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ORIGINAL RESEARCH

Predictive Value of SAPS II for 28-Day All-Cause Mortality in AECOPD Patients Admitted to the ICU

Shiyuan Yao, Yao Xu, Jin Liu, Rui Li, Yuer Li, Shaobo Ge, Yuanliang Sun, Chenyu Yao, Xia Yang, Ming Zhang

Department of Respiratory and Critical Care Medicine, the Second Affiliated Hospital of Xi'an Jiaotong University, Xi'an, Shaanxi, People's Republic of China

Correspondence: Ming Zhang; Xia Yang, Department of Respiratory and Critical Care Medicine, the Second Affiliated Hospital of Xi'an Jiaotong University, No. 157 West Fifth Road, Xi'an, Shaanxi, 710004, People's Republic of China, Email zhangmingdr@163.com; doc_yangxia@xjtu.edu.cn

Background: The Simplified Acute Physiology Score II (SAPS II), which incorporates 12 physiological variables along with age, admission type and chronic health conditions, is widely used for assessing illness severity and predicting mortality risk in critically ill patients. However, its prognostic value in patients with acute exacerbation of chronic obstructive pulmonary disease (AECOPD) remains unclear.

Methods: A total of 1087 eligible AECOPD patients admitted to intensive care unit (ICU) were included from the Medical Information Mart for Intensive Care IV database. The clinical characteristics and 28-day all-cause mortality of these patients were collected.

Results: SAPS II was significantly higher in non-survivors than in survivors among the AECOPD patients admitted to ICU. For predicting 28-day all-cause mortality, SAPS II showed superior discriminative ability compared to the scores of Sequential Organ Failure Assessment, Oxford Acute Severity of Illness Score, and Logistic Organ Dysfunction System. The combination of SAPS II with these scoring systems did not significantly enhance the predictive value. Kaplan-Meier survival analysis identified SAPS II $\geq$ 37 as a significant cut-off value, with patients scoring above this threshold showing a significantly decreased 28-day cumulative survival rate. Cox regression confirmed SAPS II $\geq$ 37 as an independent mortality predictor. Restricted cubic spline analysis revealed a linear increase in 28-day all-cause mortality risk with elevated SAPS II. Subgroup analysis revealed that the association between SAPS II and mortality risk remained consistent across the most subgroups except for coronary heart disease.

Conclusion: Our findings demonstrate that SAPS II is a significant predictor of 28-day all-cause mortality in AECOPD patients admitted to the ICU, with a score $\geq$ 37 serving as a robust indicator of poor clinical prognosis.

Keywords: chronic obstructive pulmonary disease, acute exacerbation, mortality, SAPS II, intensive care unit

Introduction

Chronic obstructive pulmonary disease (COPD) is a common chronic condition characterized by persistent airflow limitation and progressive respiratory symptoms, posing a major global public health challenge.[1] With over 400 million people affected worldwide, COPD is the third leading cause of death globally.[2] The number of cases is projected to reach 592 million by 2050, which will impose a substantial socio-economic and health burden.[3] The clinical course of COPD is frequently marked by acute exacerbations, which are events of acute worsening triggered primarily by respiratory infections (viral or bacterial) and environmental factors such as air pollutants or temperature changes.[4–7] Of particular concern are patients with acute exacerbation of COPD (AECOPD) who require intensive care unit (ICU) admission, as they face a particularly poor prognosis, with in-hospital mortality rates ranging from 20% to 40%.[8] This high mortality underscores the urgent requirements for early risk stratification and proactive management of critical ill patients with AECOPD.

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A number of prognostic biomarkers have been identified for risk stratification in AECOPD patients.[9] For instance, the stress hyperglycemia ratio specifically indicates acute stress severity, and its elevation has been independently associated with in-hospital mortality in critically ill COPD patients.[10] The ratio of blood urea nitrogen (BUN) to creatinine, an indicator of dehydration and prerenal perfusion insufficiency, has been identified as a significant predictor of in-hospital mortality of AECOPD patients.[11] The combined index of hemoglobin, albumin, lymphocyte and platelet, which integrates nutritional, inflammatory and immunological status, was associated with an increased risk of ICU mortality in patients with AECOPD.[12] Although these indicators have certain prognostic values for AECOPD patients, their accuracy and reliability in assessing outcomes for critically ill AECOPD patients still require validation in larger cohorts. This underscores the need for robust, multi-parameter prognostic tools.

Comprehensive prognostic scoring systems widely used in the ICU, integrate a range of physiological and clinical parameters to provide a more holistic risk assessment. Common tools used in ICU include the Simplified Acute Physiology Score II (SAPS II), Sequential Organ Failure Assessment (SOFA), Oxford Acute Severity of Illness Score (OASIS), and Logistic Organ Dysfunction System (LODS).[13–17] Among these, SAPS II is recommended for rapid prognostic assessment due to its standardized set of 17 clinically routine variables and straightforward calculation.[13] This score is calculated based on the worst values of 12 key physiological parameters (vital signs, laboratory markers, and the Glasgow Coma Scale) collected within the first 24 hours of ICU admission, along with patient age, admission type, and the presence of three specific comorbidities (acquired immunodeficiency syndrome, metastatic cancer, and hematologic malignancy). Each variable is assigned a weighted score, and the sum (range 0–163) predicts mortality risk, with higher scores indicating greater severity. Furthermore, evidence from the Medical Information Mart for Intensive Care III (MIMIC-III) database has confirmed that SAPS II exhibits superior predictive ability for long-term mortality in elderly septic patients compared to the Modified LODS (MLODS), Systemic Inflammatory Response Syndrome (SIRS), OASIS and SOFA,[18] highlighting its robust prognostic performance. The prognostic value of the SAPS II has been well established in general critical care populations.[13,19] Evidence also supports its predictive utility in patients with respiratory conditions, where it can predict ICU mortality and the risk of ICU-acquired infection.[20,21] However, its definitive predictive value and optimal clinical application in AECOPD patients admitted to the ICU remain to be established.

Therefore, our present study aimed to evaluate the predictive efficacy of SAPS II for 28-day all-cause mortality in AECOPD patients admitted to the ICU based on the MIMIC-IV database (version 3.1, 2008–2022),[22] with particular focus on determining its discriminative power, identifying a clinically relevant cut-off, and comparing it against contemporary scores, thereby providing evidence-based support for clinical risk stratification in these patients.

