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ORIGINAL RESEARCH

Prediction Score of *Pseudomonas Aeruginosa* Isolation in Acute Exacerbations of Chronic Obstructive Pulmonary Disease

Thotsaporn Morasert[1,2], Pichaya Tantiyavarong[1]

[1]Department of Clinical Epidemiology, Faculty of Medicine, Thammasat University, Pathum Thani, 12120, Thailand; [2]Pulmonary and Critical Care Medicine, Department of Medicine, Suratthani Hospital, Surat Thani, 84000, Thailand

Correspondence: Pichaya Tantiyavarong, Department of Clinical Epidemiology, Faculty of Medicine, Thammasat University, 99/209 Moo 18, Phaholyothin Road, Khlong Nueng, Khlong Luang, Pathum Thani, 12120, Thailand, Tel +66-89-7711576, Email pichaya_t@tu.ac.th

Background: *Pseudomonas aeruginosa* (*PA*) is an important pathogen in acute exacerbations of chronic obstructive pulmonary disease (AECOPD), yet empirical anti-*PA* coverage is often prescribed inappropriately. Accurate prediction tools are needed to guide targeted therapy.

Methods: We conducted a retrospective cohort study of hospitalized AECOPD patients at a regional referral hospital in Thailand (2015–2018). Clinical, radiographic, and laboratory data were analyzed to identify independent predictors of *PA* isolation. Multivariable logistic regression was used to develop a prediction score, which was internally validated using bootstrap resampling. Model performance was assessed by the area under the receiver operating characteristic curve (AuROC).

Results: Among 1,348 admissions (771 patients), *P. aeruginosa* was isolated in 167 cases (12.4%). A simplified prediction score was developed based on four independent predictors: home nebulizer use, prior anti-*PA* antibiotic exposure within 1 year, radiographic consolidation, and elevated serum bicarbonate. The prediction score achieved an AuROC of 0.66 (95% CI 0.62–0.70) with good calibration after internal validation. Risk groups were defined as low (0–1 points, <12% risk), intermediate (2–3 points, 16–23% risk), and high (4–6 points, ≥32% risk).

Conclusion: This simplified prediction score, developed in hospitalized AECOPD patients, may aid clinicians in guiding empirical antibiotic selection by reducing unnecessary anti-*PA* coverage in low-risk cases while ensuring timely treatment for those at high risk.

Keywords: AECOPD, acute exacerbations, chronic obstructive pulmonary disease, *pseudomonas aeruginosa*, predictive model, prediction score

Introduction

Acute exacerbation of chronic obstructive pulmonary disease (AECOPD) is defined as episodes of acute respiratory symptom worsening requiring additional therapy.[1] They contribute significantly to morbidity, hospitalization, and mortality among COPD patients.[2–4] Bacterial infection is a key factor in the pathophysiology and progression of COPD, with *Pseudomonas aeruginosa (PA)* being an important pathogen, particularly in severe cases.[5,6] *PA* is a gram-negative bacterium frequently identified in COPD patients. The prevalence of *PA* varies widely depending on disease severity and clinical setting, ranging from approximately 4% among general COPD outpatients,[7] to 18% in hospitalized patients with AECOPD,[8,9] and up to 35% in those with severe COPD.[10] Notably, in Thailand, rates as high as 27% have been reported among patients admitted to respiratory care units,[11] underscoring the relevance of this pathogen in our regional context. COPD is an established risk factor for *PA* infection, especially in severe AECOPD patients who require hospitalization.[12] Furthermore, the isolation of *PA* sputum is associated with in-hospital mortality among AECOPD.[13] Previous studies demonstrated the risk factors for *PA* isolation in sputum among COPD patients, including bronchiectasis,[12] forced expiratory volume in 1 sec (FEV_1) less than 30 to 50%,[14,15] a corticosteroid used,[16] previous hospitalizations,[16] number of antibiotic use[12] and prior *PA* isolation.[16]

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While evidence from a meta-analysis has confirmed the benefit of antibiotics in AECOPD,[17] and additional study demonstrated that bacterial eradication was associated with reduced bronchial inflammation,[18] and fewer recurrent exacerbations.[19] Accordingly, empirical antibiotics are often indicated in hospitalized AECOPD, but the choice of regimen should be guided by local bacterial resistance patterns. Standard antibiotic empirical regimens, such as aminopenicillin with clavulanic acid, macrolides, or tetracyclines, generally provide broad coverage against usual pathogens but lack activity against *PA*. Therefore, accurately identifying patients who may require broader antipseudomonal agents remains a key clinical challenge.

Empirical antipseudomonal therapy is important in AECOPD, but concern about *PA* often results in broad coverage despite uncertain risks. Consequently, some patients receive unnecessarily broad-spectrum therapy—contributing to resistance, adverse effects, and unnecessary cost—while others with unrecognized PA infection may receive inappropriate initial antibiotic therapy has been linked to increased mortality in the intensive care unit (ICU) patients with AECOPD[20] and in cases of *Pseudomonas* septicemia.[21] Despite these concerns, Planquette B et al,[22] reported a higher antipseudomonal antibiotic prescription rate after the healthcare-associated pneumonia guideline without improving prognosis. These findings underscore the importance of accurately identifying patients at high risk for *PA* infection to guide appropriate empirical therapy.

