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Original Article

Combined predictive value of age, RAR, APACHE II, and SOFA scores for 28-day mortality in severe pneumonia-induced ARDS: development and validation of a nomogram

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Abstract: Objective: This study evaluated the predictive value of red blood cell distribution width/albumin ratio (RAR) combined with Acute Physiology, Chronic Health Evaluation II (APACHE II), Sequential Organ Failure Assessment (SOFA) scores, and age for 28-day outcomes in patients with severe pneumonia-induced acute respiratory distress syndrome (ARDS), to support clinical prognostic assessment. Methods: Clinical data of 421 eligible patients hospitalized from June 2019 to June 2025 were retrospectively analyzed. Participants were split into training (n=295) and validation (n=126) sets at a 7:3 ratio. We collected baseline characteristics, 24-hour RAR, APACHE II and SOFA scores, as well as 28-day follow-up outcomes. Multivariate logistic regression was used to identify independent risk factors. ROC curves were applied to compare the predictive efficacy of single and combined indicators, and a nomogram was constructed for model validation. Indicator differences across age groups were also compared. Results: Baseline, laboratory, and scoring data were comparable between the two sets (P>0.05). Patients with adverse outcomes had older age and higher RAR, APACHE II, and SOFA scores (all P<0.001). RAR ≥55.815%, APACHE II ≥35.5, SOFA ≥12.5 and age ≥65.5 years were independent risk factors. The nomogram showed good calibration. ROC results revealed combined indicators achieved better predictive performance in both sets. Elderly patients had significantly higher RAR and scores than younger patients. Conclusion: RAR combined with APACHE II, SOFA scores, and Age is effective for predicting 28-day prognosis in severe pneumonia-related ARDS, and the combined use of these indicators can improve predictive accuracy.

Keywords: Red blood cell distribution width, albumin, APACHEII, acute respiratory distress syndrome, severe pneumonia

Introduction

Severe pneumonia is a highly prevalent pulmonary infectious disease associated with substantial morbidity and mortality rates. It is frequently complicated by secondary acute respiratory distress syndrome (ARDS), which accelerates disease progression and markedly worsens clinical outcomes [1, 2]. As one of the most life-threatening complications of severe pneumonia, ARDS is characterized by refractory hypoxemia and acute respiratory failure, which directly endangers patient survival and remains a major challenge in critical care medicine [3]. Furthermore, patients with severe pneumonia-related ARDS vary widely in disease severity and exhibit prominent prognostic heterogeneity, posing substantial challenges for clinical risk stratification [4]. Accordingly, the identification of accurate and reliable prognostic factors for ARDS is of great clinical value for disease severity evaluation and individualized intervention strategy formulation.

Red blood cell distribution width (RDW) is a routine laboratory marker that reflects erythrocyte

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volume heterogeneity. Elevated RDW levels are commonly observed in pathological conditions including inflammatory stress and nutritional and metabolic disturbances, and its prognostic value has been validated in severe pneumonia, chronic obstructive pulmonary disease, sepsis, and other critical illnesses [5, 6]. Serum albumin (ALB) is a major circulating plasma protein involved in substance transport and metabolic regulation. It has well-documented anti-inflammatory properties and plays a central role in maintaining vascular oncotic pressure. Low serum albumin levels generally indicate compromised nutritional reserve and more severe pulmonary injury [7]. The red blood cell distribution width-to-albumin ratio (RAR) integrates information on both inflammatory status and nutritional status, providing a more comprehensive reflection of pathophysiological impairment in critically ill patients. Compared with individual biomarkers, RAR offers superior prognostic performance and has been increasingly studied in various severe diseases [8, 9]. The Acute Physiology and Chronic Health Evaluation II (APACHE II) score and Sequential Organ Failure Assessment (SOFA) score are widely used quantitative assessment tools in critical care medicine. The APACHE II score captures the overall severity of systemic physiological dysfunction, whereas the SOFA score primarily reflects the progression of multi-organ failure. Although each tool has distinct clinical utility, both have inherent limitations [10-12]. Notably, the prognostic accuracy of any single indicator or score is constrained by its limited scope of assessment, and the combination of multiple parameters may further improve the precision of prognostic prediction.

The present study aimed to investigate the prognostic value of RAR combined with APACHE II and SOFA scores for 28-day outcomes in patients with severe pneumonia-induced ARDS, with a view to developing a more robust prognostic prediction model and providing a scientific basis for accurate prognostic stratification and the formulation of individualized intervention strategies.

