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Original Article

Correlation of C-reactive protein/albumin ratios and electrolytes with APACHE II score and prognosis in patients with chronic obstructive pulmonary disease

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Abstract: Objective: To investigate the correlations between the serum C-reactive protein (CRP)/albumin (Alb) ratio, electrolyte levels, and Acute Physiology and Chronic Health Evaluation (APACHE) II scores in patients with chronic obstructive pulmonary disease (COPD), as well as their associations with prognosis. Methods: Clinical data from 180 COPD patients recruited between March 2023 and August 2024 were analyzed. Patients were divided into RF (n=106) and non-RF groups (n=74). APACHE II scores were assessed within 24 hours of admission. Serum levels of CRP, Alb, Na^+, K^+, and Ca^{2+} were recorded. Pearson or Spearman correlation analysis was used to examine correlations among variables. Logistic regression was used to identify factors influencing comorbid respiratory failure (RF) and 28-day mortality. Results: APACHE II scores were positively correlated with the CRP/Alb ratio (r=0.201, P=0.007) and negatively correlated with serum Ca^{2+} levels (r=-0.201, P=0.007). A high APACHE II score was an independent risk factor for RF (OR=2.78, 95% CI: 1.98-3.91, P<0.001), while serum Na^+ levels showed a trend toward association with RF risk (OR=1.09, 95% CI: 1.00-1.20, P=0.051). Twenty-four patients died within 28 days; a high APACHE II score (OR=1.96, 95% CI: 1.55-2.48, P<0.001) and elevated CRP/Alb ratio (OR=1.43, 95% CI: 1.09-1.86, P=0.009) were significantly associated with increased 28-day mortality risk. Conclusion: The CRP/Alb ratio and electrolyte levels hold clinical value as potential biomarkers for evaluating disease severity and prognosis in COPD patients.

Keywords: C-reactive protein/albumin ratios, electrolyte levels, APACHE II score, chronic obstructive pulmonary disease, prognostic value

Introduction

Chronic Obstructive Pulmonary Disease (COPD), a prevalent condition characterized by ongoing airflow limitation, is associated with substantial global morbidity and mortality [1]. According to COPD research, an estimated 212 million people are affected globally, of whom 3.3 million die annually [2, 3]. The impact of COPD on patients' quality of life is well-established, and progression to respiratory failure (RF) during acute exacerbations further amplifies disease burden [4]. RF is a key feature of COPD deterioration, often accompanied by multi-organ dysfunction that may alter treatment strategies and increase the risk of adverse outcomes [5]. Thus, identifying biomarkers capable of accurately assessing RF severity and prognosis in COPD patients is critical for optimizing clinical management and improving outcomes.

The Acute Physiology and Chronic Health Evaluation (APACHE) is a scoring system used in Intensive Care Units (ICUs) to assess patient condition [6], enabling comprehensive evaluation of physical impairment and illness severity [7]. However, APACHE score calculation relies on numerous physiological parameters, making it complex and impractical to obtain in routine clinical settings. Consequently, there is a need for simpler yet reliable biomarkers that correlate well with APACHE scores to facilitate disease assessment and clinical decision-making.

Serum biomarkers have emerged as a focus of interest in evaluating COPD and its complications in recent years [8]. C-reactive protein (CRP) is an acute-phase reactant that rises rapidly in response to inflammation, reflecting the body's inflammatory status [9]. Albumin (Alb) - the major serum protein - is associated with

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patients' nutritional status and immune function. The serum CRP/Alb ratio is a novel, valuable indicator of inflammation-nutrition imbalance, with potential to predict disease severity and prognosis [10, 11]. Specifically, COPD patients with elevated CRP/Alb ratios have been shown to have higher 5-year mortality [12]. Additionally, cholinesterase (ChE) is a key enzymatic marker; changes in its activity are linked to liver function, neuromuscular function, and overall metabolic status. Electrolyte levels (e.g., potassium, sodium, chloride) play a crucial role in maintaining internal environmental homeostasis and normal physiological function, with abnormalities often indicating underlying organ dysfunction or metabolic disorders [13].

Currently, studies investigating correlations between the serum CRP/Alb ratio, ChE activity, electrolyte alterations, and APACHE scores in COPD patients with RF remain insufficient. Their specific manifestations and clinical utility across diverse settings require further exploration, as most existing research focuses on individual biomarkers or overall prognosis. Thus, this study's innovation lies in its integrative approach: we simultaneously evaluated the relationships of both a novel inflammatory-nutritional marker (CRP/Alb ratio) and fundamental physiological parameters (electrolytes) with the APACHE II score. Furthermore, we specifically assessed the association of these indices with poor outcomes (i.e., RF and 28-day mortality). Ultimately, we aim to provide clinicians with a simpler, faster, and more effective disease assessment tool to optimize COPD patient management and improve healthcare quality and prognosis.

