DOI: 10.4274/forbes.galenos.2026.92609
Forbes J Med 2026;7:90-7

Original Article

Early Predictors of Non-Invasive Ventilation Failure in COPD Patients with Acute Hypercapnic Respiratory Failure: A Multicenter Retrospective Study

Damla SERÇE UNAT[1], Nilay ERTEN TURAN[1], Ömer Selim UNAT[2], Mutlu Onur GÜÇSAV[1], Emine Sena DİKMENTEPE[3], Hakan KAHRAMAN[2], Aydan MERTOĞLU[2]

[1]İzmir Bakırçay University Faculty of Medicine, Department of Pulmonology, İzmir, Türkiye
[2]University of Health Sciences Türkiye, İzmir Dr. Suat Seren Chest Diseases and Surgery Training and Research Hospital, Clinic of Translational Pulmonology, İzmir, Türkiye
[3]Siirt Training and Research Hospital, Clinic of Pulmonology, Siirt, Türkiye

Cite as: Serçe Unat D, Erten Turan N, Unat ÖS, et al. Early predictors of non-invasive ventilation failure in COPD patients with acute hypercapnic respiratory failure: a multicenter retrospective study. Forbes J Med. 2026;7:90-7

ABSTRACT

Objective: Early identification of non-invasive ventilation (NIV) failure in patients with acute hypercapnic respiratory failure due to chronic obstructive pulmonary disease (COPD) exacerbation remains a critical clinical challenge, particularly in emergency departments. This study aimed to evaluate whether early arterial blood gas changes after NIV initiation predict intensive care unit (ICU) admission and in-hospital intubation and to develop a simple predictive model based on early physiological response.

Methods: This multicenter retrospective study included 319 patients with COPD exacerbation complicated by acute hypercapnic respiratory failure who were initiated on NIV in the emergency departments of three hospitals. Arterial blood gas parameters were recorded before NIV initiation and 1-3 hours thereafter. Early response was defined as the change in $PaCO_2$ ($\Delta PaCO_2$). Multivariable logistic regression models were constructed for ICU admission and intubation. Model discrimination was assessed using receiver operating characteristic curve analysis.

Results: During hospitalization, 138 patients (43.3%) required ICU admission, and 70 patients (21.9%) required intubation. Lower post-NIV pH, insufficient reduction in $\Delta PaCO_2$, and prior ICU admission independently predicted the need for ICU care and intubation. The model demonstrated good discriminative performance for ICU admission [area under the curve (AUC) =0.787; 95% confidence interval (CI): 0.737-0.837] and for intubation (AUC =0.810; 95% CI: 0.746-0.873).

Conclusion: Early physiological response to NIV, particularly post-treatment pH and the magnitude of PaCO2 reduction, provides clinically meaningful prognostic information and may assist early decision-making in emergency settings. External validation is warranted.

Keywords: Pulmonary disease, chronic obstructive lung disease, respiratory insufficiency, noninvasive ventilation, intubation, intensive care units

Received: 16.05.2026
Accepted: 03.08.2026
Epub: 05.08.2026
Publication Date: 20.08.2026

Corresponding Author:
Damla SERÇE UNAT
İzmir Bakırçay University Faculty of Medicine, Department of Pulmonology, İzmir, Türkiye
sercedamla@gmail.com
ORCID ID: 0000-0003-4743-5469

INTRODUCTION

Chronic obstructive pulmonary disease (COPD) is a progressive disorder characterized by persistent airflow limitation and represents a major public health problem associated with substantial morbidity and mortality. According to the World Health Organization, COPD is the third leading cause of death worldwide, accounting for more than 3 million deaths annually.[1] Global Burden of Disease analyses indicate that the disease burden continues to rise, particularly in low- and middle-income countries.[2] In Türkiye, the BOLD study reported a spirometry-confirmed COPD prevalence of approximately 19% among adults aged over 40 years.[3] Acute exacerbations of COPD are associated with increased hospitalizations and mortality, and each exacerbation contributes to disease progression and clinical deterioration.[4]

Severe exacerbations may lead to acute hypercapnic respiratory failure as a consequence of alveolar

hypoventilation and respiratory muscle fatigue, significantly increasing the risk of mortality.[5,6] In this setting, non-invasive mechanical ventilation (NIV) is recommended as the first-line ventilatory support modality due to its ability to improve gas exchange, reduce the work of breathing, and decrease the need for endotracheal intubation.[7-9] However, NIV failure has been reported in approximately 15-30% of cases, and delayed recognition of treatment failure may further increase mortality.[10,11] This creates a critical clinical decision-making challenge, particularly in emergency departments, where timely intubation decisions are essential.