Materials and methods

Study subjects

We retrospectively analyzed the clinical data of 421 patients with severe pneumonia-induced ARDS admitted to the First People's Hospital of Lanzhou City, Yangling Demonstration Zone Hospital, Fushun People's Hospital and Baoji High-Tech Hospital between June 2019 and June 2025. All patients received standardized treatment including invasive mechanical ventilation, anti-infective therapy, and nutritional support. Inclusion criteria were as follows: (1) met the diagnostic criteria for severe pneumonia; (2) met the diagnostic criteria for ARDS; (3) age >18 years; (4) completed 28-day follow-up after initiation of invasive mechanical ventilation; (5) complete clinical and follow-up data were available. Exclusion criteria were as follows: (1) comorbidities including hypothyroidism, acute massive hemorrhage, or other conditions that might interfere with laboratory biomarker measurement; (2) hematopoietic or immune system dysfunction; (3) concurrent malignant tumor or other severe end-stage systemic diseases; (4) pregnancy or lactation; (5) long-term use of immunosuppressive agents. Patients were allocated to a training set (n=295) and a validation set (n=126) at a 7:3 ratio. No statistically significant differences in baseline clinical characteristics were observed between the training set and validation set (all P>0.05). This study was approved by the institutional ethics committee of the First People's Hospital of Lanzhou City.

Data collection

Baseline data: Baseline characteristics of all patients were collected, including age, sex, underlying diseases (hypertension and diabetes mellitus), smoking history, drinking history, and history of chronic obstructive pulmonary disease (COPD).

Laboratory test indicators: Red blood cell distribution width (RDW) and serum albumin (ALB) levels measured within 24 hours of admission were collected, and the RDW-to-albumin ratio (RAR) was calculated as follows: RAR = red blood cell distribution width/serum albumin.

Scoring indicators: The Acute Physiology and Chronic Health Evaluation II (APACHE II) score [13] and Sequential Organ Failure Assessment (SOFA) score [14] within 24 hours after admission were recorded. The APACHE II score comprises three dimensions: acute physiology score, age score, and chronic health status score, with a total score ranging from 0 to 71; higher scores indicate more severe illness. The

Table 1. Comparison of baseline characteristics between the training and validation sets [n (%), $\bar{x} \pm s$]

Indicators	Training set (n=295)	Validation set (n=126)	t/χ^2	*P*
Age (yrs)	63.08±3.95	63.13±3.90	0.119	0.905
Sex			0.322	0.570
Male	155 (52.5)	70 (55.6)		
Female	140 (47.5)	56 (44.4)		
BMI (kg/m^2)	23.09±1.12	22.89±1.44	1.535	0.126
Hypertension			0.824	0.364
Yes	212 (71.9)	85 (67.5)		
No	83 (28.1)	41 (32.5)		
Diabetes mellitus			1.072	0.301
Yes	150 (50.8)	71 (56.3)		
No	145 (49.2)	55 (43.7)		
Smoking history			0.232	0.630
Yes	154 (52.2)	69 (54.8)		
No	141 (47.8)	57 (45.2)		
Drinking history			2.469	0.116
Yes	172 (58.3)	63 (50.0)		
No	123 (41.7)	63 (50.0)		
Chronic obstructive pulmonary disease (COPD)			0.054	0.817
Yes	23 (7.8)	9 (7.1)		
No	272 (92.2)	117 (92.9)		
RAR (%)	53.95±3.44	53.94±3.45	0.027	0.978
APACHEII	34.51±2.63	34.54±1.92	0.116	0.908
SOFA	11.80±1.23	11.77±1.29	0.226	0.821

Note: BMI, body mass index; COPD, chronic obstructive pulmonary disease; RAR, red blood cell distribution width-to-albumin ratio; APACHE II, Acute Physiology and Chronic Health Evaluation II; SOFA, Sequential Organ Failure Assessment.

SOFA score evaluates six organ systems (respiratory, coagulation, hepatic, cardiovascular, central nervous and renal systems), with each system scored 0 to 4 points and a total score ranging from 0 to 24; higher scores reflect more severe organ failure.

Prognostic outcomes: The 28-day prognostic outcomes of all patients after treatment were collected via outpatient re-examination and telephone interviews. According to the 28-day outcomes, patients were divided into the poor prognosis group and the favorable prognosis group.