Materials and methods

Patient population

Retrospective collection of clinical data was performed for 186 patients hospitalized between March 2023 and August 2024. Six patients were excluded for incomplete data, leaving 180 for final statistical analysis. Inclusion criteria were: (a) Age ≥18 years; (b) Diagnosis of COPD per Global Initiative for Chronic Obstructive Lung Disease (GOLD) criteria [14]; (c) Acute Physiology and Chronic Health Evaluation II (APACHE II) score assessed within 24 hours of admission; (d) Treatment at our institution with ≥28 days of follow-up; (e) complete clinical data. Exclusion criteria were: (a) Comorbidity with other severe respiratory conditions (e.g., bronchiectasis, tuberculosis, lung cancer); (b) Severe chronic diseases or organ failure of other systems; (c) History of major surgery within 3 months or use of medications affecting electrolyte balance; (d) Long-term glucocorticoid use (>2 weeks) prior to admission; (e) Terminal illness or palliative care initiation at admission. This study was approved by the Medical Ethics Committee of Lu'an People's Hospital.

Sample size calculation

Sample size was calculated using G*Power software (version 3.1.9.7) via a priori logistic regression formula, with 28-day mortality as the primary outcome. Preliminary pilot data from our institutional records suggested an expected mortality rate of ~15% in COPD patients with acute exacerbation. We aimed to detect a minimum odds ratio (OR) of 2.5 for the CRP/Alb ratio, with a two-sided α of 0.05 and statistical power (1-β) of 80%. An estimated minimum of 150 patients was required; thus, the final sample size of 180 patients satisfied study needs. Patients were divided into RF (n=106) and non-RF groups (n=74) according to the presence or absence of RF during hospitalization.

Data collection

Demographic and clinical data were extracted from the hospital's electronic medical record system. Demographic variables included age, gender, body mass index (BMI), smoking status, and alcohol consumption. Clinical variables included hospital length of stay, comorbid RF, serum CRP, albumin (Alb), Na^+, K^+, and Ca^{2+} levels, partial pressure of oxygen (PaO_2), partial pressure of carbon dioxide ($PaCO_2$), and APACHE II score. Venous blood samples were collected within 24 hours of admission. Serum CRP (immunoturbidimetric assay), Alb (bromocresol green assay), Na^+, K^+, and Ca^{2+} (ion-selective electrode method) concentrations were quantified. All assays were performed in the hospital's clinical laboratory per standard protocols with strict quality control. Additionally, 28-day survival status was tracked via medical records and follow-up assessments.

Patient follow-up

For inpatients who remained hospitalized or were readmitted within 28 days, 28-day survival was directly extracted from electronic medical records. For discharged patients, standardized telephone follow-up was conducted by two trained research nurses immediately after the 28-day follow-up window. A predefined script was used to respectfully confirm survival status with family members or primary caregivers.

Outcome measures

Primary outcome measures: The serum CRP/Alb ratio [15] was calculated as serum CRP divided by albumin (Alb), serving as a comprehensive measure of the patient's inflammatory and nutritional status.

The serum concentrations of Na^+, K^+, and Ca^{2+} [16] directly reflect the patient's systemic electrolyte homeostasis.

The Acute Physiology and Chronic Health Evaluation II (APACHE II) score [17] is a key indicator for assessing disease severity; it comprises the Acute Physiological Score (APS), Chronic Health Status (CHS) score, and age component, with a theoretical maximum of 71 and higher scores indicating more severe illness.

Secondary outcome measures: The risk of comorbid RF in COPD patients [18] was analyzed by grouping patients based on RF occurrence and examining its relationship with the serum CRP/Alb ratio and electrolyte levels.

The 28-day mortality risk in COPD patients [19] was evaluated by investigating its correlations with the serum CRP/Alb ratio and electrolyte levels.

Statistical analysis

Statistical analyses were performed using SPSS 27.0 software. Continuous data were presented as mean ± standard deviation (Mean ± SD) or median (interquartile range [IQR]), with between-group comparisons using independent samples t-test or Mann-Whitney U test. Categorical data were presented as frequencies (percentages), with between-group comparisons using χ^2 test or Fisher's exact test. Logistic regression models were used to identify risk factors, with ORs and 95% confidence intervals (CIs) reported. Multivariate logistic regression employed a backward stepwise selection approach. Receiver operating characteristic (ROC) curves and area under the curve (AUC) were used to assess the diagnostic performance of variables. All tests were two-tailed, with $P<0.05$ considered statistically significant.