Methods

Study Population

We conducted a retrospective cohort study using the MIMIC-IV version 3.1 database. This publicly available, longitudinal and single-center database comprises de-identified clinical data from more than 90000 ICU admissions at the Beth Israel Deaconess Medical Center (BIDMC) in Boston from 2008 to 2022. Ethical approval for the use of the MIMIC-IV database was granted by the Institutional Review Boards (IRBs) of the Massachusetts Institute of Technology (MIT) and BIDMC, and the patient consent was waived due to the de-identified nature of the data. The main author of this study (Shiyuan Yao) has completed the required Collaborative Institutional Training Initiative (CITI) program course to access the database (Certification ID: 66014454).

Inclusion criteria of this study were: (1) patients aged 18 years or older during their first ICU admission (if multiple ICU stays occurred, data from the first admission were used); (2) The diagnosis of COPD based on codes from the International Classification of Diseases, Ninth Revision (ICD-9) or the International Statistical Classification of Diseases and Related Health Problems, Tenth Revision (ICD-10); (3) The diagnosis of AECOPD based on ICD-9 or ICD-10; (4) ICU length of stay $\geq$ 24 hours. Exclusion criteria were: (1) Missing SAPS II; (2) Lack of 28-day survival status data following ICU admission. The screening flow chart is shown in Figure 1, and a total of 1087 patients were finally included in this study.

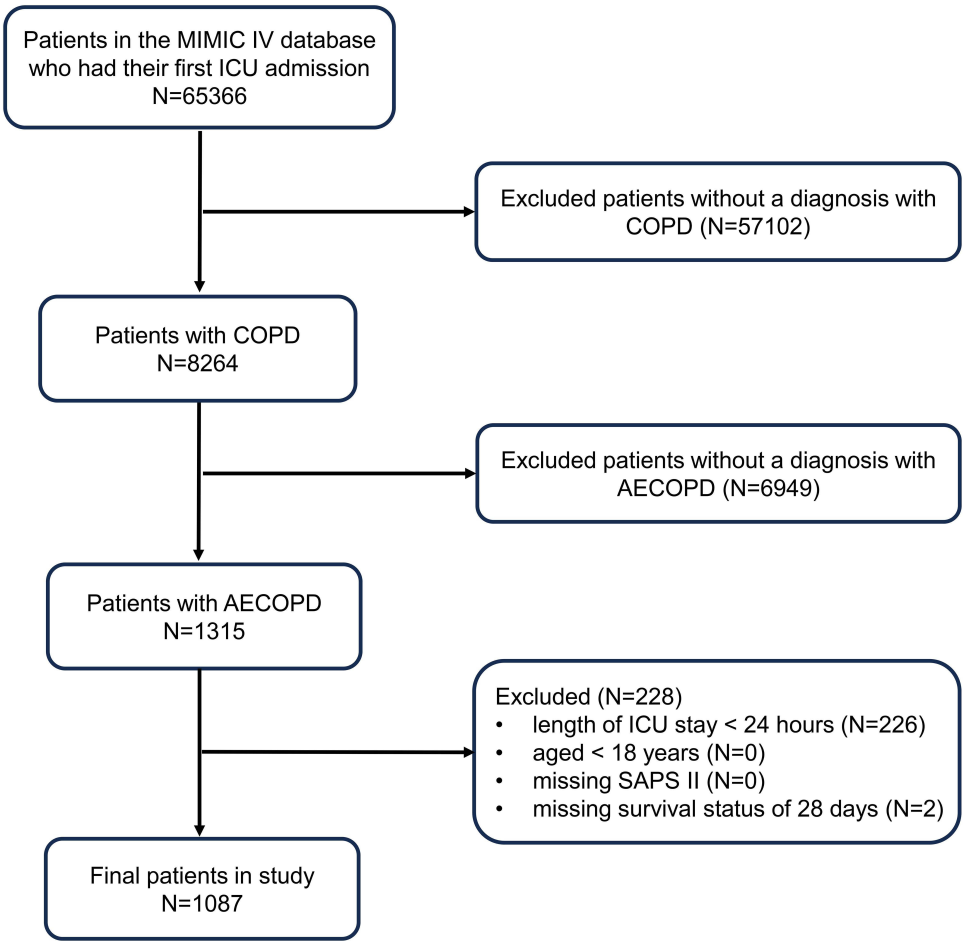

Figure 1 The flow chart of patient selection.
Abbreviations: MIMIC-IV, Medical Information Mart for Intensive Care IV; ICU, intensive care unit; SAPS II, Simplified Acute Physiology Score II.

Data Extraction

Data extraction was performed using Structured Query Language (SQL) via pgAdmin (version 8.12), with code adapted from the official MIMIC code repository (https://github.com/MIT-LCP/mimic-code), and the following variables were extracted. (1) Demographics: age, gender, race and weight. (2) Vital signs: mean heart rate, blood pressure, respiratory rate and temperature. (3) Illness severity scores: SAPS II, SOFA, OASIS and LODS. (4) Laboratory parameters: white blood cell count, neutrophil count, lymphocyte count, monocyte count, red blood cell count, hemoglobin, platelet count, BUN, creatinine, sodium, potassium, calcium, chloride, and glucose. (5) Comorbidities: asthma, hypertension, coronary heart disease, heart failure, diabetes, acute kidney injury, and sepsis were identified using ICD-9 and ICD-10 codes. (6) Outcomes: ICU length of stay, ICU admission and discharge time, as well as the time of death. Mortality data were sourced from hospital records and the US Social Security Administration Death Master File. All laboratory variables were the first available values obtained within the first 24 hours of ICU admission. Variables with missing values exceeding 20% were excluded to mitigate potential bias. Variables with less than 20% missing values were imputed using multiple imputation with the Multivariate Imputation by Chained Equations (MICE) package in R software. The primary outcome was 28-day all-cause mortality, which was defined as death from any cause within 28 days following ICU admission.