Statistical methods

Statistical analyses were performed using SPSS 26.0 software. Continuous variables conforming to normal distribution were expressed as mean ± standard deviation (SD), and intergroup comparisons were conducted using the independent samples t-test. Categorical variables were presented as counts (percentages) [n (%)], and intergroup differences were compared using the chi-square (χ^2) test. Univariate logistic regression analysis was used to screen potential risk factors for 28-day mortality. After multicollinearity assessment, variables with $P<0.05$ in the univariate analysis were entered into the multivariate logistic regression model of the training set to identify independent risk factors and establish a nomogram. Each predictor was assigned fixed point scores according to regression coefficients derived only from the training cohort.

Optimal cut-off values for RAR, APACHE II, SOFA, and age were determined by maximizing the Youden index based on ROC curves in the training set. These cut-offs were then applied to both training and validation cohorts for variable dichotomization. Separate ROC analyses for individual indicators were also performed in the validation set to simply evaluate their standalone predictive ability within the validation population; the optimal cut-off values obtain-

Table 2. Comparison of baseline characteristics between different prognosis groups [n (%), $\bar{x} \pm s$]

Indicators	Poor prognosis group (n=91)	Favorable prognosis group (n=204)	t/χ^2	*P*
Age (yrs)	65.99±3.56	61.78±3.39	9.700	<0.001
Sex			0.647	0.421
Male	51 (56.0)	104 (51.0)		
Female	40 (44.0)	100 (49.0)		
BMI (kg/m^2)	23.36±1.98	22.97±2.41	1.353	0.177
Hypertension			0.907	0.341
Yes	62 (68.1)	150 (73.5)		
No	29 (31.9)	54 (26.5)		
Diabetes mellitus			0.474	0.491
Yes	49 (53.8)	101 (49.5)		
No	42 (46.2)	103 (50.5)		
Smoking history			1.287	0.257
Yes	52 (57.1)	102 (50.0)		
No	39 (42.9)	102 (50.0)		
Drinking history			1.672	0.196
Yes	48 (52.7)	124 (60.8)		
No	43 (47.3)	80 (39.2)		
COPD			0.181	0.670
Yes	8 (8.8)	15 (7.4)		
No	83 (91.2)	189 (92.6)		

Note: BMI, body mass index; COPD, chronic obstructive pulmonary disease.

Table 3. Comparison of laboratory and scoring indicators between different prognosis groups [n (%), $\bar{x} \pm s$]

Indicators	Poor prognosis group (n=91)	Favorable prognosis group (n=204)	t/χ^2	*P*
RAR (%)	56.24±3.11	52.93±3.07	8.519	<0.001
APACHEII	36.42±2.42	33.65±2.24	9.567	<0.001
SOFA	12.63±1.14	11.43±1.08	8.664	<0.001

Note: RAR, red blood cell distribution width-to-albumin ratio; APACHE II, Acute Physiology and Chronic Health Evaluation II; SOFA, Sequential Organ Failure Assessment.

Table 4. Assignment of influencing factors

Influencing factors	Assignment
RAR	0: <55.815%
	1: ≥55.815%
APACHEII	0: <35.5
	1: ≥35.5
SOFA	0: <12.5
	1: ≥12.5
Age	0: <65.5 yrs
	1: ≥65.5 yrs

Note: RAR, red blood cell distribution width-to-albumin ratio; APACHE II, Acute Physiology and Chronic Health Evaluation II; SOFA, Sequential Organ Failure Assessment.

ed from validation-set ROC (55.02% for RAR, 64.5 years for age) were only used for auxiliary performance comparison and were not applied to model establishment or variable dichotomization, to avoid ambiguous interpretation of different threshold standards.

For standardized external validation, the fixed scoring algorithm and regression weights from the training-set nomogram were applied directly to all validation-set subjects without model refitting. Receiver operating characteristic (ROC) curve analysis was applied to evaluate the prognostic performance of individual indicators and the fixed combined nomogram model in both training and validation cohorts, and the area under the curve (AUC), sensitivity and specificity were calculated. To verify the robustness of our prediction model, stratified subgroup analyses were performed according to sex, presence of hypertension, presence of diabetes mellitus, and Berlin severity classification of ARDS. Multivariate logistic regression was used to calculate the prognostic odds ratio (OR) and 95% confidence interval (CI) of the combined indicator in each subgroup, and between-group differences were assessed by interaction tests. For subgroup analyses, the combined indicator was treated as a continuous variable (the predicted probability ranging from 0 to 1) in the logistic regression models to estimate ORs. To verify the robustness of the combined prediction model constructed in this study, sensitivity analyses were conducted using the following four methods: excluding outliers: extreme values at the upper and lower 1% of RAR, APACHE II score and SOFA score (8 cases in total) were excluded, and multivariate logistic regression analysis was re-performed; altering the split ratio: the training set (n=337) and validation set (n=84) were re-divided at an