Results

Basic information

No significant differences were found in terms of the basic information (age, gender, smoking, drinking, etc.) between groups (all $P>0.05$) See **Table 1**.

Correlations of CRP/Alb ratio and electrolyte concentrations with APACHE II score

Correlation analysis revealed a positive correlation between APACHE II score and CRP/Alb ratio (r=0.201, 95% CI: 0.057-0.338, P= 0.007) (**Figure 1**). APACHE II score was negatively correlated with serum Ca^{2+} concentration (r=-0.201, 95% CI: -0.337--0.056, P=0.007). No statistically significant correlations were observed between APACHE II score and serum Na^+ or K^+ concentrations (all $P>0.05$).

Correlations of other indicators with APACHE II score

Age, gender, hospital length of stay, body mass index (BMI), smoking status, alcohol consumption, PaO_2 and $PaCO_2$ were included in the correlation analyses. Results showed APACHE II scores were positively correlated with hospital length of stay (r=0.193, 95% CI: 0.048-0.330, P=0.010) (**Figure 2**). Additionally, APACHE II scores were negatively correlated with PaO_2 (r=-0.446, 95% CI: -0.556--0.320, $P<0.001$) and positively correlated with $PaCO_2$ (r=0.477, 95% CI: 0.357-0.583, $P<0.001$).

Univariate analysis for combined RF

Of the 180 patients, 106 (58.89%) had comorbid RF. Hospital length of stay was longer in the RF group than in the non-RF group (8.91 days vs. 7.57 days, P=0.030) (**Table 1**). Statistically significant differences between the two groups were also observed for serum Ca^{2+} concentration (P=0.037), PaO_2 ($P<0.001$), $PaCO_2$ ($P<0.001$), and APACHE II score ($P<0.001$).

Table 1. Basic characteristics and univariate analysis of patients with combined respiratory failure

Variables	Total (n=180)	Non-RF group (n=74)	RF group (n=106)	Statistic	*P*
Age, Mean ± SD	76.59 ± 7.08	76.43 ± 7.80	76.70 ± 6.56	t=-0.25	0.805
Gender, n (%)				χ^2=2.70	0.100
Female	56 (31.11)	18 (24.32)	38 (35.85)		
Male	124 (68.89)	56 (75.68)	68 (64.15)		
Duration of hospitalization, Mean ± SD	8.36 ± 4.58	7.57 ± 2.52	8.91 ± 5.54	t=-2.19	0.030
BMI, Mean ± SD	21.85 ± 2.75	22.05 ± 3.19	21.71 ± 2.40	t=0.78	0.437
Smoking, n (%)				χ^2=0.48	0.486
No	98 (54.44)	38 (51.35)	60 (56.60)		
Yes	82 (45.56)	36 (48.65)	46 (43.40)		
Drinking, n (%)				χ^2=0.97	0.325
No	114 (63.33)	50 (67.57)	64 (60.38)		
Yes	66 (36.67)	24 (32.43)	42 (39.62)		
CPR/Alb, Mean ± SD	1.78 ± 2.05	1.51 ± 1.81	1.97 ± 2.18	t=-1.49	0.137
Na^+ concentration, Mean ± SD	138.85 ± 4.44	138.32 ± 3.94	139.22 ± 4.75	t=-1.34	0.181
K^+ concentration, Mean ± SD	3.97 ± 0.67	3.91 ± 0.69	4.01 ± 0.65	t=-0.94	0.348
Ca^{2+} concentration, Mean ± SD	2.07 ± 0.18	2.11 ± 0.19	2.05 ± 0.17	t=2.11	0.037
$PaCO_2$, Mean ± SD	51.33 ± 19.02	38.37 ± 4.03	60.37 ± 20.11	t=-10.95	<0.001
PaO_2, Mean ± SD	73.52 ± 24.25	89.90 ± 13.68	62.08 ± 23.48	t=10.01	<0.001
APACHE II score, Mean ± SD	7.68 ± 2.61	6.07 ± 1.13	8.81 ± 2.76	t=-9.19	<0.001

Abbreviations: RF, respiratory failure; SD, standard deviation; BMI, body mass index; CRP, C-reactive protein; Alb, albumin; PaO_2, Partial Pressure of Oxygen; $PaCO_2$, Partial Pressure of Carbon Dioxide; APACHE, Acute Physiology and Chronic Health Evaluation.