Statistical Analysis

All continuous variables were examined using the Kolmogorov–Smirnov test for normal distribution. Quantitative variables with normal distribution are presented as mean ± standard deviation (SD), and the differences were identified

using the Student's *t*-test. Non-normally distributed are presented as median with interquartile range (IQR), and differences were explored by the Mann–Whitney *U*-test. Categorical variables are presented as frequencies (percentages) and compared using the Chi-square test or Fisher's exact test. All statistical analyses were performed using R software (version 4.4.3) and Stata/MP (version 18.0). A two-sided P-value < 0.05 was considered statistically significant. Additionally, the adequacy of the sample size was confirmed by post-hoc power analysis (G*Power, version 3.1) and Events Per Variable assessment.

Spearman's rank correlation analysis was employed to evaluate the correlations between SAPS II and several inflammatory markers. The predictive value of SAPS II, SOFA, OASIS, LODS and their combined models for 28-day all-cause mortality was assessed using receiver operating characteristic (ROC) curve analysis. The optimal cut-off value for SAPS II was identified based on the Youden Index (J = sensitivity + specificity - 1). Kaplan-Meier survival curves were generated according to the optimal cutoff value of SAPS II. Univariate and multivariate Cox proportional hazards regression models were used to quantify the association between SAPS II and 28-day all-cause mortality. Variables with either clinical significance or *P* less than 0.05 in univariable analysis were included in the multivariate Cox proportional hazards models. The association between SAPS II and 28-day all-cause mortality was further explored using restricted cubic spline models. Subgroup analyses were performed to assess the consistency of the association between SAPS II and 28-day all-cause mortality across predefined subgroups, including gender, asthma, hypertension, coronary heart disease, heart failure, diabetes, acute kidney injury and sepsis.

Results

Baseline Characteristics of the Study Population

Baseline characteristics of the enrolled AECOPD patients are shown in Table 1 according to survival status. The median age of AECOPD patients was 72.46 years, and the overall 28-day all-cause mortality rate was 20.42%. There was no significant difference in gender distribution between survivors and non-survivors (*P*>0.05). Compared to the survivors,

Table 1 Baseline Characteristics of AECOPD Patients Stratified by 28-Day All-Cause Mortality

Variable	Total (n=1087)	Survivors (n=865)	Non-Survivors (n=222)	*P* value
Age, years	72.46 [65.33, 80.09]	71.38 [64.06, 79.02]	76.36 [70.52, 84.10]	<0.001
Gender, n (%)				0.651
Female	546 (50.2)	438 (50.6)	108 (48.6)	
Male	541 (49.8)	427 (49.4)	114 (51.4)	
Race, n (%)				0.014
White	737 (67.8)	590 (68.2)	147 (66.2)	
Black	107 (9.8)	95 (11.0)	12 (5.4)	
Asian	20 (1.8)	16 (1.8)	4 (1.8)	
Other	223 (20.5)	164 (19.0)	59 (26.6)	
Weight, kg	76.85 [63.00, 94.50]	77.70 [64.80, 96.10]	71.75 [59.48, 86.30]	<0.001
Mean heart rate, bpm	86.65 [76.92, 99.16]	86.27 [76.81, 98.42]	89.82 [77.92, 104.75]	0.004
Mean MBP, mmHg	77.64 [71.66, 84.90]	77.70 [71.84, 85.12]	76.54 [70.59, 82.71]	0.077
Mean respiratory rate, times/min	20.49 [18.16, 22.96]	20.31 [18.00, 22.75]	21.60 [19.14, 24.33]	<0.001
Mean temperature, °C	36.80 [36.60, 37.01]	36.81 [36.62, 37.02]	36.75 [36.52, 36.97]	0.007
SAPS II	37.00 [30.00, 45.00]	36.00 [29.00, 43.00]	44.00 [37.00, 55.00]	<0.001
SOFA	4.00 [2.00, 7.00]	4.00 [2.00, 6.00]	5.00 [3.00, 8.00]	<0.001
OASIS	33.00 [28.00, 39.00]	33.00 [28.00, 39.00]	36.00 [31.00, 42.00]	<0.001
LODS	5.00 [3.00, 7.00]	4.00 [2.00, 6.00]	6.00 [4.00, 8.00]	<0.001
Red blood cell (M/μL)	3.73 [3.22, 4.24]	3.78 [3.26, 4.32]	3.53 [3.07, 4.00]	<0.001
White blood cell (K/μL)	10.80 [7.50, 14.65]	10.70 [7.40, 14.10]	11.45 [8.42, 17.15]	0.004
Platelets (K/μL)	205.00 [152.00, 269.50]	206.00 [156.00, 270.00]	195.00 [138.00, 264.75]	0.037

(*Continued*)

Table 1 (Continued).