Table 5. Univariate Logistic regression analysis of factors influencing patient prognosis

Influencing factors	OR	P	95% CI
RAR ≥55.815%	7.167	<0.001	4.089-12.559
APACHEII ≥35.5	6.987	<0.001	4.041-12.082
SOFA ≥12.5	7.648	<0.001	4.292-13.630
Age ≥65.5 yr	9.128	<0.001	5.088-16.378

Note: RAR, red blood cell distribution width-to-albumin ratio; APACHE II, Acute Physiology and Chronic Health Evaluation II; SOFA, Sequential Organ Failure Assessment.

Table 6. Multivariate Logistic regression analysis of factors influencing patient prognosis

Influencing factors	OR	P	95% CI
RAR ≥55.815%	2.634	0.007	1.310-5.294
APACHEII ≥35.5	2.322	0.020	1.145-4.711
SOFA ≥12.5	2.283	0.029	1.087-4.795
Age ≥65.5 yr	2.341	0.033	1.072-5.111

Note: RAR, red blood cell distribution width-to-albumin ratio; APACHE II, Acute Physiology and Chronic Health Evaluation II; SOFA, Sequential Organ Failure Assessment.

Table 7. Collinearity analysis of independent risk factors for influencing patient prognosis

Factors	B	Std. Error	B	t	P	Collinearity statistics	
						Tolerance	VIF
RAR ≥55.815%	0.186	0.064	0.182	2.923	0.004	0.629	1.591
APACHEII ≥35.5	0.154	0.063	0.157	2.442	0.015	0.584	1.712
SOFA ≥12.5	0.170	0.068	0.161	2.502	0.013	0.587	1.704
Age ≥65.5 yr	0.186	0.074	0.178	2.526	0.012	0.490	2.043

Note: RAR, red blood cell distribution width-to-albumin ratio; APACHE II, Acute Physiology and Chronic Health Evaluation II; SOFA, Sequential Organ Failure Assessment.

8:2 ratio, and changes in the AUC of the combined model were compared; Bootstrap resampling validation: 1,000 rounds of resampling with replacement were performed on the total sample to calculate the mean AUC and its 95% CI; excluding patients with COPD: patients with COPD (32 cases in total), which were not explicitly excluded in the original study but may affect prognosis, were excluded, and model performance was re-evaluated. A *P* value <0.05 was considered statistically significant.

Results

Comparison of baseline characteristics, laboratory test indicators, and scoring indicators between the training set and validation set

As shown in **Table 1**, the proportions of patients with 28-day poor prognosis were 30.8% and 31.0% in the training set and validation set, respectively. The distribution of outcome events was balanced, and the baseline prognostic risks were comparable between the two groups (P>0.05).

Comparison of baseline data between different prognosis groups

As presented in **Table 2**, there were no significant between-group differences in sex, body mass index (BMI), history of hypertension, diabetes mellitus, smoking, alcohol consumption or COPD (all P>0.05). However, patients in the poor-prognosis group were significantly older than those in the favorable-prognosis group (P< 0.05).

Comparison of laboratory test indicators and scoring indicators between different prognosis groups

As illustrated in **Table 3**, the RAR, APACHE II score and SOFA score were all markedly higher in the poor-prognosis group (all P<0.05).

Univariate and multivariate analyses

The optimal cut-off value of each predictor was determined by maximizing the Youden index of receiver operating characteristic (ROC) curves for subsequent variable assignment (**Table 4**). Univariate logistic regression (**Table 5**) and multivariate logistic regression (**Table 6**) revealed that RAR ≥55.815%, APACHE II ≥35.5 points, SOFA ≥12.5 points and age ≥65.5 years were independent risk factors for adverse 28-day outcomes. Collinearity diagnostics demonstrated that the VIF values of the four variables ranged from 1.67 to 2.15, all far below the critical threshold of 5, indicating the absence of severe multicollinearity (**Table 7**).