Factors associated with comorbid RF

Logistic regression (backward stepwise selection) was used to identify factors associated with comorbid RF. A higher APACHE II score was an independent risk factor for RF (OR=2.78, 95% CI: 1.98-3.91, P<0.001) (**Table 2**). Additionally, serum Na^+ concentration showed a trend toward association with RF risk (OR=1.09, 95% CI: 1.00-1.20, P=0.051). The AUC values for APACHE II score, serum Na^+ concentration, and their combination in predicting RF were 0.85 (95% CI: 0.79-0.91), 0.56 (95% CI: 0.48-0.64), and 0.87 (95% CI: 0.81-0.92), respectively (**Figure 3**).

Univariate analysis for 28-day mortality

Twenty-four patients (15.56%) died within 28 days of admission. Statistically significant differences between the mortality and survival groups were noted for BMI (21.01 kg/m^2 vs. 21.98 kg/m^2, P=0.036), alcohol consumption (58.33% vs. 33.33%, P=0.018), CRP/Alb ratio (3.43 vs. 1.52, P<0.001), $PaCO_2$ (61.23 mmHg vs. 49.81 mmHg, P=0.006), PaO_2 (57.75 mmHg vs. 75.94 mmHg, P<0.001), and APACHE II score (11.75 vs. 7.06, P<0.001) (**Table 3**).

Factors associated with 28-day mortality

Multivariate logistic regression analysis showed that higher APACHE II scores (OR=1.96, 95% CI: 1.55-2.48, P<0.001) and elevated CRP/Alb ratios (OR=1.43, 95% CI: 1.09-1.86, P=0.009) were significantly associated with increased 28-day mortality risk (**Table 4**). The AUC values for APACHE II score, CRP/Alb ratio, and their combination in predicting 28-day mortality were 0.92 (95% CI: 0.87-0.96), 0.77 (95% CI: 0.68-0.87), and 0.93 (95% CI: 0.88-0.97), respectively (**Figure 4**).

Discussion

COPD is a widespread condition associated with substantial global morbidity and mortality [20]. Acute exacerbations often progress to RF, exacerbating disease burden [21]. The APACHE II scoring system is a well-established tool for assessing severity and predicting outcomes in critically ill patients [22]. This study investigat-