Variable	Total (n=1087)	Survivors (n=865)	Non-Survivors (n=222)	*P* value
Hemoglobin (g/dL)	11.10 [9.60, 12.60]	11.10 [9.70, 12.70]	10.70 [9.10, 11.78]	<0.001
Neutrophils (K/μL)	9.02 [6.07, 12.89]	8.64 [5.86, 12.28]	10.20 [6.81, 15.51]	<0.001
Lymphocytes (K/μL)	0.93 [0.53, 1.47]	0.97 [0.57, 1.54]	0.78 [0.41, 1.24]	<0.001
Monocytes (K/μL)	0.55 [0.31, 0.88]	0.55 [0.31, 0.88]	0.56 [0.30, 0.85]	0.983
NLR	9.75 [4.96, 18.80]	8.92 [4.76, 16.97]	13.46 [7.40, 26.65]	<0.001
PLR	217.43 [129.69, 409.76]	208.41 [125.89, 381.91]	240.88 [148.79, 451.75]	0.01
NMLR	10.31 [5.40, 19.76]	9.66 [5.19, 17.99]	14.32 [8.03, 27.50]	<0.001
SII	2032.38 [995.17, 4153.26]	1877.85 [938.06, 3883.00]	2852.12 [1355.09, 5593.73]	<0.001
SIRI	4.83 [2.28, 11.16]	4.37 [2.17, 9.15]	7.46 [2.92, 16.15]	<0.001
PIV	1017.93 [432.54, 2380.37]	958.93 [409.41, 2207.65]	1502.55 [587.96, 3686.04]	<0.001
BUN (mg/dL)	23.00 [16.00, 36.00]	22.00 [16.00, 35.00]	29.00 [21.00, 45.00]	<0.001
Creatinine (mg/dL)	1.00 [0.70, 1.40]	1.00 [0.70, 1.40]	1.15 [0.80, 1.80]	0.001
Sodium (mEq/L)	139.00 [136.00, 142.00]	139.00 [136.00, 142.00]	140.00 [136.00, 142.00]	0.083
Potassium (mEq/L)	4.30 [3.90, 4.80]	4.30 [3.90, 4.70]	4.40 [4.00, 4.90]	0.103
Calcium (mg/dL)	8.50 [8.00, 9.00]	8.50 [8.10, 9.00]	8.50 [7.90, 8.90]	0.084
Chloride (mg/dL)	101.00 [97.00, 105.00]	101.00 [97.00, 105.00]	101.00 [97.00, 105.00]	0.313
Glucose (mg/dL)	139.00 [114.00, 176.00]	139.00 [113.00, 175.00]	139.00 [116.00, 179.75]	0.502
Asthma, n (%)	45 (4.1)	40 (4.6)	5 (2.3)	0.163
Hypertension, n (%)	650 (59.8)	515 (59.5)	135 (60.8)	0.788
Coronary heart disease, n (%)	445 (40.9)	346 (40.0)	99 (44.6)	0.244
HF, n (%)	554 (51.0)	436 (50.4)	118 (53.2)	0.512
Diabetes, n (%)	331 (30.5)	274 (31.7)	57 (25.7)	0.099
AKI, n (%)	467 (43.0)	340 (39.3)	127 (57.2)	<0.001
Sepsis, n (%)	731 (67.2)	555 (64.2)	176 (79.3)	<0.001
LOS ICU, days	3.05 [1.82, 6.06]	2.89 [1.79, 5.63]	4.02 [2.08, 7.23]	<0.001

Abbreviations: MBP, mean blood pressure; SAPS II, Simplified Acute Physiology Score II; SOFA, Sequential Organ Failure Assessment; OASIS, Oxford Acute Severity of Illness Score; LODS, Logistic Organ Dysfunction System; NLR, neutrophil to lymphocyte ratio; PLR, platelet to lymphocyte ratio; NMLR, (neutrophil + monocyte)/lymphocyte ratio; SII, (Systemic Immune-inflammation Index); SII, (platelet × neutrophil)/lymphocyte ratio; SIRI, (Systemic Inflammation Response Index); SIRI. (neutrophil × monocyte)/lymphocyte ratio; PIV, (Pan-Immune Inflammation Value); PIV, (platelet × neutrophil × monocyte)/lymphocyte ratio; BUN, blood urea nitrogen; HF, heart failure; AKI, acute kidney injury; LOS ICU, length of stay in the ICU.

non-survivors had significantly higher SAPS II [44.00 (37.00, 55.00) vs 36.00 (29.00, 43.00), $P < 0.001$]. Non-survivors were older and had higher mean heart and respiratory rates, along with elevated severity scores (SOFA, OASIS and LODS). Laboratory abnormalities were also more pronounced in the non-survivors, including increased inflammatory markers [white blood cell count, neutrophil number, neutrophil to lymphocyte ratio (NLR), (neutrophil + monocyte)/lymphocyte ratio (NMLR), Systemic Inflammation Response Index (SIRI) and Pan-Immune Inflammation Value (PIV)] and impaired renal function (higher levels of BUN and creatinine). Moreover, the prevalence of acute kidney injury and sepsis were higher in the non-survivors ($P < 0.05$). In addition, non-survivors had lower levels of weight, mean temperature, red blood cell count, platelet count, hemoglobin level and lymphocyte count compared with the survivors (all $P < 0.05$). Notably, the median ICU length of stay was longer in the non-survivors than in the survivors [4.02 (2.08, 7.23) vs 2.89 (1.79, 5.63) days, $P < 0.001$].

SAPS II Was Associated with 28-Day All-Cause Mortality of AECOPD Patients in ICU

To evaluate the association between SAPS II and inflammatory parameters, correlation coefficients were calculated using Spearman's analysis (Figure 2). SAPS II demonstrated modest yet statistically significant positive correlations with several inflammatory markers, including NLR ($\rho = 0.101$, $P < 0.001$), NMLR ($\rho = 0.101$, $P < 0.001$), SIRI ($\rho = 0.122$, $P < 0.001$), and PIV ($\rho = 0.076$, $P = 0.012$). As shown in Figure 3A, SAPS II demonstrated the highest discriminative ability for predicting 28-day all-cause mortality in AECOPD patients, with an area under the curve (AUC) of 0.695 [95% confidence interval (CI): 0.657–0.734], outperforming LODS (AUC=0.672, 95% CI: 0.632–0.711), SOFA (AUC=0.618,