Nomogram analysis

The nomogram built based on training set multivariate regression (**Figure 1A**) demonstrated

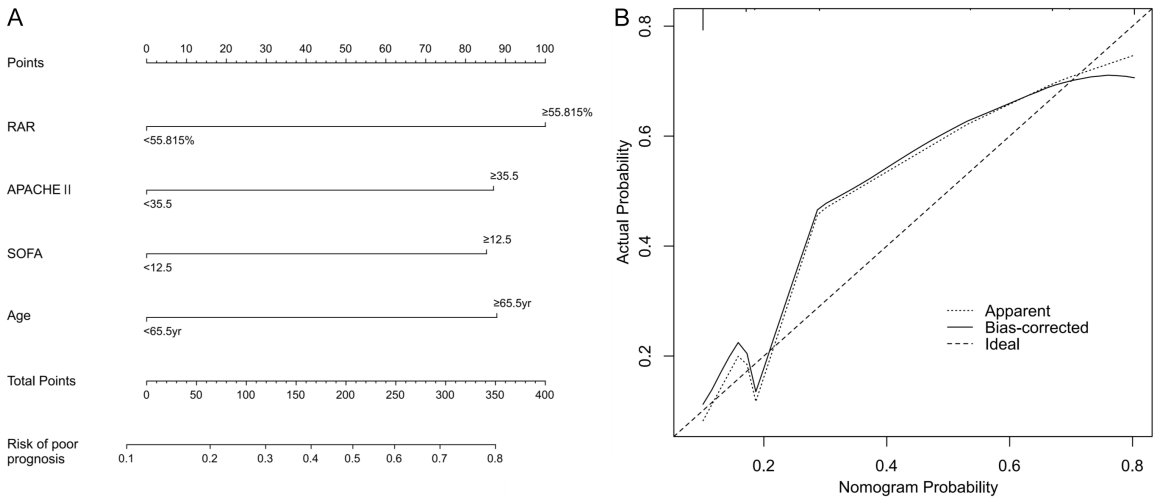


Figure 1. Nomogram and calibration curve for predicting 28-day poor prognosis in the training set. A. Nomogram constructed with four predictors in the training set; each predictor corresponds to a point scale, and the total points can be converted to the predicted risk of 28-day poor prognosis. B. Calibration curve for evaluating the agreement between model-predicted probability and actual observed probability of poor prognosis in the training set. Notes: RAR, red blood cell distribution width-to-albumin ratio; APACHE II, Acute Physiology and Chronic Health Evaluation II; SOFA, Sequential Organ Failure Assessment.

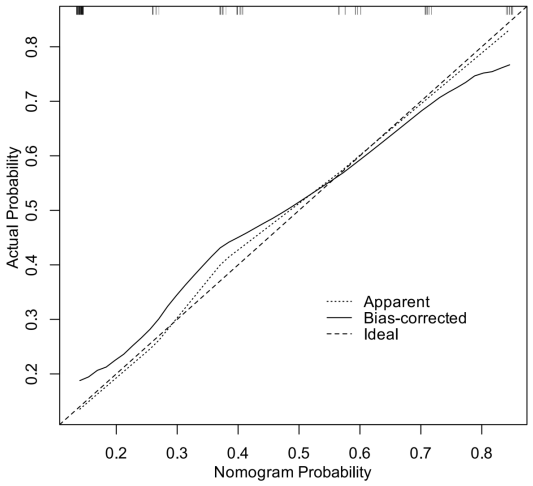


Figure 2. Calibration curve for evaluating the agreement between model-predicted probability and actual observed probability of poor prognosis in the validation set.

that RAR, APACHE II score, SOFA score and age were independent predictors of 28-day poor prognosis, and each variable provided stable contribution to risk prediction. The Hosmer-Lemeshow goodness-of-fit test of training-set calibration curve showed χ^2=1.766, P=0.622, which indicated great consistency between model predicted risk and actual observed outcome (**Figure 1B**).

For external validation, we applied the fixed scoring formula of training-set nomogram to all validation cohort patients without refitting new regression or nomogram in validation set. The Hosmer-Lemeshow test of validation-set calibration curve was χ^2=3.964, P=0.860, proving that the training-derived model maintained satisfactory calibration ability in independent populations (**Figure 2**).