In this study, we aimed to develop and internally validate a clinical prediction score to estimate the likelihood *PA* isolation in hospitalized patients with AECOPD. The score was based on routinely available clinical variables and was intended to support risk stratification and inform decision-making regarding empirical treatment.

Method

Study Design and Data Source

We conducted a retrospective cohort study to develop clinical prediction score. All data were extracted from electronic medical records of patients hospitalized with AECOPD at Suratthani Hospital, a regional referral center in southern Thailand, between October 2015 and September 2018. The Institutional Review Board and the Ethics Committee of Thammasat University approved the study protocol (Approval ID.014/2020). Informed consent was waived due to the retrospective nature of the study using existing records with no identifiable patient information and minimal risk. Data confidentiality was ensured, and the study complied with the Declaration of Helsinki. The study was conducted and reported in accordance with the Transparent Reporting of a multivariable prediction model for Individual Prognosis or Diagnosis (TRIPOD) statement.[23]

Participants

We included all adult patients with AECOPD admitted to the general medical ward and medical ICU. The diagnosis of AECOPD was based on the International Statistical Classification of Diseases and Related Health Problems, 10th Revision (ICD-10) codes J44.0, J44.1, and J44.9, as the principal diagnoses in the discharge summary. The exclusion criteria were 1) age < 40 years; 2) spirometry results that were not consistent with COPD (FEV_1/ forced vital capacity [FVC] ratio < 0.7); 3) lack of sputum culture data within 48 hours from admission; or 4) patients already receiving anti-pseudomonal therapy within 48 hours before admission. The unit of observation in this study was each hospitalized admission for each COPD patient. Thus, data were collected in multiple records for patients with recurrent admissions during the study period.

Study Endpoint

The study endpoint was the isolation of *PA*. *PA* isolation was defined as the identification of *PA* in either sputum or endotracheal tube aspirate cultures obtained within the first 48 hours of hospital admission. Patients were separated into two groups based on whether they had *PA* isolation or non-*PA* isolation.

Data Collection

Patient's demographic and clinical data for each admission were extracted from medical records, including gender, age, body mass index, smoking status, comorbidities, spirometry result (the closest result to the index admission), current inhaled

controller medications, Modified Medical Research Council dyspnea scale.[24] The number of COPD-related events in the previous year, including hospitalized and emergency department visits, was also collected. Initial clinical parameters on admission, including vital signs, the presence of respiratory failure requiring endotracheal intubation, initial chest radiographic finding interpreted by attending physicians, laboratory investigations obtained within the first 24 hours of admission, long-term home oxygen therapy use, systemic corticosteroid use within 2 weeks prior to admission (≥ 10 mg/day of prednisolone or equivalent), history of hospitalization and antibiotics usage during last 3 months and 1 year, the presence of *PA* in sputum or endotracheal tube aspirate cultures during previous 3 months. Antibiotics used against *PA* were ceftazidime, piperacillin/tazobactam, levofloxacin, meropenem, and imipenem/cilastatin.

Statistical Analysis

Descriptive data were used to summarize the baseline characteristics of hospital admission with and without *PA* isolation. Categorical variables were presented as frequency and percentage. Continuous variables were summarized as the mean and standard deviation (SD) if normally distributed, or as the median and interquartile range (IQR) for skewed distributions. Fisher's exact probability test was used to compare the difference in categorical variables between the *PA* and non-*PA* isolation admissions. The independent *t*-test was used for normally distributed continuous variables. Mann–Whitney *U*-test was used for non-normally distributed continuous variables. To estimate the probability of PA isolation, we developed a predictive score using the following steps.

Selection of Candidate Predictors

Candidate predictors for *PA* isolation were selected based on three criteria: 1) availability within the dataset, 2) established clinical relevance, and 3) prior evidence from the literature. A comprehensive list of potential predictors is presented in Supplementary Table 1.

To account for the potential non-linear associations between continuous predictors and the outcome, the multivariable fractional polynomials procedure was applied to determine the optimal functional form for continuous variables. Results were presented as odds ratios (OR) and their 95% confidence interval (CI). Given that some patients had multiple admissions during the study period, a multilevel logistic regression model was used to account for clustering at the patient level. Variance inflation factors (VIF) were computed for all predictors to assess multicollinearity. Variables with a VIF greater than 10 were considered collinear and excluded from the final model.