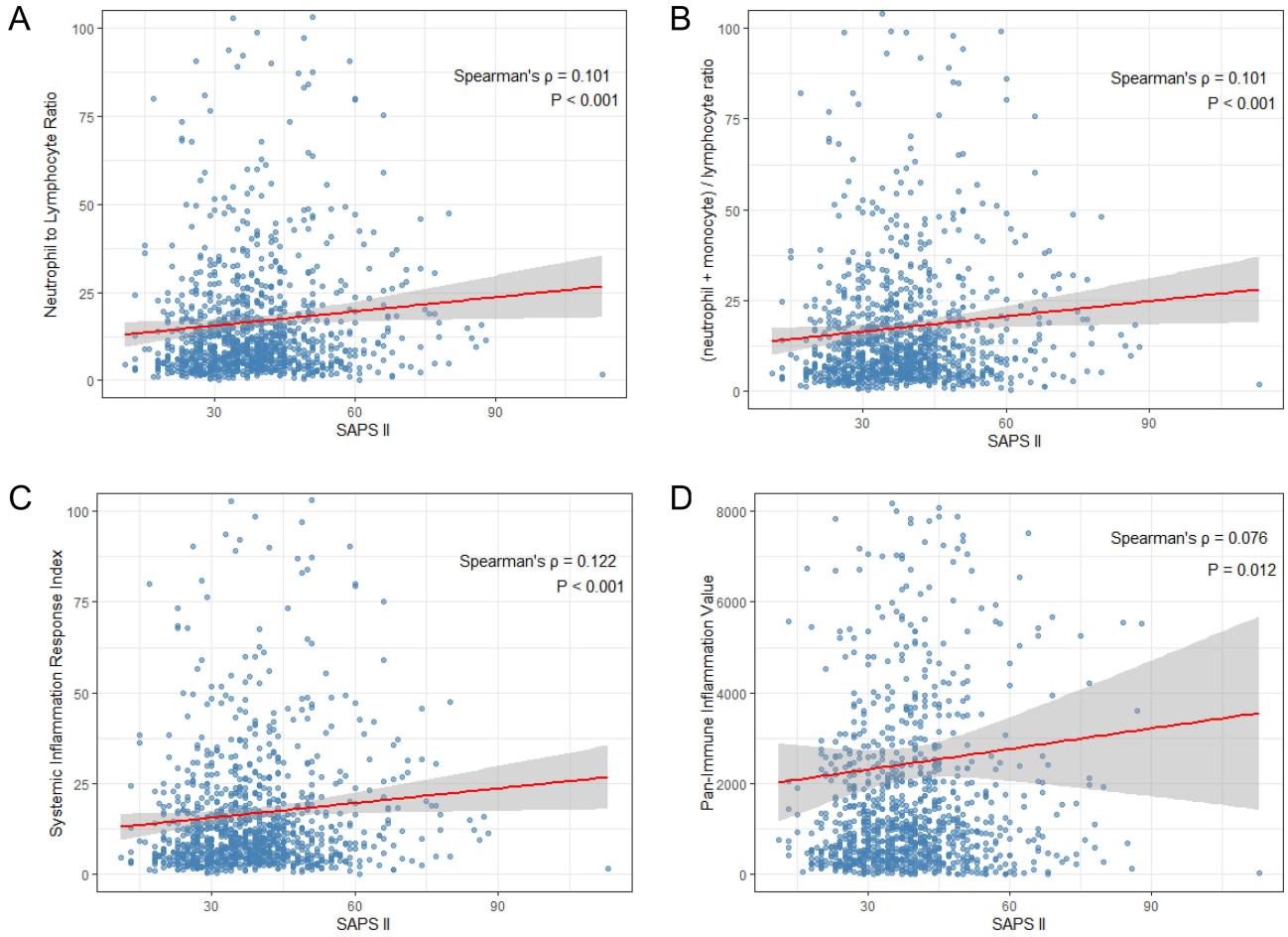

Figure 2 Correlations between SAPS II and inflammatory parameters in AECOPD patients. The correlations of SAPS II with neutrophil to lymphocyte ratio (**A**), (neutrophil + monocyte)/lymphocyte ratio (**B**), Systemic Inflammation Response Index (**C**) and Pan-Immune Inflammation Value (**D**) in AECOPD patients admitted to the ICU.
Abbreviation: Systemic Inflammation Response Index = (neutrophil × monocyte)/lymphocyte ratio; Pan-Immune Inflammation Value = (platelet × neutrophil × monocyte)/lymphocyte ratio.

95% CI: 0.578–0.658), and OASIS (AUC=0.611, 95% CI: 0.570–0.653). DeLong's test for pairwise comparisons showed that SAPS II significantly outperformed SOFA and OASIS (both $P < 0.001$), while no significant difference was observed compared to LODS ($P = 0.112$). The combinations of SAPS II with SOFA, OASIS and LODS did not significantly improve predictive performance over SAPS II alone (all $P > 0.05$, Figure 3B–G). Further DeLong's test indicated that the combined model incorporating all four scoring systems (SAPS II, SOFA, OASIS and LODS) achieved an AUC of 0.701, and its predictive value was not significantly better than SAPS II alone ($P = 0.279$, Figure 3H). The optimal cutoff value of SAPS II for predicting 28-day all-cause mortality in AECOPD patients was 37, with a sensitivity of 75.68% and a specificity of 52.60%. In addition, Kaplan-Meier analysis demonstrated that the high-risk group of AECOPD patients (defined by SAPS II ≥ 37) had a significantly poorer 28-day survival rate compared to the low-risk group (Log rank test, $\chi^2 = 58.4$, $P < 0.001$, Figure 3I).

Factors Associated with 28-Day All-Cause Mortality in AECOPD Patients

Cox proportional hazards regression models were used to explore the association between SAPS II and 28-day all-cause mortality in AECOPD patients admitted to the ICU (Table 2). In multivariable Cox regression analysis, SAPS II was a significant predictor of 28-day all-cause mortality in all three models. When analyzed as a continuous variable, the hazard ratios were 1.045 in the unadjusted model (95% CI: 1.037–1.054, $P < 0.001$), 1.041 in the partially adjusted model for age, gender and race (95% CI: 1.031–1.050, $P < 0.001$), and 1.035 in the fully adjusted model (95% CI: 1.024–1.045, $P < 0.001$). Dichotomized at a cutoff of 37, SAPS II remained significantly associated with 28-day all-cause

