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ORIGINAL RESEARCH

Association Between Neutrophil Percentage to Serum Albumin Ratio and in-Hospital Mortality of Patients with Chronic Obstructive Pulmonary Disease in Intensive Care Unit: A Retrospective Cohort Study

Yanfei Shi[1,*], Yushan Shi[2,*], Yongjuan Liu[1], Chunxiao Wang[3], Ming Qi[1], Chengwei Li[4]

[1]Department of Pulmonary Disease, The Dezhou Hospital of Traditional Chinese Medicine, Dezhou, Shandong, 253000, People's Republic of China; [2]Laboratories Department, Affiliated Hospital of Shandong University of Traditional Chinese Medicine, Jinan, Shandong, 250000, People's Republic of China; [3]School of Traditional Chinese Medicine, Shandong Second Medical University, Weifang, Shandong, 261000, People's Republic of China; [4]Department of Traditional Chinese Medicine, Dezhou Hospital of Shandong University Qilu Hospital, Dezhou, Shandong, 253000, People's Republic of China

*These authors contributed equally to this work

Correspondence: Chengwei Li, Department of Traditional Chinese Medicine, Dezhou Hospital of Shandong University Qilu Hospital, Dezhou, Shandong, 253000, People's Republic of China, Email lichengweiok@126.com

Objective: This study aimed to investigate the potential correlation between the neutrophil percentage to serum albumin ratio(NPAR) and in-hospital mortality in critically ill patients with Chronic Obstructive Pulmonary Disease (COPD).

Patients and Methods: This study employed a retrospective cohort design. A total of 599 COPD patients were included in this research. Clinical data from the MIMIC-IV (Medical Information Mart for Intensive Care IV) database were utilized. To determine whether a correlation exists between NPAR and in-hospital mortality, a multivariable logistic regression analysis was conducted. Subgroup analyses were performed, taking into account factors such as age, sex, diabetes, congestive heart failure, and ventilator use.

Results: Among the 599 patients studied, 114 (19.0%) experienced in-hospital mortality. In the multivariable logistic regression model, NPAR was positively correlated with in-hospital mortality; for each unit increase in NPAR, the in-hospital mortality rate increased by 5% (Odds Ratio [OR] = 1.05; 95% Confidence Interval [95% CI] = 1.02–1.09). Compared to the lowest NPAR group, the highest NPAR group had a significantly greater risk of in-hospital mortality (OR [95% CI] = 2.15 [1.11–4.17]). Furthermore, the results of the subgroup analyses were consistent across all groups.

Conclusion: Our study reveals a correlation between NPAR levels and mortality in COPD patients. Further research is warranted to validate these findings.

Keywords: chronic obstructive pulmonary disease, neutrophil percentage to serum albumin ratio, MIMIC-IV, hospital mortality, retrospective cohort study

Introduction

Chronic obstructive pulmonary disease (COPD) is a common, treatable, and preventable disease that is characterized by ongoing respiratory symptoms and restricted airflow. These abnormalities are caused by abnormalities in the airways and/or alveoli, which are typically brought on by prolonged exposure to harmful particles or gases. Additionally, abnormal lung development is one of the host factors that can contribute to the development of COPD.[1] According to estimates, 544.9 million persons worldwide suffered from a chronic respiratory condition in 2017, with COPD accounting for almost 55% of cases.[2] Globally, COPD ranked as the third most common cause of death in 2019.[3]

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Different degrees of emphysema, inflammation, pathologic mucus production, and vascular dysfunction are seen in patients with COPD.[4] Neutrophils are crucial innate immune cells that play a vital role in the pathophysiological processes associated with chronic obstructive pulmonary disease (COPD). They also have a considerable impact on the progression of emphysema and ongoing inflammatory conditions.[4] Apart from inflammation, the body's nutritional state plays a significant role in determining the prognosis of individuals suffering from COPD.[5] A useful biochemical biomarker of nutritional status is albumin (ALB). ALB, a protein with several physiological roles including lipid metabolism, inflammatory response, thrombosis, intravascular transport of certain chemicals, and maintenance of plasma colloid osmotic pressure, is traditionally regarded as a biomarker of malnourishment and ill health.[6] In patients with COPD, malnutrition may be linked to a dismal prognosis.[7] The serum albumin concentration alone should not be viewed as the sole measure of a patient's nutritional health, since low levels of albumin often occur alongside chronic systemic inflammation and various other medical issues that may not directly relate to nutrition.[8] The NPAR serves as a practical and cost-effective biomarker that combines both neutrophil and albumin metrics, easily obtained from standard blood tests.

To the best of our knowledge, Chou-Chin Lan et al conducted the first study to compare the predictive performance of NPAR, NLR, and ELR in COPD patients, revealing that NPAR outperforms other inflammatory biomarkers in predicting 5-year all-cause mortality.[9] The innovation of this study lies in its pioneering use of the MIMIC-IV database to explore the predictive value of the NPAR in critically ill COPD patients admitted to the intensive care unit (ICU), with a specific focus on its association with in-hospital mortality.