Among patients initiated on NIV in the emergency department, early clinical and arterial blood gas responses play a decisive role in determining whether to continue NIV or to escalate to invasive mechanical ventilation. Previous studies have demonstrated that persistent acidosis and insufficient reduction in $PaCO_2$ during the first hours of NIV are associated with treatment failure.[12,13] Nevertheless, most available data are derived from intensive care unit (ICU) populations, and evidence focusing specifically on the early response to NIV initiated in the emergency department remains limited.

The present study aimed to evaluate the association between early clinical and arterial blood gas parameters and clinical outcomes in patients with acute hypercapnic respiratory failure due to COPD exacerbation who were started on NIV in the emergency department and to identify variables that may predict the need for intubation.

METHODS

Study Design and Setting

This multicenter retrospective observational study was conducted across three hospitals in Türkiye: a secondary-level state hospital, this multicenter retrospective observational study was conducted across three hospitals in Türkiye: Giresun Dr. Ali Menekşe Chest Diseases Hospital, a secondary care hospital; İzmir Bakırçay University, a tertiary multidisciplinary training and research hospital; and University of Health Sciences Türkiye, İzmir Dr. Suat Seren Chest Diseases and Surgery Training and Research Hospital, a tertiary hospital specialized in chest diseases. Patients presenting to the emergency departments with acute hypercapnic respiratory failure due to COPD exacerbation and who were initiated on NIV were included. Differences in data collection periods across centers were due to institutional transitions involving members of the research team. The study was reported in accordance with the STROBE statement for observational studies.

Ethics Statement

This study was approved by the Clinical Research Ethics Committee of İzmir Bakırçay University Faculty of Medicine (approval no: 2702, date: 04.03.2026). The study was conducted in accordance with the principles of the Declaration of Helsinki. Institutional permissions were obtained from all three participating centers, and administrative approval for data use was granted by the respective hospital authorities. Due to the retrospective design and use of anonymized data, the requirement for informed consent was waived by the Ethics Committee.

Patient Selection

All patients presenting to the emergency department with a diagnosis of COPD exacerbation complicated by acute hypercapnic respiratory failure and who were initiated on NIV were screened for eligibility. COPD exacerbation was defined clinically as worsening dyspnea and/or changes in sputum volume or purulence requiring acute medical treatment. Acute hypercapnic respiratory failure was diagnosed based on baseline arterial blood gas analysis demonstrating hypercapnia accompanied by respiratory acidosis.

Patients were included if NIV was initiated in the emergency department, a baseline arterial blood gas measurement was obtained prior to NIV initiation, and a follow-up arterial blood gas measurement was available within 1-3 hours after NIV initiation. Patients were excluded if only venous blood gas analysis was available, if the follow-up arterial blood gas measurement was missing, if cardiac arrest occurred within the first 2 hours after NIV initiation, or if endotracheal intubation was required within the first 2 hours after NIV initiation.

When multiple arterial blood gas measurements were available within the 1-3-hour window, the measurement closest to 2 hours after NIV initiation was selected for analysis to ensure consistency in the assessment of early response.

NIV Application and Monitoring

NIV was delivered via a face mask using bilevel positive airway pressure (BPAP). Initial ventilator settings were determined by the treating physician based on clinical status and patient tolerance. Patients were closely monitored for respiratory effort, oxygenation, mental status, and hemodynamic stability. Intubation decisions were made according to standard clinical criteria, including deterioration in level of consciousness, hemodynamic instability, refractory hypercapnia/hypoxemia, or NIV intolerance.

Data Collection and Variables

Data collection focused on demographic and clinical characteristics, including comorbidities, history of ICU admission and intubation, use of home oxygen and BPAP, and hospitalization within the previous year. Laboratory variables included hemoglobin, white blood cell count, and C-reactive protein (CRP). Arterial blood gas measurements (pH, $PaCO_2$, PaO_2, and HCO_3-) were obtained at baseline (before NIV initiation) and repeated 1-3 hours after NIV initiation. Early physiological response to NIV was quantified as the change in $PaCO_2$ over this interval and calculated as $\Delta PaCO_2$ = $PaCO_2$ (post-NIV)-$PaCO_2$ (baseline).

Two primary outcomes were prespecified: (i) requirement for ICU admission at any time during the index hospitalization; and (ii) requirement for endotracheal intubation during the index hospitalization. For the purposes of this study, NIV failure was defined as the need for endotracheal intubation and transition to invasive mechanical ventilation during the index hospitalization.