Evaluation of Prediction Model Performance and Internal Validation

We applied a multivariable stepwise backwards elimination order to derive a more parsimonious prediction model, retaining predictors with p-values < 0.05 in the final model. The final prediction model was tested for the discrimination power of the model in predicting *PA* isolation using the c-statistic (area under the curve, AuROC). Prediction model calibration was evaluated by comparing predicted probabilities to observed outcomes using a calibration plot, and goodness-of-fit was assessed with the Hosmer–Lemeshow test. To perform internal validation, we applied bootstrap resampling with 1,000 iterations using the original dataset. The optimism-corrected performance was used to estimate potential overfitting.

Predictive Score Assignment

We assigned a score to each predictor in the final model based on the regression coefficient value. The points of scores assigned to each predictor were obtained by dividing each β coefficient by the smallest β coefficient significantly different from zero and rounding to the nearest integer. The prediction scores were summed and retested on the patient to evaluate the performance of the final score.

Clinical Decision of the Prediction Score

The total prediction scores for clinical application were categorized into three risk groups to guide clinical decisions regarding empirical anti-*PA* coverage: 1) not recommended, 2) conditionally recommended, and 3) recommended. The appropriate cut-off values for these groups were determined based on sensitivity, specificity, and the predicted probabilities of *PA* isolation. The lowest risk group (ie, not recommended) was defined by a predicted *PA* isolation probability

lower than the overall prevalence of *PA* observed in the study cohort. The investigator consensus determined this threshold to avoid unnecessary anti-*PA* antibiotic use in low-risk patients.

A two-sided p-value < 0.05 was considered statistically significant. Data with more than 20% missing were excluded, and complete case analysis was performed. Statistical analyses were performed using Stata 16 (StataCorp, College Station, TX, USA).

Result

Study Population and Prevalence

Between October 2015 and September 2018. A total of 1,919 admissions of AECOPD patients were screened. A total of 571 admissions were excluded due to age < 40 years (n = 5), FEV_1/FVC ratio ≥ 0.7 (n = 28), or the absence of sputum culture result within 48 hours of admission (n = 538). No patients were receiving anti-*PA* therapy within 48 hours prior to admission. After exclusion, 1,348 admissions from 771 patients were included in the final analysis. Of these numbers, *PA* was isolated in 167 admissions, yielding a prevalence of 12.4%. Study flow is shown in Figure 1.

Characteristics of AECOPD Admissions and Patients

The study population was predominantly male (86.8%) with a mean ± SD age of 75 ± 11 years. A history of smoking was present in approximately 90% of patients, with a median smoking exposure of 25 pack-years (IQR 15, 40). A history of bronchiectasis and pulmonary tuberculosis was noted in 3.2% and 14.8% of cases, respectively. Spirometry data were available in 21.4% of admissions. Among those with data, the mean FEV_1/FVC ratio was 0.49 ± 0.10, and the mean predicted FEV_1 was 40.8 ± 17.2%, respectively. Due to more than 20% missing data, spirometry and arterial blood gas variables were omitted from subsequent final modelling. On initial presentation, 87% of patients experienced respiratory failure requiring intubation, and 37% had radiographic evidence of pneumonia. Comparisons of baseline characteristics, medical treatment, and clinical findings between admissions with and without *PA* isolation are shown in Tables 1–3, respectively. Approximately 40% of admissions yielded positive cultures for gram-negative bacteria from sputum or endotracheal tube aspirates, with *Klebsiella pneumoniae* (12.9%) and *PA* (12.4%) being the most frequently isolated pathogens (Supplementary Table 2).

Candidate Predictors

All pre-selected candidate predictors were available within the dataset and were chosen based on established clinical relevance, prior evidence from the literature, or both, as demonstrated in the Supplementary Table 3. After excluding variables due to collinearity, 18 candidate clinical predictors remained for model development. When examined as

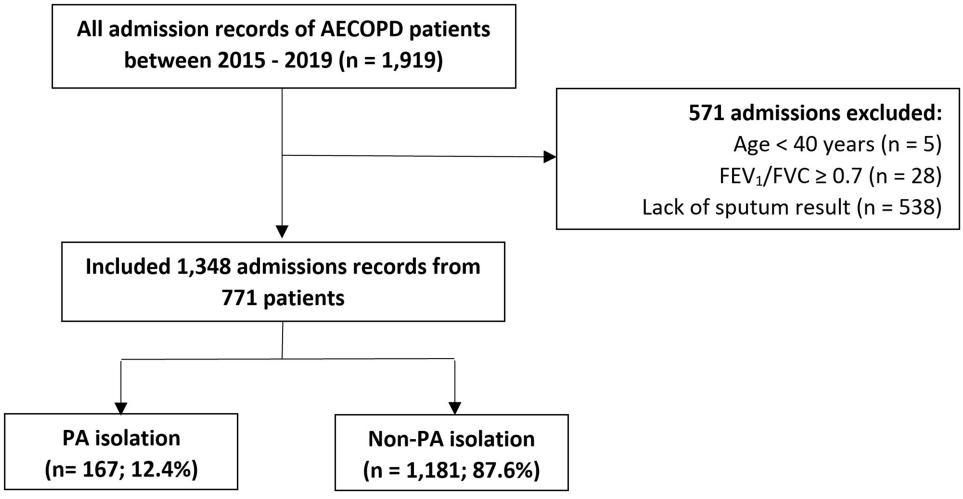

Figure 1 The study flow chart of hospitalized patients with acute exacerbation of COPD.