Materials and Methods

Introduction to Databases

The data were extracted from the Medical Information Mart for Intensive Care IV (MIMIC-IV), an upgrade to MIMIC-III and an open-source clinical database that included information on over 50,000 patients hospitalized to Beth Israel Deaconess Medical Center's critical care unit (ICU) between 2008 and 2019.[10] Yushan Shi, the co-first author, completed the online tests, signed a data usage agreement, and was granted access to the database (Certification No. 54017638). The creation of the MIMIC-IV database has received approval from the institutional review boards at MIT Affiliates and Beth Israel Deaconess Medical Center.Consent that was informed was not necessary since the database is anonymous. This specific study has received approval for exemption from evaluation by the Ethics Committee at the Affiliated Hospital of Shandong University of Traditional Chinese Medicine (ethics number: 2023–0020).

Selection of Study Population

50,920 of the 73.181 patients in the MIMIC IV database were first admitted to the intensive care unit. All COPD patients from the MIMIC-IV database were included in this research, which was based on the real-world study idea. These were our inclusion criteria: (1) Patients spent more than 24 hours in the intensive care unit and were older than 40;[11–13](2)The diagnosis of chronic obstructive pulmonary disease (COPD) in the patients was confirmed using ICD-9 codes (49120, 49,121, 49122) and ICD-10 codes (J44, J440, J441, and J442).Patients who did not have access to neutrophils or albumin on the first day of their ICU admission were also eliminated, as was any stay in the ICU for fewer than twenty-four hours. In our thorough investigation of patients with multiple admissions to the intensive care unit (ICU), we exclusively included data from individuals who experienced their first hospital admission and initial stay in the ICU.[14]

Extraction of Variables and Results

Data were obtained using PostgreSQL (version 13.9).The dataset included essential scores, comorbid conditions, vital signs, test results, and treatment interventions. Baseline information was gathered during the first twenty-four hours following admission to the ICU. For any variable assessed multiple times within this 24-hour timeframe, only the initial measurement was considered.

Gender, age, race, insurance status, frequency of hospital visits, and hospital mortality indicators are examples of demographic data.

Heart rate (HR), respiratory rate (RR),systolic blood pressure (SBP),mean blood pressure (MBP), and oxygen saturation (SpO2) are the vital signs.

Laboratory data: routine blood tests included platelet (PLT), white blood cell (WBC), blood urea nitrogen (BUN), creatinine, glucose, neutrophil percentage, albumin, hemoglobin (HB), anion gap, bicarbonate, calcium, chloride and sodium, potassium.

The following conditions are recognized as comorbidities: malignant tumors, metastatic solid cancers, diabetes mellitus, congestive heart failure, peripheral vascular diseases, cerebrovascular disorders, moderate liver diseases, severe liver diseases, kidney dysfunctions, and myocardial infarction. In the ninth and tenth versions of the International Classification of Diseases (ICD-9 and ICD-10), chronic hepatitis and cirrhosis are categorized as either mild to moderately severe liver diseases or as severe liver conditions, which may or may not involve portal hypertension.[15]

Essential metrics include the Charlson Comorbidity Index, the Simplified Acute Physiology Score II (SAPS II), and the Sequential Organ Failure Assessment (SOFA) scores.

Neutrophil percentage divided by serum albumin concentration was used to determine NPAR. Based on NPAR at 24 hours, all patients were grouped into quartiles.

The study outcome was hospital mortality.

Statistical Analysis

Participants were divided into quartiles based on their NPAR levels, with the following ranges: NPAR less than 22.50; between 22.50 and 26.09; from 26.09 to 30.75; and NPAR equal to or greater than 30.75.

The *T*-test or one-way ANOVA is used to test regularly distributed continuous variables, which are reported as mean ± standard deviation (SD). On the other hand, the Kruskal–Wallis H-test is used to test non-normally distributed variables, which are stated as median and interquartile range (IQR). Categorical variables are assessed using the Fisher exact test or the Chi-square test and are represented as proportions (%).

In order to ascertain if hospital mortality was correlated with the NPAR and other biochemical markers, a univariate model was used. Hospital mortality was examined for any independent relationship between NPAR and hospital death using multivariable logistic regression models.In the analysis of multivariable logistic regression, covariates were identified as those variables that showed a statistically significant difference with P values below 0.05 in univariate logistic regression. NPAR was analyzed through both continuous and categorical regression methods. To evaluate multicollinearity, the variance inflation factor (VIF) values were employed.A variety of variance inflation factors (VIFs) greater than ten indicated the presence of multicollinearity. Five distinct models were developed: the unadjusted raw model; Model 1, which accounted for age, gender, and race; Model 2, which built upon Model 1 by including additional variables such as heart rate, systolic blood pressure (SBP), mean blood pressure (MBP), respiratory rate, oxygen saturation (SPO2), white blood cell count (WBC), platelet count, hemoglobin concentration, anion gap, bicarbonate level, blood urea nitrogen (BUN), creatinine levels, calcium levels, glucose levels, and sodium levels; Model 3 was further refined based on all variables from Model 2 while also incorporating congestive heart failure status along with histories of mild and severe liver disease, metastatic solid tumors presence, renal disease status, diabetes mellitus (DM), and the Charlson comorbidity index; in the end, we developed Model 4, which incorporates all aspects of Model 3 while also taking into account the Simplified Acute Physiology Score II (SAPS II), Sequential Organ Failure Assessment (SOFA) score, and the status of ventilation.