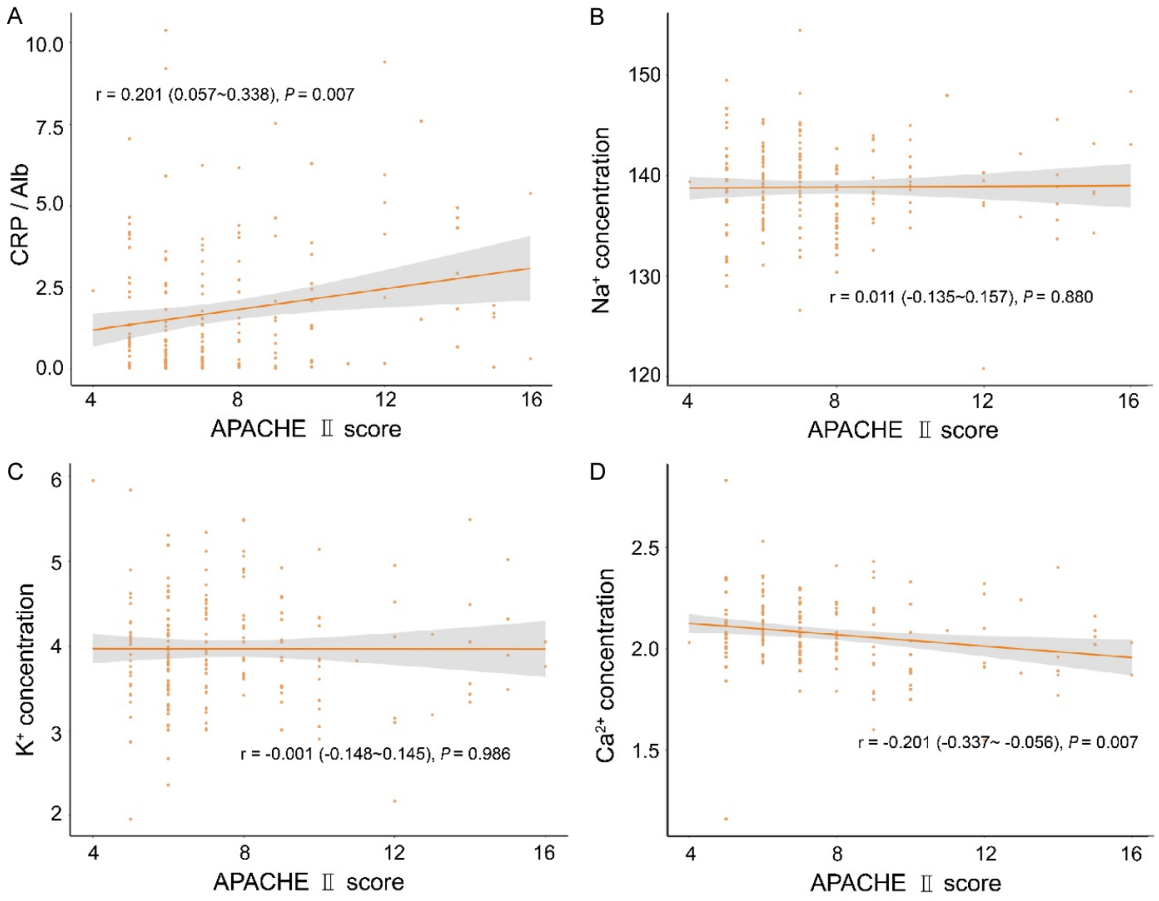

Figure 1. Correlation analysis of CRP/Alb ratio and electrolyte level with APACHE II score. A. CRP/Alb ratio; B. Na^+ concentration; C. K^+ concentration; D. Ca^{2+} concentration. Abbreviations: CRP, C-reactive protein; Alb, albumin; APACHE, Acute Physiology and Chronic Health Evaluation.

ed whether serum CRP/Alb ratio and electrolyte levels correlate with APACHE II scores in COPD patients, and their associations with adverse outcomes (i.e., RF and 28-day mortality). Our findings showed that APACHE II scores were positively correlated with the CRP/Alb ratio and negatively correlated with serum Ca^{2+} concentrations. Moreover, higher APACHE II scores emerged as an independent risk factor for comorbid RF, while both APACHE II scores and CRP/Alb ratios were linked to increased 28-day mortality risk.

The positive correlation between APACHE II scores and the CRP/Alb ratio aligns with previous studies highlighting this inflammatory-nutritional marker's prognostic value in COPD. For example, Ao et al. reported that elevated CRP/Alb ratios were significantly associated with COPD risk in a cross-sectional study of 1,809 participants [23]. Shen et al. further demonstrated a strong association between the CRP/Alb ratio and mortality in a retrospective COPD cohort [12], consistent with our finding that higher ratios predict increased 28-day mortality. Yao et al. also identified the CRP/Alb ratio as an independent risk factor for short-term death in COPD patients with heart failure [24], underscoring its broad prognostic utility. Our study extends these insights by linking the CRP/Alb ratio to acute disease severity (via APACHE II), supporting its potential role in early risk stratification of hospitalized COPD patients. Mechanistically, CRP is an acute-phase reactant whose levels rise rapidly with inflammation [25], while Alb reflects nutritional status and immune function [26]. Persistent inflammation in COPD consumes nutrients, reducing albumin levels and increasing inflammatory mediator secretion-driving up CRP levels and the CRP/Alb ratio. Higher APACHE II scores indicate severe disease [27], so an elevated CRP/Alb