Table 1 Characteristics of *PA* Isolation and Non-*PA* Isolation Among Hospitalized Acute Exacerbation of COPD Patients (N= 1,348 Admissions)

Characteristics	Missing Data n (%)	*PA* Isolation n (%)	Non-*PA* Isolation n (%)	p-value
Total		167 (12.4)	1181 (87.6)	
Age, years, mean ± SD	0 (0)	75.1 ± 9.2	75.3 ± 11.1	0.800
Male	0 (0)	147 (88.0)	1023 (86.6)	0.710
BMI, kg/m^2, mean ± SD	570 (42.3)	20.1 ± 4.6	19.9 ± 4.1	0.740
Smoking status				0.440
Non-smoker	40 (3.0)	16 (9.6)	111 (9.4)	
Ex-smoker	40 (3.0)	129 (77.2)	856 (72.5)	
Active smoker	40 (3.0)	19 (11.4)	177 (15.0)	
No. of cigarettes smoked (pack-year), median [IQR]	379 (28.1)	30.0 [20.0, 40.0]	25.0 [15.0, 40.0]	0.160
Underlying diseases				
Diabetes mellitus	0 (0)	29 (17.4)	195 (16.5)	0.820
Left ventricular dysfunction	0 (0)	2 (1.2)	20 (1.7)	1.000
Chronic kidney disease	0 (0)	14 (8.4)	147 (12.4)	0.160
Cerebrovascular disease	0 (0)	19 (11.4)	121 (10.2)	0.680
Bronchiectasis	0 (0)	4 (2.4)	40 (3.4)	0.640
COPD severity				
Spirometry done	1,059 (78.6)	26 (15.6)	263 (22.3)	0.055
Post-bronchodilator				
FEV_1, % predicted, mean ± SD	1,059 (78.6)	41.3 ± 19.1	40.8 ± 17.0	0.880
FEV_1 < 35% of predicted value	1,059 (78.6)	14 (8.4)	118 (10.0)	0.410
FVC, % predicted, mean ± SD	1,059 (78.6)	69.2 ± 21.0	63.4 ± 18.3	0.130
FEV_1/FVC ratio, mean ± SD	1,059 (78.6)	0.45 ± 0.11	0.49 ±0.10	0.066
Hospitalization in the previous 1 year	0 (0)	73 (43.7)	449 (38.0)	0.170
ED visits in the previous 1 year	0 (0)	88 (52.7)	548 (46.4)	0.140
Prior *PA* isolation in 3 months	0 (0)	13 (7.8)	42 (3.6)	0.028
Home oxygen therapy	0 (0)	18 (10.8)	68 (5.8)	0.018
Home nebulization	0 (0)	23 (13.8)	69 (5.8)	<0.001

Abbreviations: PA, Pseudomonas aeruginosa; COPD, chronic obstructive pulmonary disease; SD, standard deviation; IQR, interquartile range; BMI, body mass index; FEV_1, forced expiratory volume-one second; FVC, forced vital capacity; ED, emergency department.

Table 2 Medical Treatment of COPD Prior to Admission (n=1,348 Admissions)

Medications	Missing Data n (%)	*PA* Isolation n (%)	Non-*PA* Isolation n (%)	p-value
Inhaled controller medications	0 (0)	126 (75.4)	834 (70.6)	0.240
Salmeterol/fluticasone	0 (0)	106 (63.5)	727 (61.6)	0.670
Formoterol/budesonide	0 (0)	8 (4.8)	34 (2.9)	0.230
Tiotropium	0 (0)	46 (27.5)	253 (21.4)	0.090
Budesonide	0 (0)	8 (4.8)	50 (4.2)	0.690
Antibiotics used during the previous 3 months	0 (0)	36 (21.6)	249 (21.1)	0.920
Antibiotics used during the previous 1 year	0 (0)			
Any	0 (0)	68 (40.7)	402 (34.0)	0.099
Ceftriaxone	0 (0)	37 (22.2)	253 (21.4)	0.840
Clarithromycin	0 (0)	38 (22.8)	232 (19.6)	0.350
Roxithromycin	0 (0)	3 (1.8)	16 (1.4)	0.720
Azithromycin	0 (0)	8 (4.8)	59 (5.0)	1.000
Amoxicillin/Clavulanic acid	0 (0)	22 (13.2)	94 (8.0)	0.037

(*Continued*)

Table 2 (Continued).