Statistical Analysis

Continuous variables were assessed for normality and expressed as mean ± standard deviation or median (interquartile range). Group comparisons were performed using Student's t-test, Mann-Whitney U test, and chi-square test, as appropriate. Variables that were significant in univariate analysis (p<0.10) or that were clinically relevant were entered into multivariable logistic regression models. Separate models were constructed for ICU admission and intubation.

Model Development and Probability Estimation

Multivariable logistic regression coefficients were used to estimate each patient's predicted probability of the outcome. The optimal probability threshold was identified from the receiver operating characteristic (ROC) curve using the Youden index, and a spreadsheet-based calculator was prepared to facilitate bedside application.

Model Performance

Discrimination was evaluated using ROC curve analysis and the area under the curve (AUC) with a 95% confidence interval (CI). At the optimal probability threshold identified by ROC analysis, the sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) of each model were calculated. A p value <0.05 was considered statistically significant.

RESULTS

Study Population

A total of 319 patients were included from three centers: Giresun Dr. Ali Menekşe Chest Diseases Hospital (n=110), a secondary care hospital; İzmir Bakırçay University (n=109), a tertiary multidisciplinary training and research hospital; and University of Health Sciences Türkiye, İzmir Dr. Suat Seren Chest Diseases and Surgery Training and Research Hospital (n=100), a tertiary hospital specialized in chest diseases. During hospitalization, 138 patients (43.3%) required ICU admission, and 70 patients (21.9%) required endotracheal intubation.

Findings According to ICU Requirement

Patients requiring ICU admission were significantly older than those managed without ICU care (71.9±12.0 vs. 69.1±10.8 years; p=0.032). Baseline arterial blood gas analysis demonstrated lower pH levels in the ICU group (7.29±0.07 vs. 7.31±0.06; p=0.001), and post-NIV pH remained significantly lower in these patients (7.32±0.10 vs. 7.36±0.05; p<0.001).

The median baseline $PaCO_2$ level was higher in patients requiring ICU admission [69.5 mmHg (59.4-82.0) vs. 65.0 mmHg (55.1-71.2); p=0.001]. Similarly, post-NIV $PaCO_2$ values were significantly higher in the ICU group [65.5 mmHg (56.2-78.9) vs. 57.9 mmHg (49.4-64.4); p<0.001]. The early physiological response reflected by $\Delta PaCO_2$ was significantly smaller among patients who required ICU care (-3.51±16.88 mmHg vs. -8.30±10.39 mmHg; p=0.002).

CRP levels were markedly higher in the ICU group [47.5 mg/L (19.4-97.6) vs. 26.5 mg/L (8.1-67.9); p=0.003]. The length of hospital stay was also significantly longer in these patients [12.5 days (8-20) vs. 8 days (5-12); p<0.001]. Prior ICU admission (63.8% vs. 23.3%), previous intubation (26.1% vs. 3.3%), and hospitalization within the previous year (97.1% vs. 82.2%) were strongly associated with ICU requirement (all p<0.001) (Table 1).

In multivariable logistic regression analysis, lower post-NIV pH, insufficient reduction in $\Delta PaCO_2$, and prior ICU admission remained independent predictors of ICU requirement. The model demonstrated good discriminative ability (AUC =0.787; 95% CI: 0.737-0.837; p<0.001). The ROC curve is presented in Figure 1 .At the optimal predicted probability cut-off value of 0.430, the model predicted ICU requirement with a sensitivity of 67.4%, specificity of 76.7%, PPV of 68.9%, and NPV of 75.4%.

Findings According to Intubation Requirement

Patients who required intubation had significantly lower hemoglobin levels compared with those who did not [12.5 g/dL (11.2-14.5) vs. 13.3 g/dL (11.8-15.1); p=0.016]. CRP levels were significantly higher in the intubation group [55.0 mg/L (23.4-86.7) vs. 27.4 mg/L (8.1-68.1); p<0.001].

Baseline pH was significantly lower in patients who required intubation [7.28 (7.24-7.33) vs. 7.31 (7.27-7.35); p<0.001]; the

pH difference was more pronounced after NIV initiation [7.28 (7.22-7.34) vs. 7.37 (7.32-7.40); p<0.001]. Baseline $PaCO_2$ levels were higher in the intubation group [69.8 mmHg (60.1-90.5) vs. 65.7 mmHg (56.4-72.8); p=0.022], and post-NIV $PaCO_2$ remained markedly elevated [72.8 mmHg (60.1-95.4) vs. 58.9 mmHg (50.2-65.7); p<0.001]. The reduction in $PaCO_2$ ($\Delta PaCO_2$) was significantly smaller among patients who required intubation [-0.8 mmHg (-11.2 to 13.4) vs. -7.4 mmHg (-14.1 to -3.5); p<0.001].