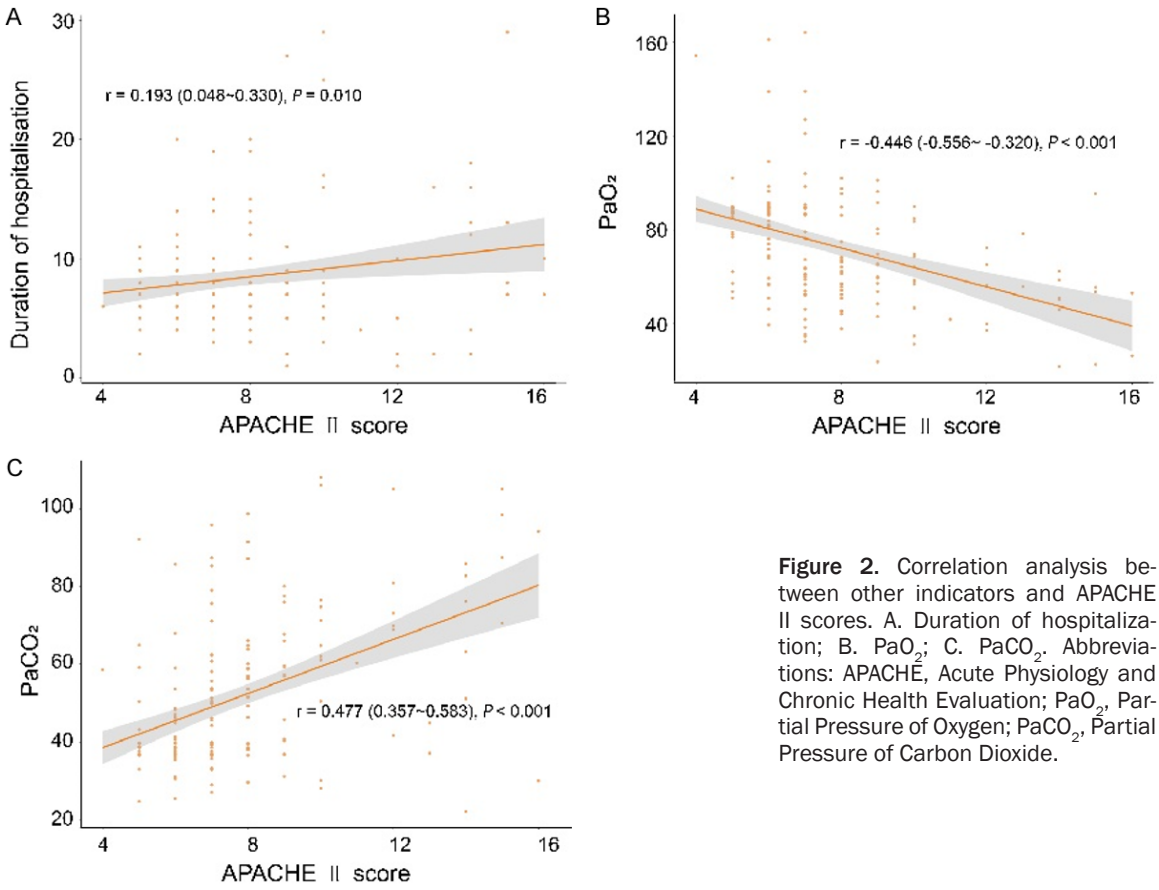

Figure 2. Correlation analysis between other indicators and APACHE II scores. A. Duration of hospitalization; B. PaO_2; C. $PaCO_2$. Abbreviations: APACHE, Acute Physiology and Chronic Health Evaluation; PaO_2, Partial Pressure of Oxygen; $PaCO_2$, Partial Pressure of Carbon Dioxide.

Table 2. Multivariate Logistic regression analysis of respiratory failure

Variables	β	S.E	Z	*P*	OR (95% CI)
APACHE II score	1.02	0.17	5.91	<0.001	2.78 (1.98-3.91)
Na^+ concentration	0.09	0.05	1.95	0.051	1.09 (1.00-1.20)

Abbreviations: SE, standard error; OR, odds ratio; APACHE, Acute Physiology and Chronic Health Evaluation.

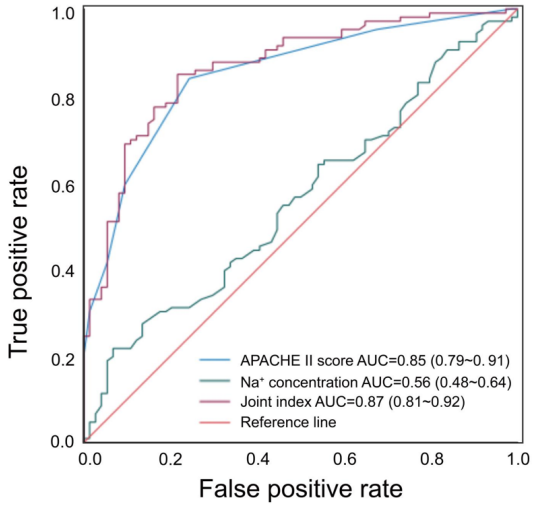

Figure 3. ROC curve analysis for predicting combined respiratory failure. Abbreviations: APACHE, Acute Physiology and Chronic Health Evaluation; ROC, receiver operating characteristic; AUC, area under curve.

ratio may signal disease progression by reflecting synergistic inflammatory and nutritional imbalance. This imbalance can impair immunity, increasing susceptibility to infections and complications that worsen outcomes and hinder recovery [28], though further mechanistic studies are needed to confirm these pathways.