Medications	Missing Data n (%)	*PA* Isolation n (%)	Non-*PA* Isolation n (%)	p-value
Anti-pseudomonas antibiotics used during the previous 1 year	0 (0)	41 (24.6)	158 (13.4)	<0.001
Ceftazidime	0 (0)	8 (4.8)	38 (3.2)	0.260
Piperacillin/Tazobactam	0 (0)	31 (18.6)	105 (8.9)	<0.001
Levofloxacin	0 (0)	12 (7.2)	44 (3.7)	0.058
Meropenem	0 (0)	4 (2.4)	16 (1.4)	0.300
Imipenem/Cilastatin	0 (0)	2 (1.2)	10 (0.8)	0.650
Systemic steroids used during				
Previous 3 months	50 (3.7)	31 (18.6)	217 (18.4)	0.830
Previous 1 year	50 (3.7)	55 (32.9)	349 (29.6)	0.310

Abbreviations: PA, Pseudomonas aeruginosa; COPD, chronic obstructive pulmonary disease.

Table 3 Clinical Parameters During Admission of *PA* Isolation and Non-*PA* Isolation Among Acute Exacerbation of COPD Patients (n=1,348 Admissions)

Clinical Parameters	Missing Data n (%)	*PA* Isolation n (%)	Non-*PA* Isolation n (%)	p-value
Initial vital signs, mean ± SD				
Body temperature, °C	1 (0.1)	37.3 ± 0.8	37.3 ± 0.9	0.270
Heart rate, per minute	1 (0.1)	105.9 ± 22.9	107.5 ± 22.3	0.390
Systolic BP, mmHg	1 (0.1)	136.8 ± 29.9	136.7 ± 27.9	0.960
Diastolic BP, mmHg	1 (0.1)	81.7 ± 16.4	81.8 ± 16.0	0.960
Respiratory rate, per minute	1 (0.1)	29.5 ± 7.9	29.7 ± 8.2	0.770
Intubation with mechanical ventilation	0 (0)	139 (83.2)	1034 (87.6)	0.140
Radiographic consolidation	2 (0.2)	79 (47.3)	424 (35.9)	0.006
Laboratory investigations, mean ± SD				
pH	890 (66.0)	7.35 ± 0.13	7.37 ± 0.13	0.220
PaO_2, mmHg	924 (68.6)	196.1 ± 124.7	189.1 ± 107.2	0.670
$PaCO_2$, mmHg	890 (66.0)	47.3 ± 18.2	42.5 ± 17.2	0.054
Bicarbonate, mmol/l	6 (0.5)	26.2 ± 6.0	24.1 ± 5.2	<0.001
Blood urea nitrogen, mg/dl	15 (1.1)	21.2 ± 15.9	19.6 ± 13.4	0.160
Serum creatinine, mg/dl	4 (0.3)	1.07 ± 0.91	1.08 ± 0.57	0.800
Serum albumin, g/dl	547 (40.6)	3.62 ± 0.66	3.73 ± 0.59	0.095
Hemoglobin, g/dl	3 (0.2)	12.4 ± 1.9	12.5 ± 1.9	0.400
White blood cell count, /mm^3	3 (0.2)	15,791 ± 7,635	14,342 ± 6,488	0.008
Neutrophil count, /mm^3	3 (0.2)	13,969 ± 6,966	12,383 ± 6,191	0.002

Abbreviations: PA, Pseudomonas aeruginosa; COPD, chronic obstructive pulmonary disease; SD, standard deviation; BP, blood pressure.

a continuous variable, age exhibited a non-linear relationship with *PA* isolation as determined by fractional polynomial modelling. Consequently, we investigated a threshold of ≥ 60 years, which is frequently utilized to categorize elderly patients and was similarly employed in a previously published *PA* prediction score from Thailand.[25]

In univariable analysis, 7 of 18 pre-selected candidate clinical predictors were significantly associated with *PA* isolation (Table 4), including home oxygen therapy, prior isolation of *PA* within the previous 3 months, use of home nebulization, receipt of anti-*PA* antibiotics within the past year, radiographic consolidation, elevated serum bicarbonate levels, and increased white blood cell count.

Prediction Model Performance and Internal Validation

All 18 candidate predictors were included in the multivariable logistic regression model. Stepwise selection analysis identified 4 of the 18 evaluated variables as independent predictors of *PA* isolation, including a history of home nebulization

Table 4 Predictors Associated with *Pseudomonas Aeruginosa* Isolation Among Hospitalized AECOPD Patients by Univariable and Multivariable Logistic Regression Analyses