We conducted interaction and subgroup analyses following the guidelines of sex (Female and Male), age (<65 years and ≥65 years), diabetic mellitus (DM) status (Absent and Present), congestive heart failure (CHF) status (Absent and Present), and ventilation utilization (Absent and Present) to further investigate the robustness of our findings. Except for the stratification factor itself, all other covariates in Model 4 of the multivariable logistic regression analysis were appropriately calibrated.

About 40% of variables had missing data; these covariate values were imputed using multiple imputations.[16] More specifically, we selected one set of missing data to undergo subgroup and logistic regression analysis after imputed five sets of missing data.Additionally, using just the non-missing population, we conducted multivariable analysis after

sensitivity analysis with variable deletion for missing data. Supplementary Table 1 contains the findings of this investigation.

In all of our investigations, we employed R version 3.3 and Free Statistics version 1.7 for statistical analysis.[17] A two-tailed approach was used for each statistical test, with a significance threshold set at $P < 0.05$.

Results

Population of the Study

In the final cohort, 599 patients were identified, which included 485 individuals who survived and 114 who did not. The flowchart illustrating the selection of research participants is presented in Figure 1, following the inclusion and exclusion criteria outlined earlier.

Initial Qualities of the Research Participants

Table 1 displays the patients' initial features. 19.0% (114/599) is the total hospital mortality rate. Overall mean ± SD age was 71.1±11.0 years and 306 (51.1%) of patients were male, most of whom were white.

We divided the patients into four groups according to the quartiles of NPAR. NPAR<22.50 was considered as the reference group, 22.50≤NPAR<26.09 was considered as the lower group, 26.09≤NPAR<30.75 was considered as the intermediary group, and ≥30.75 was considered as the highest quartile. Patients in the higher NPAR group had elevated WBC counts, BUN, neutrophil percentage, anion gap, and chloride levels, but lower albumin, hemoglobin, bicarbonate, and calcium levels.Patients with higher NPAR also had a higher SOFA and SAPSII scores than those with lower NPAR (<23.71). There was no significant correlation observed among the four groups regarding anion gap, sodium and