We also observed a significant negative correlation between serum Ca^{2+} levels and APACHE II

Table 3. Basic characteristics and univariate analysis of 28-day mortality risk

Variables	Total (n=180)	Survival group (n=156)	Death group (n=24)	Statistic	*P*
Age, Mean ± SD	76.59 ± 7.08	76.47 ± 7.22	77.38 ± 6.19	t=-0.58	0.560
Gender, n (%)				χ^2=0.48	0.487
Female	56 (31.11)	50 (32.05)	6 (25.00)		
Male	124 (68.89)	106 (67.95)	18 (75.00)		
Duration of hospitalization, Mean ± SD	8.36 ± 4.58	8.21 ± 3.57	9.33 ± 8.70	t=-0.63	0.537
BMI, Mean ± SD	21.85 ± 2.75	21.98 ± 2.84	21.01 ± 1.89	t=2.17	0.036
Smoking, n (%)				χ^2=3.21	0.073
No	98 (54.44)	89 (57.05)	9 (37.50)		
Yes	82 (45.56)	67 (42.95)	15 (62.50)		
Drinking, n (%)				χ^2=5.60	0.018
No	114 (63.33)	104 (66.67)	10 (41.67)		
Yes	66 (36.67)	52 (33.33)	14 (58.33)		
CPR/Alb, Mean ± SD	1.78 ± 2.05	1.52 ± 1.87	3.43 ± 2.40	t=-3.73	<0.001
Na^+ concentration, Mean ± SD	138.85 ± 4.44	138.99 ± 4.49	137.90 ± 4.09	t=1.12	0.264
K^+ concentration, Mean ± SD	3.97 ± 0.67	4.00 ± 0.65	3.79 ± 0.77	t=1.40	0.163
Ca^{2+} concentration, Mean ± SD	2.07 ± 0.18	2.08 ± 0.17	2.04 ± 0.23	t=0.73	0.471
$PaCO_2$, Mean ± SD	51.33 ± 19.02	49.81 ± 18.62	61.23 ± 19.00	t=-2.79	0.006
PaO_2, Mean ± SD	73.52 ± 24.25	75.94 ± 24.48	57.75 ± 15.48	t=4.89	<0.001
APACHE II score, Mean ± SD	7.68 ± 2.61	7.06 ± 1.96	11.75 ± 2.69	t=-8.21	<0.001

Abbreviations: SD, standard deviation; BMI, body mass index; CRP, C-reactive protein; Alb, albumin; PaO_2, Partial Pressure of Oxygen; $PaCO_2$, Partial Pressure of Carbon Dioxide; APACHE, Acute Physiology and Chronic Health Evaluation.

Table 4. Multivariate Logistic regression analysis of 28-day mortality risk

Variables	β	S.E	Z	*P*	OR (95% CI)
APACHE II score	0.67	0.12	5.59	<0.001	1.96 (1.55-2.48)
CPR/Alb	0.36	0.14	2.62	0.009	1.43 (1.09-1.86)

Abbreviations: SE, standard error; OR, odds ratio; APACHE, Acute Physiology and Chronic Health Evaluation; CRP, C-reactive protein; Alb, albumin.

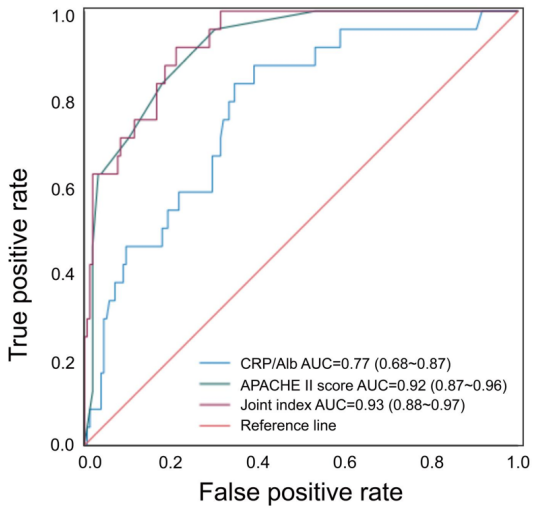

Figure 4. ROC curve analysis for predicting 28-day mortality. Abbreviations: CRP, C-reactive protein; Alb, albumin; APACHE, Acute Physiology and Chronic Health Evaluation; ROC, receiver operating characteristic; AUC, area under curve.