ROC curve analysis

ROC analysis of the training set (**Figure 3A**) demonstrated satisfactory discriminative power for RAR, APACHE II, SOFA and age, and the combined panel exhibited superior predictive efficacy over any single variable. Consistent findings were observed in the validation set (**Figure 3B**), where all individual indicators showed acceptable diagnostic value and the combined model achieved better performance. Detailed ROC results are summarized in **Table 8**. Cut-off of validation set in **Table 8** is only the optimal threshold derived from independent single-marker ROC fitting in validation cohort, which is completely different from the unified modeling cut-off from training set shown in **Table 4**. The slight discrepancy is caused by inconsistent sample distribution between two subgroups, while all multivariate analyses and

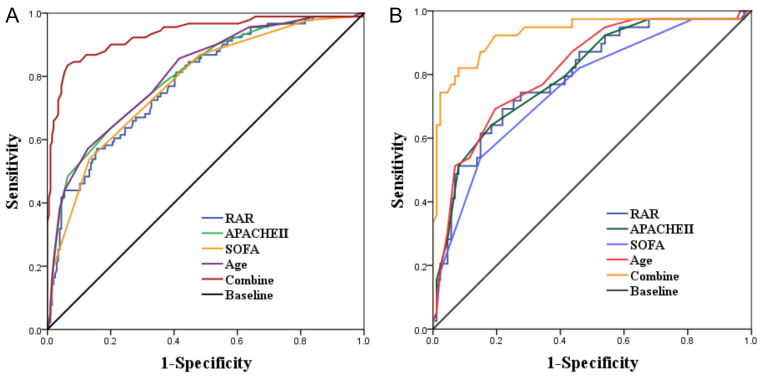


Figure 3. Receiver operating characteristic (ROC) curves for evaluating the predictive performance of each indicator and the combined model for 28-day poor prognosis. A. ROC curves in the training set. B. ROC curves in the validation set. Notes: ROC, receiver operating characteristic; RAR, red blood cell distribution width-to-albumin ratio; APACHE II, Acute Physiology and Chronic Health Evaluation II; SOFA, Sequential Organ Failure Assessment.

nomogram construction consistently adopted the training-set cut-off.

Subgroup analysis

Subgroup analyses showed that the combined model maintained stable predictive value for poor prognosis across all subgroups (all $P<0.05$). Interaction tests detected no significant inter-subgroup differences (all $P>0.05$), which suggested excellent generalizability of the model to diverse patient populations (**Figure 4**; **Table 9**).

Sensitivity analysis

Sensitivity analyses using four distinct strategies yielded identical independent risk factors as the primary analysis, with no meaningful shifts in odds ratios OR and 95% CI. The AUC of the combined model fluctuated between 0.921 and 0.937, highly consistent with the original AUC of 0.934, which verified strong robustness of the prediction model (**Table 10**).

Discussion

Severe pneumonia is a prevalent critical illness characterized by rapid progression and substantial threats to patient survival [15]. ARDS constitutes a leading fatal complication of severe pneumonia. Early identification and precise risk stratification of patients at high risk for ARDS are critical for optimizing clinical interventions and improving outcomes [16]. The present study investigated the prognostic performance of the RAR combined with APACHE II and SOFA scores in patients with severe pneumonia-related ARDS. Our analyses identified RAR, APACHE II score, SOFA score and age as independent prognostic risk factors, and confirmed superior discriminative capacity of the four-variable combined model. These findings offer novel evidence to support clinical prognostic assessment, and we interpret our results alongside previously published literature in the following discussion.

This study found that advanced age was an independent predictor of adverse clinical outcomes, consistent with the conclusions reported by Patel et al. [17]. The underlying mechanisms are multifactorial. Physiological aging impairs immune function, reduces alveolar elasticity and ventilatory capacity; older patients also frequently have multiple chronic comorbidities, all of which amplify the risk of dysregulated inflammatory responses following pulmonary infection [18]. Furthermore, elderly individuals possess limited organ reserve capacity. When challenged by oxidative stress and systemic inflammatory response syndrome triggered by severe pneumonia, their organs fail to mount sufficient compensatory responses, triggering sequential multiple organ dysfunction and ultimately worsening prognosis [19].

We identified RAR as an independent prognostic factor for severe pneumonia-associated ARDS, consistent with findings reported by He et al. [20] on prognostic biomarkers in ARDS. The potential biological mechanisms are explained as follows: RDW quantifies erythrocyte volume heterogeneity. In severe pneumonia, elevated inflammatory cytokines such as tumor necrosis factor-α and interleukin-6 suppress bone marrow hematopoiesis and disrupt erythrocyte membrane stability, leading to increased RDW [21]. Serum ALB, a major circulating plasma protein, mediates substance transport and metabolic homeostasis while exerting anti-inflammatory effects and sustaining vascular oncotic pressure. Hypoalbuminemia typically indicates systemic nutritional depletion and aggravated pulmonary tissue injury [22]. By