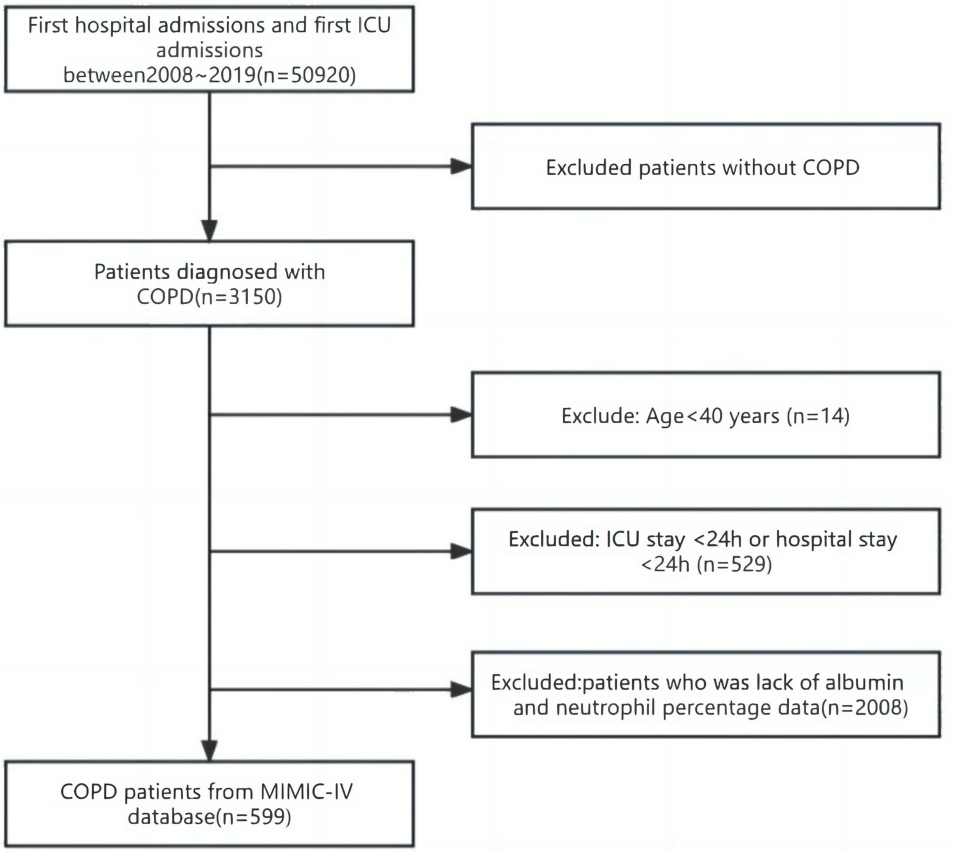

Figure 1 Diagram Illustrating the Enrollment of Participants. Symbols: (n=XXX): Represents the number of patients at each step.
Abbreviations: COPD, Chronic Obstructive Pulmonary Disease; ICU, Intensive Care Unit; MIMIC-IV, Medical Information Mart for Intensive Care IV.

Table 1 Characteristics of Study Patients by NPAR Quartiles

Variables	Total (n = 599)	Quartile1 (n = 150) NPAR<22.50	Quartile2 (n = 149) 22.50≤NPAR<26.09	Quartile3 (n = 150) 26.09≤NPAR<0.75	Quartile4 (n = 150) NPAR≥30.75	*P*
Gender, n (%)						0.333
Female	293 (48.9)	69 (46)	76 (51)	67 (44.7)	81 (54)	
Male	306 (51.1)	81 (54)	73 (49)	83 (55.3)	69 (46)	
Age, years	71.1 ± 11.0	68.7 ± 11.1	71.7 ± 11.9	72.7 ± 10.1	71.2 ± 10.7	0.013
Race, n (%)						0.05
White	386 (64.4)	87 (58)	105 (70.5)	97 (64.7)	97 (64.7)	
Non-white	58 (9.7)	23 (15.3)	9 (6)	17 (11.3)	9 (6)	
Other	155 (25.9)	40 (26.7)	35 (23.5)	36 (24)	44 (29.3)	
Vital signs						
Heart rate, beats/minute	88.5 ± 16.5	88.3 ± 14.8	87.2 ± 17.0	87.9 ± 16.4	90.6 ± 17.6	0.33
Respiratory rate, beats/minute	20.6 ± 4.0	19.7 ± 3.7	20.4 ± 4.0	21.0 ± 4.1	21.4 ± 4.2	0.001
Systolic blood pressure, mmHg	116.0 ± 15.7	119.9 ± 16.9	118.0 ± 15.8	114.2 ± 14.7	111.9 ± 14.2	< 0.001
Mean blood pressure, mmHg	77.7 ± 10.5	81.7 ± 12.1	78.3 ± 10.4	75.9 ± 9.6	74.7 ± 8.5	< 0.001
Spo_2, %	95.7 ± 2.6	95.9 ± 2.4	95.6 ± 3.1	95.7 ± 2.4	95.8 ± 2.6	0.731
Laboratory parameters						
Platelet, 10^9 /L	203.0 (137.5, 288.0)	181.5 (116.2, 241.0)	205.0 (151.0, 290.0)	220.0 (145.0, 308.2)	214.5 (137.8, 313.5)	< 0.001
White blood cell, 10^9 /L	13.8 (9.6, 19.5)	10.9 (7.4, 15.6)	13.3 (9.5, 18.5)	15.2 (10.2, 19.7)	16.5 (12.1, 22.7)	< 0.001
BUN, mg/dL	28.0 (18.0, 46.0)	25.5 (15.2, 40.0)	25.0 (18.0, 45.0)	33.5 (22.0, 49.8)	29.5 (19.0, 45.8)	0.001
Creatinine, mg/dL	1.3 (0.9, 2.0)	1.3 (0.8, 1.8)	1.1 (0.8, 1.9)	1.5 (1.0, 2.2)	1.3 (0.8, 2.0)	0.015
Glucose, mg/dL	157.0 (123.0, 209.0)	144.0 (116.0, 175.0)	164.0 (125.0, 198.0)	169.5 (135.2, 236.0)	152.0 (121.2, 212.8)	< 0.001
Neutrophil percentage, %	78.8 ± 15.1	63.7 ± 19.8	80.3 ± 9.8	84.6 ± 8.0	86.7 ± 5.9	< 0.001
NPAR	26.9 ± 8.1	18.0 ± 5.0	24.3 ± 0.9	28.4 ± 1.3	36.7 ± 7.0	< 0.001
Albumin, g/dL	3.1 ± 0.6	3.5 ± 0.5	3.3 ± 0.4	3.0 ± 0.3	2.4 ± 0.4	< 0.001
Hemoglobin, g/dL	11.0 ± 2.2	11.3 ± 2.2	11.4 ± 2.2	10.8 ± 2.3	10.6 ± 2.0	0.001
Anion gap, mmol/L	17.5 ± 5.5	17.1 ± 4.3	17.3 ± 4.9	17.9 ± 5.4	17.8 ± 6.9	0.508
Bicarbonate, mmol/L	25.2 ± 5.3	25.1 ± 5.1	26.4 ± 5.6	25.4 ± 5.5	24.1 ± 4.7	0.002
Calcium, mmol/L	8.6 ± 0.8	8.7 ± 0.8	8.8 ± 0.7	8.6 ± 0.9	8.2 ± 0.8	< 0.001
Chloride, mmol/L	103.8 ± 6.9	104.1 ± 6.8	102.2 ± 6.2	104.2 ± 7.2	104.9 ± 7.2	0.005
Sodium, mmol/L	140.0 ± 5.6	140.4 ± 5.1	139.2 ± 5.4	140.6 ± 5.9	139.9 ± 5.8	0.151
Potassium, mmol/L	4.8 ± 0.9	4.7 ± 1.0	4.8 ± 0.9	4.8 ± 0.9	4.8 ± 0.9	0.653