Predictors	Univariable Model*		Multivariable Model†	
	OR (95% CI)	p-value	OR (95% CI)	p-value
Age ≥ 60 years‡	1.66 (0.64, 4.32)	0.298	–	
Male	1.14 (0.69, 1.86)	0.617	–	
Smoking status				
Non-smoker	Reference			
Ex-smoker	1.05 (0.60, 1.82)	0.875	–	
Active smoker	0.74 (0.37, 1.51)	0.413	–	
Underlying disease				
Diabetes mellitus	1.06 (0.69, 1.63)	0.781	–	
Left ventricular dysfunction	0.70 (0.16, 3.04)	0.638	–	
Chronic kidney disease	0.64 (0.36, 1.14)	0.132	–	
Cerebrovascular disease	1.12 (0.67, 1.88)	0.654	–	
Bronchiectasis	0.70 (0.24, 2.02)	0.509	–	
Home oxygen therapy	1.97 (1.15, 3.40)	0.014		
Home nebulization	2.57 (1.43, 4.62)	0.002	2.35 (1.33, 4.13)	0.003
ED visit in the previous year	1.29 (0.93, 1.78)	0.128	–	
Prior *PA* isolation in 3 months	2.23 (1.10, 4.75)	0.016	–	
Anti-*PA* antibiotic used during the previous 1 year	2.11 (1.28, 3.47)	0.003	1.79 (1.09, 2.93)	0.021
Steroids used during the previous 1 year	1.21 (0.76, 1.92)	0.420	–	
Intubation with mechanical ventilation	0.71 (0.45, 1.10)	0.122	–	
Radiographic consolidation	1.60 (1.15, 2.23)	0.006	1.51 (1.07, 2.12)	0.019
Bicarbonate, every 1 mmol/l increase	1.07 (1.03, 1.10)	<0.001	1.07 (1.03, 1.10)	<0.001
WBC, every 1000/mm^3 increase	1.03 (1.01, 1.05)	0.023	–	

Notes: *Univariable logistic regression model with cluster-robust standard errors. †Multivariable logistic regression model with cluster-robust standard errors, using backward stepwise selection with a p-value threshold of < 0.05. ‡Age ≥ 60 years was used, reflecting a non-linear association with *PA* isolation and common clinical categorization of older adults.
Abbreviations: OR, odds ratio; CI, confidence interval; ED, emergency department; *PA*, Pseudomonas aeruginosa; WBC, white blood cell count.

(OR 2.35), use of anti-*PA* antibiotics in the preceding 1 year (OR 1.79), radiographic consolidation on admission (OR 1.51) and elevated serum bicarbonate level (per mmol/L) (OR 1.07). The OR with 95% CI of the final model were presented in Table 4, and logit regression coefficients (β) and p-values were presented in the Supplementary Table 4.

The discriminative performance of the multivariable model was evaluated using the AuROC. This model had 4 predictors and achieved an AuROC of 0.67 (95% CI, 0.62–0.70). Internal validation using bootstrap resampling with 1,000 iterations demonstrated by the AuROC and slope from the test set were 0.66 (optimism 0.01) and 0.93 (optimism 0.07), respectively.

Prediction Score Assignment

The score assignment was based on the magnitude of the regression coefficients from the final logistic regression model. Serum bicarbonate was categorized using clinically relevant thresholds (≤ 24, 25–29, and ≥ 30 mmol/L) to simplify score

development. These cut-offs are supported by respiratory physiology, as elevated bicarbonate reflects renal compensation for chronic respiratory acidosis in patients with COPD.[26] Prior studies have demonstrated that bicarbonate levels around or above 30 mmol/L serve as a pragmatic surrogate marker of chronic hypercapnia when arterial blood gas measurements are unavailable.[27]

The assigned points were as follows: 2 points for a history of home nebulization and serum bicarbonate level of more than 30 mmol/L; 1 point for anti-*PA* antibiotics use within the previous year, the presence of radiographic consolidation and serum bicarbonate level between 25 and 29 mmol/L (Supplementary Table 4).

The prediction score demonstrated an AuROC of 0.66 (95% CI, 0.62–0.70) for *PA* isolation, which was similar to that of the final prediction model (Figure 2). It demonstrated strong concordance with the observed risk, as the anticipated risk closely correlated with the observed risk. The probability of isolating *PA* increased with higher clinical risk scores: scores of 0–1 indicated low risk (< 12.4%, less than the prevalence), scores of 2–3 indicated intermediate risk, while scores of 4–6 represented high risk (> 30%). The calibration of the prediction score was evaluated by comparing predicted probabilities of *PA* isolation with the observed outcomes through probability plots and calibration plots (Supplementary Figure 1 and 2, respectively). The Hosmer–Lemeshow goodness-of-fit test revealed no significant difference between predicted and observed outcomes (P = 0.802), indicating that the score was well-calibrated and appropriate for predictive application.

Clinical Decision of Predictive Score

For the clinical applicability of the prediction score, the predicted probabilities, sensitivity and specificity were presented in Table 5. The clinical decisions for anti-*PA* coverage were categorized into three groups. Scores 0–1 (predicted probability < 15%): Anti-*PA* coverage is not recommended due to high sensitivity and low specificity. Scores 2–3 (predicted probability 16–23%): Conditional recommendation, particularly in pneumonia or suspected sepsis cases. Scores 4–6 (predicted probability ≥ 32%): Empirical anti-PA coverage is recommended due to high specificity despite low sensitivity. Furthermore, the decision curve analysis was conducted to assess the clinical utility of the prediction score. The finding suggests that, within a predicted probability of 5 to 20%, using the prediction score to inform decisions regarding the initiation of antipseudomonal coverage yields a significant therapeutic advantage. (Supplementary Figure 3).