Table 8. ROC curve results for each predictor and the combined model for predicting 28-day poor prognosis

Group	Factor	AUC	P	95% CI	Sensitivity	Specificity	Youden index	Cut-off value
Training set	RAR	0.782	<0.001	0.725-0.838	0.571	0.843	0.414	55.815%
	APACHEII	0.802	<0.001	0.748-0.857	0.637	0.799	0.436	35.5
	SOFA	0.778	<0.001	0.721-0.836	0.538	0.868	0.406	12.5
	Age	0.808	<0.001	0.755-0.862	0.571	0.873	0.444	65.5yrs
	Combine	0.934	<0.001	0.899-0.968	0.835	0.936	0.771	-
Validation set	RAR	0.795	<0.001	0.710-0.880	0.692	0.782	0.474	55.02%
	APACHEII	0.800	<0.001	0.716-0.884	0.641	0.816	0.457	35.5
	SOFA	0.758	<0.001	0.666-0.850	0.538	0.851	0.389	12.5
	Age	0.817	<0.001	0.738-0.897	0.692	0.805	0.497	64.5
	Combine	0.929	<0.001	0.871-0.987	0.821	0.920	0.741	

Note: RAR, red blood cell distribution width-to-albumin ratio; APACHE II, Acute Physiology and Chronic Health Evaluation II; SOFA, Sequential Organ Failure Assessment.

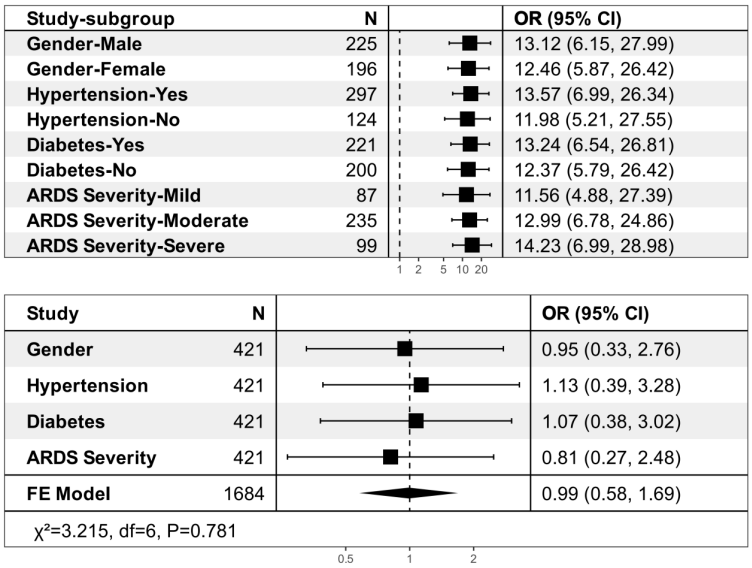


Figure 4. Forest plot of subgroup analyses for the four-factor combined model in predicting 28-day poor prognosis. Upper panel: Subgroup-specific ORs and 95% CIs stratified by sex, comorbidities and ARDS severity. Black squares represent the effect size of each subgroup; horizontal lines indicate 95% CIs; the vertical solid line at OR=1 indicates the line of no effect. Lower panel: Results of interaction tests across subgroups. FE Model = fixed-effect pooled model; χ^2 (chi-square statistic), df (degrees of freedom) and *P* value were used to assess statistical differences in effect sizes between subgroups. Abbreviations: OR, odds ratio; CI, confidence interval; ARDS, acute respiratory distress syndrome; FE, fixed effect.

integrating markers of inflammatory activation and nutritional status, RAR provides a more holistic assessment of overall pathophysiological disturbance in severe pneumonia-related ARDS, overcoming the limited predictive value of single laboratory indicators [23, 24].

Higher APACHE II and SOFA scores were independent predictors of poor outcomes in our cohort, consistent with previous reports by Zhao et al. [25] and Song et al. [26]. The two scoring systems offer complementary prognostic information based on distinct evaluation frameworks. The APACHE II scale integrates acute physiological derangements, age and chronic comorbidities; higher total scores correspond to more severe disruption of physiological homeostasis and diminished organ compensatory capacity [27]. The SOFA score quantifies dysfunction across six vital organ systems (respiratory, coagulation, hepatic, cardiovascular, neurological and renal) to dynamically track the progression of multiple organ failure [28]. Combined use of these tools enables comprehensive risk evaluation by covering both global severity and individual organ function, yielding more robust risk stratification [29].