(*Continued*)

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Table 1 (Continued).

Variables	Total (n = 599)	Quartile1 (n = 150) NPAR<22.50	Quartile2 (n = 149) 22.50≤NPAR<26.09	Quartile3 (n = 150) 26.09≤NPAR<0.75	Quartile4 (n = 150) NPAR≥30.75	*P*
Comorbidities, n (%)						
Myocardial infarct	163 (27.2)	46 (30.7)	41 (27.5)	40 (26.7)	36 (24)	0.634
Congestive heart failure	289 (48.2)	69 (46)	85 (57)	71 (47.3)	64 (42.7)	0.077
Peripheral vascular disease	105 (17.5)	28 (18.7)	26 (17.4)	24 (16)	27 (18)	0.94
Cerebrovascular disease	77 (12.9)	28 (18.7)	20 (13.4)	15 (10)	14 (9.3)	0.062
Mild liver disease	82 (13.7)	24 (16)	13 (8.7)	21 (14)	24 (16)	0.214
Severe liver disease	42 (7.0)	15 (10)	6 (4)	10 (6.7)	11 (7.3)	0.247
Renal disease	161 (26.9)	38 (25.3)	42 (28.2)	48 (32)	33 (22)	0.248
Malignant cancer	111 (18.5)	24 (16)	19 (12.8)	31 (20.7)	37 (24.7)	0.043
Metastatic solid tumor	48 (8.0)	4 (2.7)	11 (7.4)	15 (10)	18 (12)	0.019
Ventilation use, n (%)	315 (52.6)	67 (44.7)	77 (51.7)	88 (58.7)	83 (55.3)	0.09
Scores						
Charlson comorbidity index	7.7 ± 2.6	7.3 ± 2.4	7.6 ± 2.5	7.9 ± 2.8	7.7 ± 2.6	0.234
SAPSII	43.4 ± 13.8	40.3 ± 14.6	41.0 ± 12.2	46.0 ± 13.2	46.5 ± 14.3	< 0.001
SOFA						
ICU stay, days	6.0 ± 6.5	5.1 ± 5.7	5.8 ± 7.3	6.1 ± 5.2	6.9 ± 7.5	0.117
Hospital mortality, n (%)						< 0.001
No	485 (81.0)	131 (87.3)	126 (84.6)	124 (82.7)	104 (69.3)	
Yes	114 (19.0)	19 (12.7)	23 (15.4)	26 (17.3)	46 (30.7)	

Notes: Continuous variables are presented as mean ± SD or median (quartile), while categorical variables are presented as absolute numbers (percentages).

Abbreviations: NPAR, neutrophil percentage to serum albumin ratio; SpO_2, pulse oximetry derived oxygen saturation; BUN, blood urea nitrogen; SAPS II, simplified acute physiology score II; SOFA, sequential organ failure assessment; ICU,Intensive Care Unit.

potassium levels, as well as the history of admissions to the intensive care unit (ICU) for conditions such as myocardial infarction, congestive heart failure, peripheral vascular disease, cerebrovascular disease, mild liver dysfunction, severe liver dysfunction, and renal disease. Compared to patients in the lower group, patients in the higher NPAR group had a reduced risk of developing Congestive heart failure, a greater risk of Metastatic solid tumors, and a higher risk of Malignant cancer (all P<0.05).As the NPAR increased, Respiratory rate, White blood cell, Neutrophil percentage, SAPSII scores increased, whereas Systolic blood pressure, Mean blood pressure, Albumin decreased.

Results Obtained from the Logistic Regression Analysis

A univariate regression analysis was conducted to identify the factors associated with in-hospital mortality (see Supplementary Table 2).The results indicated that heart rate, respiratory rate, platelet count, white blood cell count, anion gap, NPAR, blood urea nitrogen (BUN), creatinine levels, severe liver disease, metastatic solid tumors, Charlson comorbidity index score, Simplified Acute Physiology Score II (SAPS II) score, Sequential Organ Failure Assessment (SOFA) score, and the use of ventilation were all significant risk factors for in-hospital mortality (all P < 0.05).