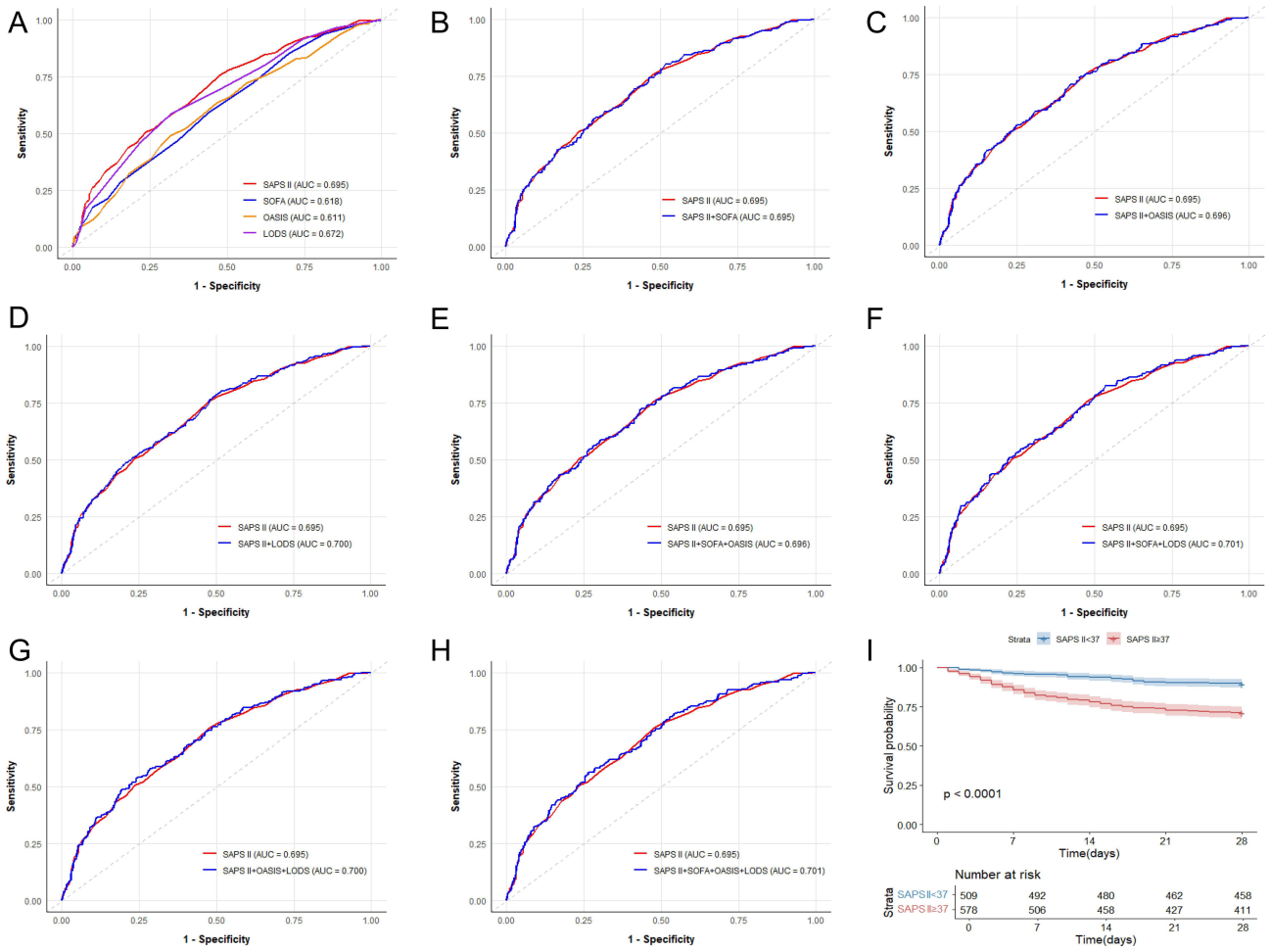

Figure 3 ROC curves of the scoring system and Kaplan-Meier curve of the 28-day all-cause mortality in AECOPD patients. ROC curves of SAPS II, SOFA, OASIS and LODS (**A**). The ROC curves of SAPS II combined with SOFA (**B**), OASIS (**C**), LODS (**D**). The ROC curve of SAPS II combined with SOFA and OASIS (**E**). The ROC curve of SAPS II combined with SOFA and LODS (**F**). The ROC curve of SAPS II combined with OASIS and LODS (**G**). The ROC curve of SAPS II combined with SOFA, OASIS and LODS (**H**). Kaplan-Meier curve of the 28-day all-cause mortality in AECOPD patients according to the cut-off of SAPS II (**I**). Blue line refers to SAPS II <37, and red line refers to SAPS II ≥ 37.
Abbreviations: ROC, receiver operating characteristic; SAPS II, Simplified Acute Physiology Score II; SOFA, the Sequential Organ Failure Assessment; OASIS, the Oxford Acute Severity of Illness Score; LODS, the Logistic Organ Dysfunction System.

mortality of AECOPD patients, with hazard ratios of 3.110 in the unadjusted model (95% CI: 2.288–4.226, $P < 0.001$), 2.455 in the partially adjusted model (95% CI: 1.784–3.378, $P < 0.001$), and 2.160 in the fully adjusted model (95% CI: 1.540–3.031, $P < 0.001$).

Restricted cubic splines were used to investigate the association between SAPS II and 28-day all-cause mortality in patients with AECOPD admitted to the ICU. The analysis demonstrated a significant positive association between SAPS

Table 2 Cox Proportional Hazard Ratios for 28-Day All-Cause Mortality in AECOPD Patients

Variable	Model1		Model 2		Model 3	
	HR (95% CI)	***P* value**	**(95% CI)**	***P* value**	**HR (95% CI)**	***P* value**
SAPS II[a]	1.045(1.037,1.054)	<0.001	1.041(1.031,1.050)	<0.001	1.035(1.024,1.045)	<0.001
SAPS II≥37[b]	3.110(2.288,4.226)	<0.001	2.455(1.784,3.378)	<0.001	2.160(1.540,3.031)	<0.001
SAPS II<37[b]	Ref		Ref		Ref	

Notes: Model 1: no adjusted. Model 2: adjusted for age, gender, race. Model 3: adjusted for Model 2 plus weight, mean heart rate, mean respiratory rate, mean temperature, white blood cell, platelets, hemoglobin, creatinine, asthma, hypertension, coronary heart disease, heart failure, diabetes, acute kidney injury, sepsis. [a]Included the continuous variable SAPS II. [b]Included the categorical variable SAPS II.