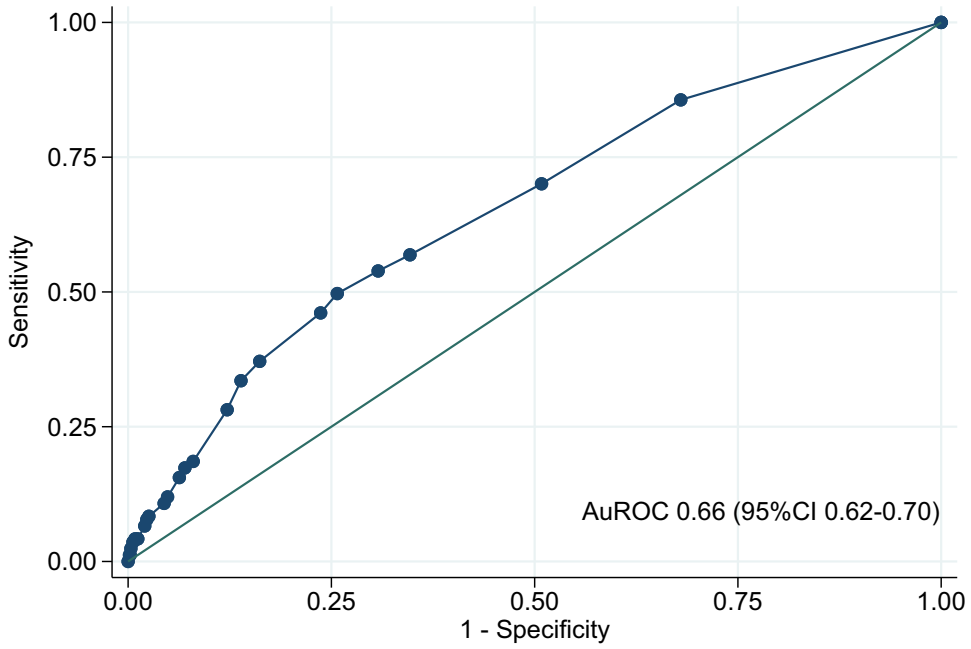

Figure 2 Receiver Operating Characteristic (ROC) curve of prediction score for Pseudomonas aeruginosa isolation.

Table 5 The Clinical Decision for Anti-Pseudomonal Coverage

Prediction Score	Predicted Probability	*PA* isolation	Non-*PA* isolatIon	Sensitivity (%)	Specificity (%)	Decision for Anti-*PA* Coverage
0	7%	24	376	100	1.0	Not recommended
1	10%	53	437	85.6	32.0	
2	16%	43	218	53.9	69.3	Conditional recommended in pneumonia or sepsis
3	23%	33	113	28.1	87.8	
4	32%	8	23	8.4	97.4	Recommended
5	42%	4	5	3.6	99.4	
6	54%	2	2	1.2	99.8	

Note: Prevalence of PA isolation (Pre-test probability): 12.4%.
Abbreviation: PA, Pseudomonas aeruginosa.

Discussion

In this study, we developed a prediction score based on four independent predictors—home nebulizer use, prior receipt of anti-*PA* antibiotics, radiographic consolidation and elevated serum bicarbonate—to estimate the risk of *PA* isolation in hospitalized AECOPD patients. The score is designed to help clinicians guide empirical therapy, particularly by reducing unnecessary anti-*PA* coverage in patients at low risk of complications. Notably, the prevalence of *PA* in our cohort, which included both ICU and non-ICU admissions, was approximately 12%, consistent with previous studies reporting rates of 6–16%.[8,16] This finding suggests that while *PA* is not uncommon, it does not justify routine broad-spectrum coverage.

Previous exposure to antibiotics—including fluoroquinolones and β-lactams (such as cephalosporins and carbapenems)—has been consistently recognized as an important risk factor for *PA* isolation.[28,29] In our cohort, both anti-pseudomonal agents (eg, piperacillin/tazobactam) and non-anti-pseudomonal regimens (eg, amoxicillin/clavulanic acid) were more frequently prescribed among patients with *PA* isolation. However, to address multicollinearity among antibiotic classes, only prior receipt of anti-*PA* agents was retained in the final prediction model.

High serum bicarbonate may serve as a surrogate marker of COPD severity, as chronic hypercapnia leads to renal bicarbonate retention in advanced disease states,[26] and is associated with worse COPD outcomes, independent of spirometry.[27] In our cohort, spirometry and arterial blood gas data were largely unavailable, making bicarbonate a pragmatic alternative.