Five distinct models were created for the multivariable logistic regression analysis, and Table 2 displays the odds ratios (OR) and 95% confidence intervals (95% CI). The initial crude model was left unchanged; Model 1 included adjustments for gender, age, and race. Building on Model 1, Model 2 added further parameters such as heart rate, systolic blood pressure (SBP), mean blood pressure (MBP), respiratory rate, oxygen saturation (SPO2), white blood cell count (WBC), platelet count, hemoglobin levels, anion gap, bicarbonate levels, blood urea nitrogen (BUN), creatinine levels, calcium levels, glucose levels, and sodium levels. In addition to these factors in Model 3 were considerations for congestive heart failure, mild liver disease, severe liver disease, metastatic solid tumors, renal disease diabetes mellitus along with the Charlson comorbidity index. Finally, Model 4 adjusted the parameters from Model 3 while also taking into account the Simplified Acute Physiology Score II (SAPS II), Sequential Organ Failure Assessment (SOFA) score and ventilation status. When analyzing NPAR as a continuous variable showed a significant association with hospital mortality in both the fully adjusted Model 4 (odds ratio [OR] = 1.05; 95% confidence interval [CI]: 1.02–1.09; P = 0.003) and the unadjusted model (OR = 1.06; 95% CI: 1.03–1.08; P <0 0.001). Specifically within the second and third tertiles of fully adjusted Model 4 when comparing categorized NPAR against the lower group yielded odds ratios of 1.04 (95% CI:0 0.53 −2 0.02; P=0 0.914) and 2 0.15 (95% CI:1 0.11–4 0.17;P=0 0.023).

Analyses of Subgroup Stratification and Sensitivity Evaluation

To evaluate the consistency of the relationship between NPAR and in-hospital mortality in COPD patients who are admitted to the intensive care unit (ICU),we conducted subgroup and sensitivity analyses. Subgroups and interactive analyses were used in accordance with sex (Female and Male), age (<65 and ≥65 years), CHF (No and Yes), DM (No and Yes), ventilation use (No and

Table 2 Multivariable Logistic Analysis of NPAR and Hospital Mortality (Post-Interpolation)

Variable	Crude Model		Model 1		Model 2		Model 3		Model 4	
	OR (95% CI)	P	OR (95% CI)	P	OR (95% CI)	P	OR (95% CI)	P	OR (95% CI)	P
NPAR continuous	1.06 (1.03–1.08)	< 0.001	1.06 (1.03–1.08)	< 0.001	1.06 (1.03–1.1)	< 0.001	1.06 (1.02–1.09)	< 0.001	1.05 (1.02–1.09)	0.003
NPAR tertiles										
T1 (NPAR < 23.71)	1(Ref)		1(Ref)		1(Ref)		1(Ref)		1(Ref)	
T2 (23.71 ≤ NPAR < 29.24)	1.18 (0.68–2.07)	0.557	1.16 (0.66–2.06)	0.602	1.18 (0.63–2.2)	0.613	1.1 (0.58–2.1)	0.766	1.04 (0.53–2.02)	0.914
T3 (NPAR ≥ 29.24)	2.49 (1.5–4.15)	< 0.001	2.45 (1.46–4.13)	< 0.001	2.41 (1.3–4.45)	0.005	2.1 (1.11–3.96)	0.022	2.15 (1.11–4.17)	0.023

Notes: Crude model was not adjusted. Model 1 was adjusted for gender + age + race. Model 2 was adjusted for model 1 + heart rate + SBP + MBP + respiratory rate + SPO_2 + WBC + platelets + hemoglobin + anion gap + bicarbonate+ bun + creatinine + calcium + glucose + sodium. Model 3 was adjusted for model 2 + congestive heart failure + mild liver disease + severe liver disease + metastatic solid tumor + renal disease + diabetes + charlson comorbidity index. Model 4 was adjusted for model 3 + sapsii + sofa score + ventilation status.

Abbreviations: OR, odds ratio; CI, confidence interval; Ref, reference; NPAR, neutrophil percentage to serum albumin ratio; T1,Tertile 1;T2,Tertile 2;T3,Tertile 3.