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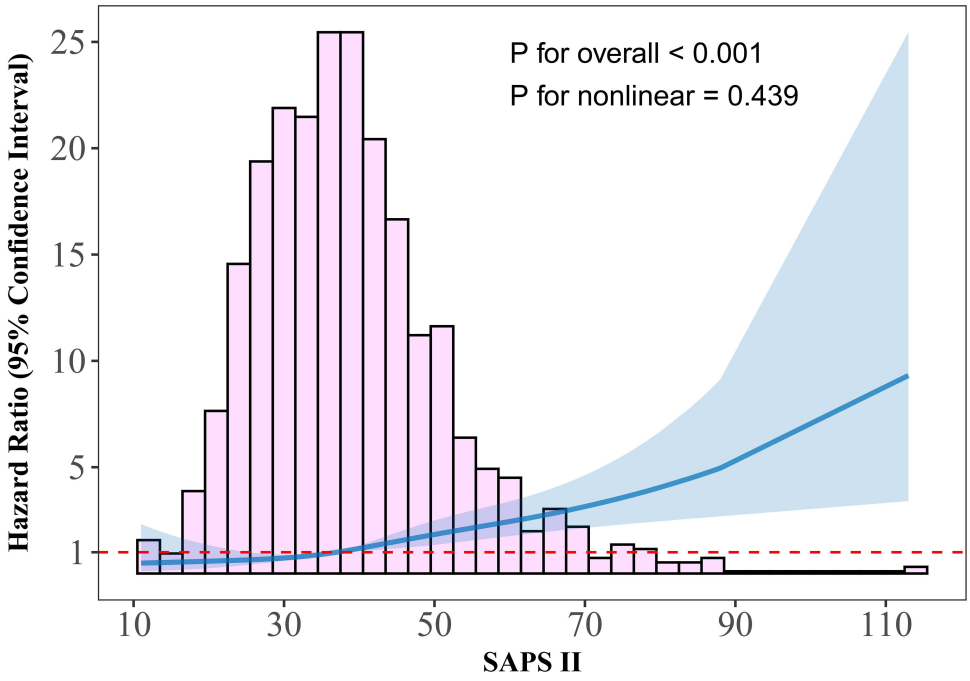

Figure 4 Restricted cubic spline analysis on the association between SAPS II and 28-day all-cause mortality in AECOPD patients. The restricted cubic spline analysis of the association between SAPS II and 28-day all-cause mortality in AECOPD patients was adjusted for age, gender, race, weight, mean heart rate, mean respiratory rate, mean temperature, white blood cell count, platelet number, hemoglobin, creatinine as well as comorbidities (asthma, hypertension, coronary heart disease, heart failure, diabetes, acute kidney injury and sepsis).
Abbreviation: SAPS II, Simplified Acute Physiology Score II.

II and 28-day all-cause mortality after adjustment for covariates, with higher SAPS II corresponding to an increased risk of mortality ($P < 0.001$, Figure 4). Restricted cubic spline analysis revealed no significant evidence of nonlinearity in the association between SAPS II and 28-day all-cause mortality ($P = 0.439$), supporting a linear pattern in their relationship. Further statistical test confirmed a significant linear association between SAPS II and 28-day all-cause mortality in AECOPD patients admitted to the ICU ($P < 0.001$).

Subgroup Analysis

To further determine whether the association between SAPS II and 28-day all-cause mortality in AECOPD patients was influenced by other common comorbidities, subgroup analysis was performed (Figure 5). The association between SAPS II and 28-day all-cause mortality remained consistent across most subgroups, including gender, asthma, hypertension, heart failure, diabetes, acute kidney injury and sepsis (all P for interaction > 0.05). However, a statistically significant interaction was observed in the subgroup of coronary heart disease (P for interaction = 0.018).

Discussion

Acute exacerbations are critical events in COPD, often necessitating intensive care for advanced support,[23] which underscores the vital need for early and accurate risk stratification. Various prognostic scoring systems, such as SAPS II, SOFA, OASIS and LODS, are routinely utilized in the ICU.[24] Among these, SOFA and LODS primarily focus on tracking organ dysfunction, whereas SAPS II and OASIS are specifically designed for mortality prediction.[25] However, their application values in patients with AECOPD remain inadequately validated. Our study has found non-survivors had significantly higher SAPS II scores than survivors, indicating its potential use in predicting 28-day all-cause mortality for AECOPD patients in the ICU. Furthermore, our analysis revealed a significant positive correlation between the SAPS II score and key inflammatory markers (NLR, NMLR, SIRI and PIV) that are established predictors of AECOPD mortality,[26–30] suggesting that its predictive value may be partly derived from reflecting systemic inflammation.