Length of hospital stay was significantly longer in intubated patients [15.5 days (9-23) vs. 9 days (5-13); p<0.001]. Prior ICU admission (74.3% vs. 31.7%), previous intubation (40.0% vs. 6.0%), home oxygen use (80.0% vs. 66.7%), and hospitalization within the previous year (98.6% vs. 85.9%) were significantly associated with the requirement for intubation (p<0.05) (Table 2).

In multivariable analysis, lower post-NIV pH, insufficient reduction in $\Delta PaCO_2$, and prior ICU admission remained independent predictors of intubation. The model demonstrated good discriminative performance (AUC =0.810; 95% CI: 0.746-0.873; p<0.001), and the ROC curve is shown in Figure 2. At the optimal predicted probability cut-off value of 0.303, the model predicted the need for intubation with a sensitivity of 64.3%, specificity of 86.3%, PPV of 57.0%, and NPV of 89.6%.

Table 1. Comparison of clinical, laboratory and arterial blood gas variables according to ICU requirement

Parameters	No ICU (n=181)	ICU (n=138)	p value
Age, years	69.1±10.8	71.9±12.0	**0.032**
pH (baseline)	7.31±0.06	7.29±0.07	**0.001**
pH (post-NIV)	7.36±0.05	7.32±0.10	**<0.001**
HCO_3- (baseline), mmol/L	30.47±4.96	30.85±5.93	0.535
HCO_3- (post-NIV), mmol/L	30.86±4.76	32.74±10.85	**0.039**
PaO_2 (baseline), mmHg	63.5 (52.4-74.8)	63.5 (54.1-72.6)	0.576
$PaCO_2$ (baseline), mmHg	65.0 (55.1-71.2)	69.5 (59.4-82.0)	**0.001**
PaO_2 (post-NIV), mmHg	66.8 (55.3-80.6)	67.8 (54.9-84.1)	0.531
$PaCO_2$ (post-NIV), mmHg	57.9 (49.4-64.4)	65.5 (56.2-78.9)	**<0.001**
$\Delta PaCO_2$ (post-baseline), mmHg	-8.30±10.39	-3.51±16.88	**0.002**
Hemoglobin, g/dL	13.4 (11.9-14.9)	12.8 (11.1-14.4)	0.100
Leukocyte count, /mm^3	11.150 (7.800-13 760)	11.205 (7.200-14 800)	0.293
CRP, mg/L	26.5 (8.1-67.9)	47.5 (19.4-97.6)	**0.003**
Length of hospital stay, days	8 (5-12)	12.5 (8-20)	**<0.001**
Female sex, n (%)	56 (31.1)	41 (29.7)	0.788
Smoking status, n (%)			
Non-smoker	29 (16.1)	21 (15.2)	0.113
Ex-smoker	75 (41.7)	73 (52.9)	
Current smoker	76 (42.2)	44 (31.9)	
Hypertension, n (%)	103 (57.2)	91 (65.9)	0.114
Diabetes mellitus, n (%)	40 (22.2)	37 (26.8)	0.320
History of cerebrovascular disease, n (%)	5 (2.8)	7 (5.1)	0.287
Cardiovascular disease, n (%)	63 (35.0)	46 (33.3)	0.756
Previous ICU admission, n (%)	42 (23.3)	88 (63.8)	**<0.001**
History of intubation, n (%)	6 (3.3)	36 (26.1)	**<0.001**
Home oxygen therapy, n (%)	118 (65.6)	103 (74.6)	0.081
Home BPAP use, n (%)	72 (40.0)	45 (32.6)	0.176
Hospitalization within previous year, n (%)	148 (82.2)	134 (97.1)	**<0.001**

Data are expressed as mean ± standard deviation or median (25^{th}-75^{th} interquartile range) for continuous variables, and as number (percentage) for categorical variables. p values were calculated using appropriate parametric or non-parametric tests based on data distribution. Statistically significant p values are shown in bold. BPAP: Bilevel positive airway pressure, CRP: C-reactive protein, HCO_3-: Bicarbonate, ICU: Intensive care unit, NIV: Non-invasive ventilation, $PaCO_2$: Arterial partial pressure of carbon dioxide, PaO_2: Arterial partial pressure of oxygen, $\Delta PaCO_2$: Change in arterial carbon dioxide level calculated as post-NIV, $PaCO_2$ minus baseline $PaCO_2$