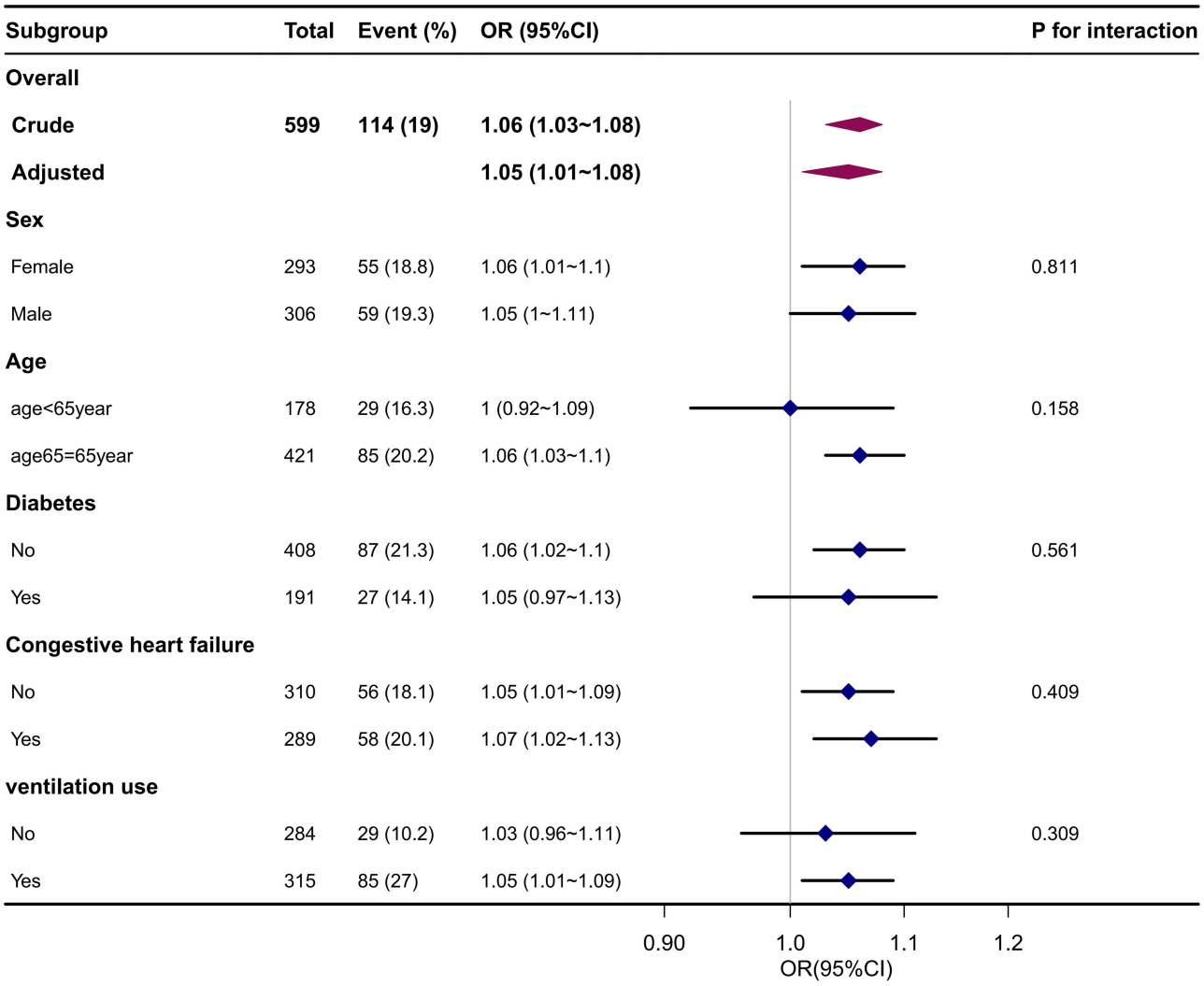

Figure 2 Illustrates a forest plot that shows the relationship between the NPAR and mortality rates in hospitals. Bold text (eg, "Overall", "Crude", "Adjusted") highlights key categories or analysis types. Symbols:OR (95% CI): Odds ratio with 95% confidence interval. P for interaction: P-value for interaction tests between subgroups. Event (%): Percentage of in-hospital mortality events in each subgroup. The crude analysis is presented without adjustments, while the adjusted analysis incorporates various covariates including gender, age, race, heart rate, systolic blood pressure (SBP), mean blood pressure (MBP), respiratory rate, oxygen saturation (SPO2), white blood cell count (WBC), platelet count, hemoglobin levels, anion gap, bicarbonate levels, blood urea nitrogen (BUN), creatinine levels, calcium levels, glucose levels, sodium levels; as well as whether or not there is congestive heart failure present along with mild liver disease, severe liver disease, metastatic solid tumors, renal disease diabetes mellitus. Additionally, the Charlson Comorbidity Index is taken into account alongside the Simplified Acute Physiology Score II (SAPS II) and the Sequential Organ Failure Assessment (SOFA) score, as well as the patient's ventilation status.
Abbreviations: OR, odds ratio; CI, confidence interval.

Yes) (Figure 2). The NPAR's constant effect size on hospital mortality was seen in subgroups. In the subgroups, no significant interactions were found (all P for interaction > 0.05).

The results are shown in Supplementary Table 1. Following this, a sensitivity analysis was conducted through variable removal to address the issue of missing data, and a multivariable analysis was carried out using only the complete cases.

Discussion

In our investigation, we discovered a strong positive correlation between COPD patients' deaths and their NPAR levels. This study showed that, after adjusting for gender, age, and race, higher NPAR levels were associated with increased in-hospital mortality among COPD patients admitted to the ICU.Once other possibly confusing variables were taken into account, this association remained substantial. The impact value in fully adjusted model 4 was 1.05 (95% CI: 1.02–1.09),

meaning that for every unit increase in NPAR, there is a 5% increase in the risk of hospital mortality. The outcome was dependable and stable when NPAR was converted to a categorical variable, and it remained constant across all subgroups in the absence of any interaction.