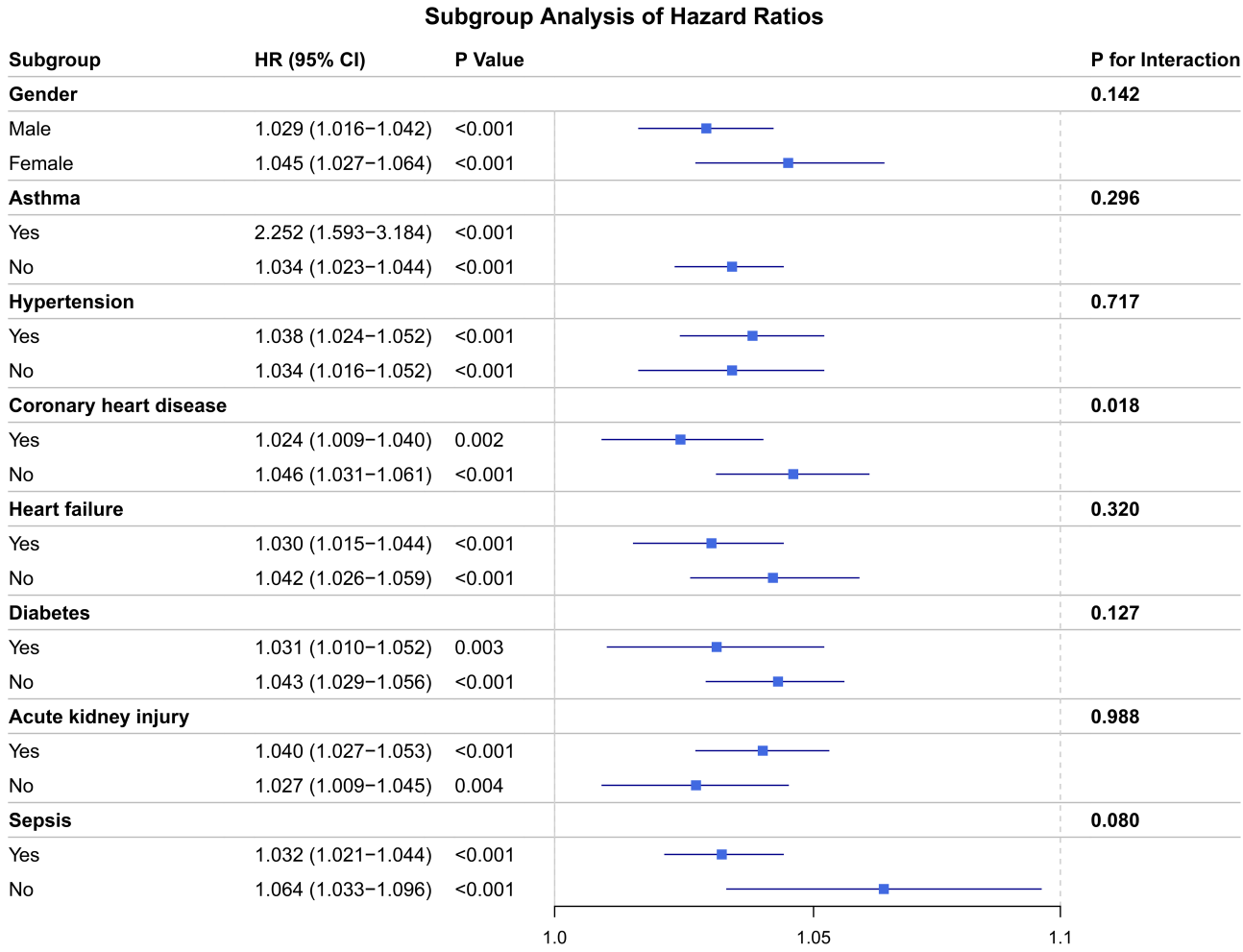

Figure 5 Forest plots of hazard ratios for 28-day mortality across subgroups. For each subgroup, HR is plotted as a solid square with its 95% CI shown as a horizontal line. Subgroup analysis was performed to assess the influence of comorbidities on the association between SAPS II and 28-day all-cause mortality in AECOPD patients.
Abbreviations: SAPS II, Simplified Acute Physiology Score II; HR, hazard ratios; CI, confidence interval.

The SAPS II system is calculated from 12 physiological variables, age, admission type, and chronic health conditions, thereby providing a comprehensive reflection of patients' physiological reserve, acute disease severity as well as chronic disease burden.[31] Its components capture key prognostic dimensions in AECOPD, including physiological reserve, systemic stress response, and risks of respiratory failure and renal dysfunction, which are supported by established clinical evidence.[32–34] In our cohort, ROC analysis validated a good predictive ability of SAPS II for 28-day all-cause mortality. This finding is strongly supported by consistent evidence across diverse critically ill populations. For example, SAPS II has shown superior prognostic performance compared to SOFA and Acute Physiology and Chronic Health Evaluation II (APACHE II) in sepsis,[35] and outperformed SOFA in post-cardiac arrest patients.[36] Moreover, a study comparing seven prognostic scores (including SAPS II, SOFA, OASIS, and several other common systems) in ICU patients with sleep apnea-hypopnea syndrome found that SAPS II ranked among the best in predictive performance.[37] In addition, our study further confirmed that combining it with other scores did not enhance predictive efficacy, thereby affirming its role as an independent and core prognostic tool.

Our present study has identified SAPS II of 37 as a critical prognostic threshold for AECOPD patients admitted to ICU. Kaplan-Meier analysis revealed a significantly elevated 28-day all-cause mortality among patients with scores at or above this threshold. This finding was further supported by multivariable Cox regression, which confirmed that SAPS II $\geq$ 37 remained an independent risk factor for mortality after the adjustment for age, gender, comorbidities, and other

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potential clinical confounders. Moreover, a positive linear correlation was observed between SAPS II and mortality risk, indicating that AECOPD patients exhibited poorer outcomes with higher scores of SAPS II. Therefore, these findings highlight the necessity for heightened clinical attention and more aggressive management in AECOPD patients with SAPS II $\geq$ 37.

Subgroup analysis revealed that the association between SAPS II and mortality risk remained consistent across the most subgroups, indicating the stable predictive value and good generalizability of the score among AECOPD patients with various clinical features. However, a significant interaction was observed in the subgroup of patients comorbid with coronary heart disease, suggesting that the predictive power of SAPS II may differ in this specific population. The acute-on-chronic pathophysiology exacerbates underlying coronary inflammation and plaque instability, thereby increasing the risk of acute cardiac decompensation or ischemic events.[38] This cascade ultimately alters the mortality risk profile of AECOPD patients comorbid with coronary heart disease. Given the limitations of SAPS II in assessing cardiac-specific risk, we recommend its combination with cardiac biomarkers (such as N-terminal pro-B-type natriuretic peptide or high-sensitivity troponin) to improve risk stratification and prognosis in AECOPD patients with coronary heart disease.[39]

Several limitations of this study should be addressed. First, the retrospective single-center design based on the MIMIC-IV database carries inherent risks of selection bias and unmeasured confounding factors. Second, the analysis was limited to the SAPS II upon ICU admission, and the potential prognostic value of its serial measurements during the ICU stay remains to be explored. Finally, the clinical applicability of the current findings requires external validation through independent, prospective, and multi-center studies.

In summary, this study validates the SAPS II as an independent predictor of 28-day all-cause mortality in ICU-admitted AECOPD patients. We establish a clinically actionable cutoff of 37 points for risk stratification, and confirm its standalone utility. For clinicians, this readily available tool enables the early identification of high-risk patients (SAPS II $\geq$ 37), who may thus be targeted for intensified monitoring and therapy. Future prospective multicenter studies are warranted to refine its clinical application.

Data Sharing Statement

The datasets generated and analyzed during the current study are available from the corresponding author on reasonable request.

Ethical Statement

This study was conducted in accordance with the principles of the Declaration of Helsinki. The use of the MIMIC-IV database was approved by the Institutional Review Board of the Massachusetts Institute of Technology and Beth Israel Deaconess Medical Center. Based on a publicly available database containing de-identified patient information, this study qualified for exemption from full ethical review. Formal approval for this exemption was granted by the Medical Ethics Committee of the Second Affiliated Hospital of Xi'an Jiaotong University.

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Disclosure

The authors declare that there are no conflicts of interest in this work.

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