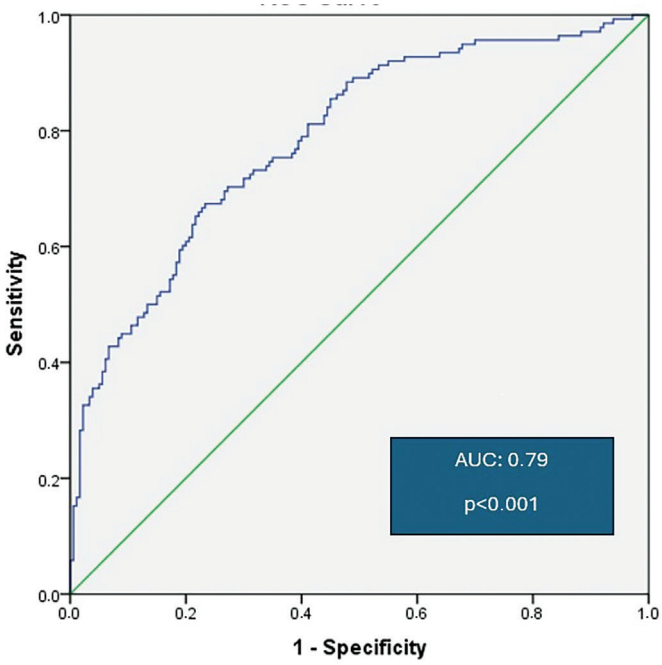

Figure 1. Receiver operating characteristic curve of the regression-based model predicting intensive care unit admission in patients with acute hypercapnic respiratory failure due to chronic obstructive pulmonary disease exacerbation treated with non-invasive ventilation in the emergency department. The model demonstrated good discriminative performance with an AUC of 0.787 (95% confidence interval: 0.737-0.837; p<0.001)

AUC: Area under the curve

DISCUSSION

In this multicenter cohort of patients with acute hypercapnic respiratory failure due to COPD exacerbation who were treated with NIV in the emergency department, early post-treatment physiological response emerged as the strongest determinant of clinical trajectory. Lower post-NIV pH, insufficient reduction in $PaCO_2$ within the first 1-3 hours, and a history of prior ICU admission independently predicted both ICU requirement and in-hospital intubation. The discriminative performance of the derived models was clinically meaningful, with AUC values of 0.787 for ICU admission and 0.810 for intubation. These findings suggest that early dynamic changes following NIV initiation provide prognostic information beyond baseline severity markers.

Several prognostic tools have been developed to predict mortality in acute exacerbations of COPD. The NIVO score estimates in-hospital mortality in patients requiring assisted ventilation, using admission variables such as age and acidosis.[14] Similarly, the DECAF score predicts hospital mortality based on clinical and laboratory parameters at presentation.[15] While these tools offer valuable risk stratification for mortality, they are primarily static and not specifically designed to predict NIV failure or early need for escalation. Our model differs by incorporating early treatment response variables, particularly post-NIV pH and $\Delta PaCO_2$, thus reflecting the physiological evolution under ventilatory support rather than admission status alone.

Beyond mortality-focused scores, efforts have been made to predict NIV failure directly. Duan et al.[16] developed and validated a simple early risk score for NIV failure in COPD patients, and van Gemert et al.[17] identified factors associated with intubation following NIV failure in the emergency department. Although these studies highlight the importance of early identification of high-risk patients, most models rely heavily on baseline characteristics. In contrast, our findings demonstrate that the magnitude of $PaCO_2$ reduction during the initial hours of therapy independently predicts deterioration, reinforcing the concept that response to treatment is as important as initial severity.

The efficacy of NIV in acute hypercapnic COPD has been well established since the landmark randomized trial by Brochard et al.,[18] which demonstrated reduced intubation rates and mortality. The benefits of early NIV initiation were further confirmed by Plant et al.,[19] even in non-ICU ward settings. More recent real-world data from large national cohorts have shown that, despite widespread NIV adoption, outcomes remain heterogeneous, and failure continues to occur in a significant proportion of patients.[20] Our study builds upon this foundation by addressing a clinically relevant but underexplored question: how to identify patients early who are unlikely to benefit from continued NIV. These observations are consistent with current guideline recommendations: the ERS/ATS clinical practice guidelines endorse NIV as the first-line ventilatory strategy in acute hypercapnic respiratory failure due to COPD exacerbation while emphasising close monitoring for early signs of treatment failure,[7] and the 2025 Global Initiative for Chronic Obstructive Lung Disease (GOLD) report similarly recommends NIV as the preferred initial modality and highlights the importance of timely recognition of non-response to avoid delayed intubation.[21] Our findings help to operationalise these recommendations by providing objective early physiological indicators (post-NIV pH and $\Delta PaCO_2$ reduction) that may support such monitoring.