ROC analyses in both training and validation sets demonstrated that the four-variable predictive model incorporating the RAR, APACHE II score, SOFA score and age achieved superior discriminative performance, with higher sensitivity and specificity compared with any single marker alone. This model integrates indicators of inflammation, nutritional status, physiological derangement, organ dysfunction, and age,

Table 9. Predictive efficacy of combined indicators for 28-day prognosis in different subgroups [n (%)]

Subgroup	n	OR	95% CI	*P*-value	Interaction *P*-value
Sex					0.682
Male	225	13.124	6.152-27.987	<0.001	
Female	196	12.458	5.876-26.432	<0.001	
Hypertension					0.543
Yes	297	13.567	6.987-26.341	<0.001	
No	124	11.982	5.213-27.564	<0.001	
Diabetes					0.497
Yes	221	13.245	6.543-26.812	<0.001	
No	200	12.367	5.789-26.421	<0.001	
ARDS Severity					0.312
Mild	87	11.564	4.876-27.345	<0.001	
Moderate	235	12.987	6.789-24.876	<0.001	
Severe	99	14.231	6.987-28.965	<0.001	

Note: ARDS, acute respiratory distress syndrome.

Table 10. Sensitivity analysis: predictive performance of the combined model under different analytical strategies

Sensitivity Analysis Method	Sample Size	AUC	95% CI	Sensitivity	Specificity	Youden Index
Original Study	421	0.934	0.899-0.968	0.835	0.936	0.771
Excluding Outliers	413	0.931	0.895-0.967	0.827	0.932	0.759
Training set (8:2 Split)	337	0.928	0.887-0.969	0.819	0.928	0.747
Validation set (8:2 Split)	84	0.921	0.856-0.986	0.806	0.917	0.723
Bootstrap Resampling	421	0.931	0.902-0.957	0.829	0.931	0.760
Excluding COPD Patients	389	0.937	0.901-0.973	0.842	0.941	0.783

Note: COPD, chronic obstructive pulmonary disease.

enabling more accurate prognostic stratification than isolated indicators. Further subgroup stratified analyses revealed consistent predictive performance for adverse 28-day outcomes across subgroups stratified by sex, comorbid hypertension or diabetes, and ARDS severity grades, with no significant interaction effects between subgroups. These findings confirm that the combined model maintains stable predictive capacity regardless of patients' underlying comorbidities and disease severity, supporting broad clinical generalizability. Sensitivity analyses, including outlier removal, adjusted split ratios, bootstrap resampling, and exclusion of COPD patients, yielded identical independent prognostic factors and minimal AUC fluctuations [30, 31]. Such stable outputs verify that our core findings are not biased by extreme observations or cohort partitioning strategies, and reflect robust statistical reliability. From a clinical perspective, readily available admission laboratory tests and early scoring systems can facilitate early identification of high-risk patients and rational allocation of critical care resources. Patients with high combined scores may be prioritized for ICU admission, enhanced respiratory support, optimized anti-infective therapy, and targeted nutritional support. Additionally, this multi-marker scoring framework allows rapid bedside estimation of 28-day adverse prognosis risk, assisting clinicians in designing personalized therapeutic strategies.

The present study does have several limitations. First, this was a retrospective, single-center cohort study, and only patients receiving invasive mechanical ventilation were enrolled according to the inclusion criteria, which may introduce selection bias. Second, several potential confounders, including genetic polymorphisms and individualized treatment regimens, were not adjusted for in the analysis. Third, cut-off values were determined by the Youden index from training-set ROC curves before conducting dichotomous logistic regression, which

may carry a minor risk of overfitting and slight OR overestimation. Fourth, the follow-up duration was limited to 28 days, and long-term patient outcomes were not assessed. Fifth, the relatively narrow standard deviations of baseline variables may reflect strict eligibility criteria and the single-center design, which could limit generalizability to more heterogeneous real-world populations. Future large-scale, multicenter studies with extended follow-up are warranted to refine this prognostic model. Further analyses incorporating potential confounders (e.g., genetic polymorphisms and treatment heterogeneity) and basic experimental studies would help elucidate the underlying pathophysiological mechanisms.

In conclusion, RAR, APACHE II score, SOFA score, and age are independent risk factors for 28-day outcomes in severe pneumonia-induced ARDS. The predictive model built upon these four indicators exhibits favorable prognostic performance. This model may assist clinicians in early identification of high-risk individuals and formulation of personalized interventions, thereby improving patient prognosis.

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Disclosure of conflict of interest

None.

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