In addition to systemic inflammation, COPD is linked to chronic inflammation of the lung parenchyma and airways, which intensifies during acute exacerbations.[18] Over time, systemic inflammatory markers rise, and in COPD, inflammatory indicators are linked to a quicker deterioration in lung function.[19] According to related research, 16% of patients with COPD had chronic inflammation and 70% of patients had some degree of systemic inflammation, as measured by six different indicators of inflammation, including white blood cells.[20] It has been shown that inflammation is essential to the pathophysiology of COPD. Neutrophils are involved in inflammation in the lungs of patients with COPD as part of the innate immune response, and there is a characteristic pattern of inflammation in this.[21–23] A statement from European Respiratory Society suggested that dietary condition was a significant factor in determining the COPD's prognosis.[24] Patients with COPD often have malnutrition as a result of increased energy use, problems with digestion and absorption, and COPD itself. In addition, the chronic inflammatory process can trigger catabolic stress, which exerts an adverse effect on the patients' nutritional status.[25] In the inflammatory area, the material metabolism of tissue cells is disrupted, leading to the necrosis and disintegration of cell tissues. At the same time, white blood cells begin to infiltrate. Once the white blood cells are damaged, a large amount of proteolytic enzymes will be released. These enzymes extensively decompose and metabolize proteins, causing a large number of protein decomposition products such as free amino acids and peptones to continuously accumulate in the inflammatory area. Eventually, this situation leads to a decline in the patient's nutritional status. Patients with COPD have a poor prognosis due to a drop in blood albumin levels caused by both systemic inflammatory responses and malnutrition.[26,27] A previous study showed that low albumin (≤ 36.50 g/l) alone produces an approximately 20% risk of death during hospitalization and that albumin declines in acute systemic disease.[28] A number of emerging biomarkers are good predictors of hospitalization outcomes in patients with severe chronic obstructive pulmonary disease (COPD) and help clinicians monitor the progress of patients with COPD. For example, in patients experiencing acute exacerbations of COPD, the C-reactive protein to serum albumin ratio (CAR) may be an independent predictor of rehospitalization and frequent exacerbations.[29] The red cell index (RCI) shows a notable positive correlation with in-hospital mortality rates for patients suffering from chronic obstructive pulmonary disease (COPD) in intensive care settings.[17] NPAR is also a relatively new and readily available biomarker that combines neutrophil percentage and serum albumin levels. It integrates the percentage of neutrophils (reflecting acute inflammation) and serum albumin (reflecting chronic inflammation and nutritional status), and it may more comprehensively capture the multidimensional pathophysiological state of patients with COPD. A high NPAR may indicate a vicious cycle of inflammation and malnutrition, exacerbating the risk of organ failure, which is consistent with the independent predictive value of inflammatory markers (such as C-reactive protein, CRP) and nutritional indicators (such as prealbumin [30]) in previous studies. Peng Yangpei et al showed that NAR levels correlate with mortality in patients with cardiogenic shock and that the prognostic value of NAR is more sensitive than neutrophil percentage or serum albumin levels.[31] Hu Zesong et al [32] demonstrated that NPAR serves as an independent predictor of mortality in heart failure patients and shows a notable relationship with the duration of hospital stays.Chunying Hu et al [33] studied the relationship between neutrophil albumin ratio and 28-day mortality in patients with sepsis. Based on the above studies, it can be supposed that NPAR can also predict mortality in patients with CDPD.

However, our study also has some limitations. First and foremost, it was a retrospective cohort study. In retrospective cohort studies, all potential confounding factors cannot be taken into account.There may still be unaccounted for potential confounders even after recognized confounders have been taken into account.Although we adjusted for variables such as age, gender, and comorbidities, potential confounding factors like smoking history, body mass index (BMI), pulmonary function classification, and the frequency of acute exacerbations could not be included in the analysis due to data missing, which may lead to residual confounding of the results.Secondly, we excluded patients younger than 18 and 40 years of age.As a result, it is not practical to apply our findings to these patients. Additionally, around 40% of the data for ALT, AST, and SOFA related to individual variables were missing.Nevertheless, in order to overcome the difficulties caused by the missing data, we used repeated interpolation. Furthermore, when we used multivariable regression analysis to exclude the missing data, the results were still reliable.Third, there may have been some biases

since NPAR was only evaluated when patients were first brought to the ICU.Among summary, we discovered that among critically sick COPD patients, a greater NPAR was positively correlated with a higher chance of mortality.More studies are required to verify our results.

Conclusion

The death rate of COPD patients was correlated with their NPAR level. For COPD patients, NPAR was a possible predictive biomarker of death. To verify our findings in the future, however, meticulously designed, prospective, multicenter trials are essential.

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Disclosure

The authors disclose no conflicts of interest for this work.

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