Data from ICU populations demonstrate considerable morbidity and mortality among hypercapnic COPD patients.[22] However, most of these analyses evaluate outcomes after ICU admission rather than evaluating predictors available at presentation to the emergency department. In addition, systematic reviews confirm

Table 2. Comparison of clinical, demographic and laboratory characteristics according to intubation requirement			
Parameters	**No intubation (n=249)**	**Intubation (n=70)**	**p value**
Age, years	70.0±11.1	71.3±12.6	0.403
Hemoglobin, g/dL	13.3 (11.8-15.1)	12.5 (11.2-14.5)	**0.016**
Leukocyte count, /mm^3	10.960 (7.800-13 650)	12 440 (9 100-15 677)	0.067
CRP, mg/L	27.4 (8.1-68.1)	55.0 (23.4-86.7)	**<0.001**
pH (baseline)	7.31 (7.27-7.35)	7.28 (7.24-7.33)	**<0.001**
pH (post-NIV)	7.37 (7.32-7.40)	7.28 (7.22-7.34)	**<0.001**
PaO_2 (baseline), mmHg	62.9 (52.9-72.9)	67.5 (55.0-78.0)	0.090
PaO_2 (post-NIV), mmHg	66.4 (53.9-79.1)	71.25 (55.5-88.9)	**0.039**
HCO_3- (baseline), mmol/L	30.72±4.99	30.33±6.65	0.592
HCO_3- (post-NIV), mmol/L	31.39±6.09	32.64±12.73	0.250
$PaCO_2$ (baseline), mmHg	65.7 (56.4-72.8)	69.8 (60.1-90.5)	**0.022**
$PaCO_2$ (post-NIV), mmHg	58.9 (50.2-65.7)	72.8 (60.1-95.4)	**<0.001**
Δ$PaCO_2$ (post-baseline), mmHg	-7.4 (-14.1 to -3.5)	-0.8 (-11.2 to 13.4)	**<0.001**
Length of hospital stay, days	9 (5-13)	15.5 (9-23)	**<0.001**
Male sex, n (%)	169 (67.9)	53 (75.7)	0.210
Smoking status, n (%)			
Non-smoker	41 (16.5)	9 (12.9)	**0.015**
Ex-smoker	105 (42.2)	43 (61.4)	
Current smoker	103 (41.4)	18 (25.7)	
Hypertension, n (%)	148 (59.4)	47 (67.1)	0.241
Diabetes mellitus, n (%)	57 (22.9)	20 (28.6)	0.557
Cardiovascular disease, n (%)	83 (33.3)	26 (37.1)	0.553
History of cerebrovascular disease, n (%)	8 (3.2)	4 (5.7)	0.336
Previous ICU admission, n (%)	79 (31.7)	52 (74.3)	**<0.001**
History of intubation, n (%)	15 (6.0)	28 (40.0)	**<0.001**
Home oxygen therapy, n (%)	166 (66.7)	56 (80.0)	**0.032**
Home BPAP use, n (%)	90 (36.1)	28 (40.0)	0.562
Hospitalization within previous year, n (%)	214 (85.9)	69 (98.6)	**0.003**

Data are expressed as mean ± standard deviation or median (25th-75th interquartile range) for continuous variables, and as number (percentage) for categorical variables. p values were calculated using appropriate parametric or non-parametric tests based on data distribution. Statistically significant p values are shown in bold. BPAP: Bilevel positive airway pressure, CRP: C-reactive protein, HCO_3-: Bicarbonate, ICU: Intensive care unit, NIV: Non-invasive ventilation, $PaCO_2$: Arterial partial pressure of carbon dioxide, PaO_2: Arterial partial pressure of oxygen, Δ$PaCO_2$: Change in arterial carbon dioxide level calculated as post-NIV, $PaCO_2$ minus baseline $PaCO_2$

that although NIV reduces mortality and intubation rates overall, failure rates remain clinically significant, underscoring the need for early predictive tools.[23] Case-based and management-oriented discussions further emphasize the difficulty clinicians face in determining the optimal timing of intubation for hypercapnic respiratory failure.[24] Our model directly addresses this decision point by providing objective early indicators of potential NIV failure.