An independent association was observed between home nebulizer use and *PA* isolation. Patients with chronic respiratory diseases, particularly those with severe COPD, frequently use home nebulizers. Harris et al[30] demonstrated that the pathogenic bacteria—including *PA, Staphylococcus aureus or Stenotrophomonas maltophilia*—on the contaminated reusable home nebulizer surface pose a risk of bacterial inhalation. Furthermore, the use of improperly dried nebulizers contaminated with *PA* has been linked to respiratory infections in patients with cystic fibrosis.[31] In contrast to Gram-positive bacteria and fungi, cleaning the nebulizer set only partially eliminated Gram-negative organisms, likely due to biofilm formation.[32] Additionally, COPD patients with pathogenic bacteria present on their nebulizer equipment—which may serve as potential reservoirs—were more likely to experience exacerbations.[32]

The radiographic consolidation may reflect either pneumonia or infection of pre-existing bronchiectasis. Therefore, the presence of consolidation on chest radiography, when combined with a higher prediction score, may indicate *PA* as the likely pathogen. This finding could warrant initiation of empirical anti-*PA* therapy.

However, broad anti-*PA* coverage should be reserved for high-risk patients, as indiscriminate use has not been shown to improve outcomes such as hospital length of stay[33] or mortality[34] compared with guideline-directed therapy targeting common pathogens such as *Streptococcus pneumoniae* and *Haemophilus influenzae*. Aarts et al[35] reported increased mortality associated with prolonged empirical antibiotic use among ICU patients without confirmed infection. Similarly,

Planquette et al[22] found no benefit from increased anti-*PA* prescriptions following the implementation of healthcare-associated pneumonia guidelines, possibly reflecting low prevalence of *PA* at admission (7%).

Distinguishing colonization from true infection in AECOPD patients remains a major diagnostic challenge, often resulting in overcautious prescribing and unnecessary use of broad-spectrum antibiotics. Although approximately half of COPD exacerbations are thought to be bacterial in origin,[36] and several studies have linked *PA* to higher mortality in hospitalized AECOPD patients.[13,36,37] Furthermore, colonization or sputum cultures positive for *PA* have also been associated with an increased risk of acute exacerbations and the need for mechanical ventilation in some studies.[13,15,20] However, these cultures have not consistently predicted worse long-term outcomes in stable COPD outpatients,[38] and the treatment response and clinical role of *PA* remain unclear.[8,14,39]

Recent research has identified three distinct patterns of *PA* behavior in COPD patients: 1) transient carriage with spontaneous clearance, 2) acquisition of a new strain associated with an acute exacerbation, and 3) chronic colonization with uncertain clinical implications.[40] Recognizing this heterogeneity underscores why clinical decisions cannot rely solely on culture results. Our prediction score addresses this gap by integrating clinical, radiographic, and laboratory variables to stratify risk, enabling clinicians to avoid unnecessary anti-*PA* therapy in low-risk patients while ensuring timely coverage for those most likely to have true infection.

To our knowledge, no prediction model has been developed specifically to identify *PA* isolation in COPD. A recent score designed for elderly patients with community-acquired pneumonia —including 30% with COPD—demonstrated good discrimination (AuROC 0.77) but reported an unusually high *PA* prevalence of 44%.[25] These findings highlight the challenge of developing broadly applicable tools, as *PA* prevalence varies widely across populations, and no existing score has yet demonstrated an impact on patient outcomes or antibiotic stewardship.

This study has notable strengths. It is among the few to develop and internally validate a clinical prediction score specifically for *PA* isolation in hospitalized AECOPD patients, using a large, real-world cohort that includes both ICU and non-ICU admissions. The model incorporates readily available clinical, radiographic, and laboratory variables, enhancing its potential applicability in routine practice.

However, several limitations should also be acknowledged. First, the single-center, retrospective design may limit its generalizability to settings with different patient populations, microbiological profiles, or antibiotic prescribing practices. Second, the lack of standardized spirometry and incomplete pulmonary function data restricted the inclusion of lung function parameters, which might have improved model performance and likely contributed to the fair AuROC rather than a higher value. Nevertheless, in high-COPD-burden and limited-resource settings, where spirometry is often unavailable, this limitation may reflect real-world practice. Third, reliance on culture results made it impossible to distinguish colonization from true infection, raising the possibility of misclassification bias. Fourth, the small number of patients in the highest-risk category—especially those with *PA* isolation—may constrain the predictive reliability within this subgroup, while the large percentage of intubated patients in this cohort could limit the generalizability of the identified predictive factors to non-intubated patients. Finally, although internal validation was performed, external validation in independent cohorts is necessary before the score can be recommended for widespread clinical use.

Conclusion

This simplified prediction score, incorporating readily available clinical, radiographic, and laboratory parameters, estimates the probability of *PA i*solation in hospitalized AECOPD patients. It may facilitate more judicious empirical antibiotic selection, promoting antimicrobial stewardship by reducing unnecessary anti-*PA* coverage while ensuring timely therapy in high-risk patients.

AI Declaration

AI (ChatGPT, OpenAI) was used to assist with English grammar correction, formatting, and improving readability.

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Disclosure

The authors report no conflicts of interest in this work.

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