scores, consistent with prior research in critically ill populations. Dey et al. reported more pronounced hypocalcemia in patients with APACHE II scores >20, suggesting a link between calcium homeostasis and disease severity [29]. In COPD acute exacerbations, reduced Ca^{2+} may reflect underlying metabolic disturbances or organ dysfunction that exacerbates clinical status. Ca^{2+} is critical for maintaining normal cellular function, including neuromuscular excitability and myocardial contractility [30]. During exacerbations, respiratory acidosis or acid-base imbalance can alter intracellular and extracellular Ca^{2+} distribution, reducing serum levels [31]. Severe disease may also impair renal Ca^{2+} reabsorption and

excretion [32], further lowering concentrations. Reduced serum Ca^{2+} can then compromise myocardial contractility and neuromuscular function, worsening illness severity-explaining the negative correlation with APACHE II scores. In contrast, Na^+ and K^+ concentrations showed no significant correlation with APACHE II scores, likely due to their relative stability in COPD patients and weaker impact on disease severity compared to Ca^{2+}. Nevertheless, electrolyte abnormalities still merit clinical attention, as they may indicate unrecognized metabolic or organ dysfunction requiring intervention.

Of the 180 patients, 106 (58.89%) had comorbid RF. Univariate analysis showed longer hospital stays and higher $PaCO_2$ in the RF group, with lower Ca^{2+} concentrations and PaO_2 compared to the non-RF group. RF causes hypoxia and carbon dioxide retention: hypoxia induces pulmonary vasoconstriction, increasing right heart load and potentially leading to cardiac insufficiency that impairs systemic perfusion and prolongs hospitalization [33]. Hypercapnia can dilate cerebral blood vessels, raising intracranial pressure and worsening outcomes [34]. Reduced Ca^{2+} may stem from acid-base imbalance or renal dysfunction in RF, with hypocalcemia impairing respiratory muscle contraction and exacerbating RF. Multivariate logistic regression confirmed higher APACHE II scores as an independent risk factor for RF, reinforcing its utility in assessing RF risk [34]. Serum Na^+ concentrations showed a trend toward association with RF risk, suggesting a potential role of Na^+ metabolic disorders in RF pathogenesis that warrants further investigation.

For 28-day mortality, 24 patients (15.56%) died within the follow-up period. Univariate analysis revealed lower BMI and PaO_2, and higher CRP/Alb ratios, $PaCO_2$, APACHE II scores, and alcohol consumption rates in the mortality group. Low BMI reflects poor nutritional status, with insufficient reserves impairing immune function and tissue repair, increasing death risk [35]. A high CRP/Alb ratio indicates severe inflammation-nutrition imbalance, with persistent inflammation damaging multiple organ systems and weakening host resistance [36]. Elevated $PaCO_2$ and reduced PaO_2 signal severe respiratory impairment, with hypoxia and carbon dioxide retention causing dysfunction of vital organs (e.g., heart, brain, kidneys). Alcohol consumption may compromise immune function and metabolism, increase organ burden, and worsen outcomes in COPD patients with RF [37]. Multivariate logistic regression identified higher APACHE II scores and elevated CRP/Alb ratios as independent predictors of 28-day mortality. This echoes Yao et al.'s finding that the CRP/Alb ratio predicts 28-day mortality in COPD patients with heart failure [24], and extends this evidence to a broader cohort of COPD patients with acute exacerbations-strengthening its clinical relevance as a readily accessible prognostic tool.

This study has several limitations. First, its retrospective, single-center design is inherently prone to selection bias and unmeasured confounding factors. Second, while the sample size was a priori calculated and sufficient for primary analyses, larger multi-center prospective cohorts would enhance the generalizability and stability of findings, particularly for subgroup analyses. Most importantly, as noted during review, the correlations between the CRP/Alb ratio, calcium levels, and outcomes-along with their predictive value from ROC analyses-require external validation. While our results are biologically plausible and promising, they should be interpreted as generating testable hypotheses for future validation studies rather than definitive proof of clinical utility. Future prospective, multi-center studies with larger samples are needed to validate these findings, explore underlying mechanisms, and rigorously evaluate their impact on guiding clinical management of COPD patients.

Conclusion

APACHE II scores were significantly positively correlated with the CRP/Alb ratio and negatively correlated with serum Ca^{2+} concentrations. Patients with comorbid RF had longer hospital stays, higher $PaCO_2$, and lower Ca^{2+} concentrations and PaO_2. Multivariate logistic regression confirmed higher APACHE II scores as an independent risk factor for comorbid RF, and elevated CRP/Alb ratios as a significant predictor of 28-day mortality. These findings deepen our understanding of COPD pathophysiology and provide clinicians with an intuitive, rapid tool for assessing severity and predicting prognosis. Serum CRP/Alb ratio and electrolyte levels thus

serve as valuable indicators for evaluating COPD severity and prognosis, enabling optimized clinical management strategies to improve healthcare quality and patient outcomes.

Disclosure of conflict of interest

None.

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