With increasing availability of advanced analytical methods, machine-learning-based prediction models have recently been introduced. Jiang et al. developed and validated a machine-learning model to predict the need for invasive mechanical ventilation in AECOPD patients with respiratory failure, demonstrating high discriminative performance.[25] While such approaches may improve predictive accuracy, they often require complex computational infrastructure and may limit bedside interpretability. Notably, our regression-based model achieved comparable discrimination while remaining transparent and implementable through a simple Excel-based calculator, potentially enhancing clinical applicability.

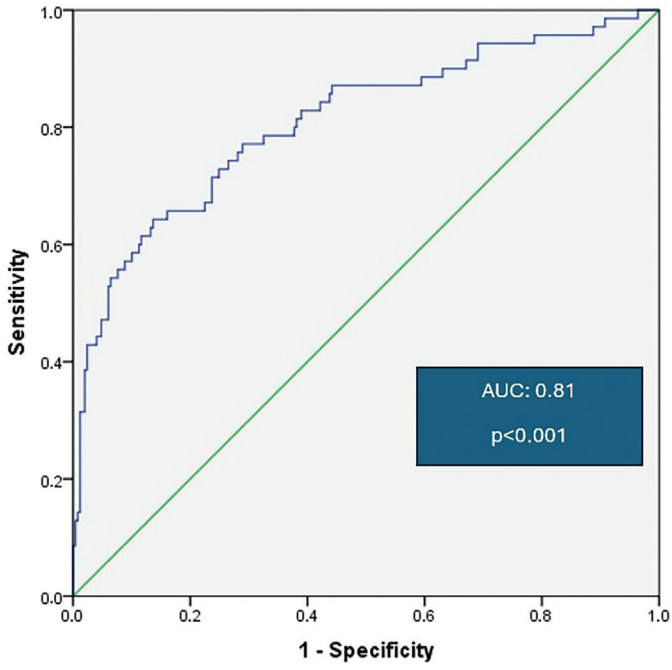

Figure 2. Receiver operating characteristic curve of the regression-based model predicting in-hospital endotracheal intubation in patients with acute hypercapnic respiratory failure due to chronic obstructive pulmonary disease exacerbation treated with non-invasive ventilation in the emergency department. The model showed good discriminative ability with an AUC of 0.810 (95% confidence interval: 0.746-0.873; p<0.001)
AUC: Area under the curve

Study Limitations

This study has several notable strengths. It is based on a multicenter cohort that includes patients from both secondary- and tertiary-level institutions, thereby enhancing the generalizability of the findings across healthcare settings. In contrast to many prior studies focusing predominantly on intensive care populations, this study evaluates patients in whom NIV was initiated in the emergency department, which represents a critical and underexplored time window for clinical decision-making. Moreover, the incorporation of dynamic changes in arterial blood gases, rather than reliance solely on baseline measurements, allows the assessment of the early physiological response to therapy and provides a more clinically meaningful evaluation of treatment trajectory.

Nevertheless, several limitations should be considered. The retrospective design inherently carries a risk of selection bias and residual confounding. In addition, ICU admission was used as one of the primary outcomes; however, because the decision to admit a patient to intensive care may be influenced by external factors such as ICU bed availability, institutional admission policies, and individual physician preference, it may not represent a fully objective clinical endpoint. Endotracheal intubation and in-hospital mortality are less susceptible to these influences and may be regarded as more robust outcome measures. Baseline COPD severity indicators (e.g., GOLD stage, FEV_1, and mMRC score) were not consistently available in this emergency department cohort, which limits full characterisation of disease severity. External validation in independent cohorts was not performed, and formal calibration analyses were not conducted. In addition, long-term outcomes beyond hospital discharge were not assessed, thereby limiting the interpretation to short-term, in-hospital endpoints. These factors should be taken into account when interpreting the predictive performance of the model.

CONCLUSION

Early physiological response to NIV provides important prognostic information in patients with COPD exacerbation complicated by acute hypercapnic respiratory failure. In this multicenter cohort, lower post-treatment pH, insufficient reduction in $PaCO_2$, and a history of prior ICU admission were independently associated with both ICU requirement and in-hospital intubation. The regression-based model incorporating these variables demonstrated good discriminative performance and may support early risk stratification in emergency departments following external validation. External validation in independent populations and confirmation through prospective studies are necessary to further establish its clinical utility.

Ethics

Ethics Committee Approval: This study was approved by the Clinical Research Ethics Committee of İzmir Bakırçay University Faculty of Medicine (approval no: 2702, date: 04.03.2026). The study was conducted in accordance with the principles of the Declaration of Helsinki.

Informed Consent: As this was a retrospective observational study using anonymized data, the requirement for informed consent was waived by the Ethics Committee.

Footnotes

Authorship Contributions

Surgical and Medical Practices: D.S.U., N.E.T., Ö.S.U., M.O.G., E.S.D., H.K., Concept: D.S.U., Ö.S.U., Design: D.S.U., Ö.S.U., Data Collection or Processing: D.S.U., Ö.S.U., H.K., A.M., Analysis or Interpretation: D.S.U., Ö.S.U., A.M., Literature Search: D.S.U., N.E.T., M.O.G., A.M., Writing: D.S.U., M.O.G., A.M.

Conflict of Interest: No conflict of interest was declared by the authors.

Financial Disclosure: The authors declared that this study received no financial support.

REFERENCES

1. World Health Organization. Chronic obstructive pulmonary disease (COPD). Geneva: WHO; 2023. Available from: https://www.who.int/news-room/fact-sheets/detail/chronic-obstructive-pulmonary-disease-(copd)
2. GBD 2019 Chronic Respiratory Diseases Collaborators. Global burden of chronic respiratory diseases and risk factors, 1990-2019: an update from the Global Burden of Disease Study 2019. EClinicalMedicine. 2023;59:101936.
3. Buist AS, McBurnie MA, Vollmer WM, et al. International variation in the prevalence of COPD (the BOLD Study): a population-based prevalence study. Lancet. 2007;370:741-50.
4. Agustí A, Celli BR, Criner GJ, et al. 2025 Global Initiative for Chronic Obstructive Lung Disease 2023 report: GOLD executive summary. Eur Respir J. 2023;61:2300239.
5. Wedzicha JA, Seemungal TA. COPD exacerbations: defining their cause and prevention. Lancet. 2007;370:786-96.
6. Connors AF Jr, Dawson NV, Thomas C, et al. Outcomes following acute exacerbation of severe chronic obstructive lung disease. The SUPPORT investigators (Study to Understand Prognoses and Preferences for Outcomes and Risks of Treatments). Am J Respir Crit Care Med. 1996;154:959-67.
7. Rochwerg B, Brochard L, Elliott MW, et al. Official ERS/ATS clinical practice guidelines: noninvasive ventilation for acute respiratory failure. Eur Respir J. 2017;50:1602426.
8. Squadrone E, Frigerio P, Fogliati C, et al. Noninvasive vs invasive ventilation in COPD patients with severe acute respiratory failure deemed to require ventilatory assistance. Intensive Care Med. 2004;30:1303-10.
9. Osadnik CR, Tee VS, Carson-Chahhoud KV, Picot J, Wedzicha JA, Smith BJ. Non-invasive ventilation for the management of acute hypercapnic respiratory failure due to exacerbation of chronic obstructive pulmonary disease. Cochrane Database Syst Rev. 2017;7:CD004104.
10. Davidson AC, Banham S, Elliott M, et al. BTS/ICS guideline for the ventilatory management of acute hypercapnic respiratory failure in adults. Thorax. 2016;71(Suppl 2):ii1-ii35.
11. Demoule A, Girou E, Richard JC, Taille S, Brochard L. Benefits and risks of success or failure of noninvasive ventilation. Intensive Care Med. 2006;32:1756-65.
12. Confalonieri M, Garuti G, Cattaruzza MS, et al. A chart of failure risk for noninvasive ventilation in patients with COPD exacerbation. Eur Respir J. 2005;25:348-55.
13. Ozyilmaz E, Ugurlu AO, Nava S. Timing of noninvasive ventilation failure: causes, risk factors, and potential remedies. BMC Pulm Med. 2014;14:19.
14. Hartley T, Lane ND, Steer J, et al. The noninvasive ventilation outcomes (NIVO) score: prediction of in-hospital mortality in exacerbations of COPD requiring assisted ventilation. Eur Respir J. 2021;58:2004042.
15. Echevarria C, Steer J, Heslop-Marshall K, et al. Validation of the DECAF score to predict hospital mortality in acute exacerbations of COPD. Thorax. 2016;71:133-40.
16. Duan J, Wang S, Liu P, et al. Early prediction of noninvasive ventilation failure in COPD patients: derivation, internal validation, and external validation of a simple risk score. Ann Intensive Care. 2019;9:108.
17. van Gemert JP, Brijker F, Witten MA, Leenen LP. Intubation after noninvasive ventilation failure in chronic obstructive pulmonary disease: associated factors at emergency department presentation. Eur J Emerg Med. 2015;22:49-54.
18. Brochard L, Mancebo J, Wysocki M, et al. Noninvasive ventilation for acute exacerbations of chronic obstructive pulmonary disease. N Engl J Med. 1995;333:817-22.
19. Plant PK, Owen JL, Elliott MW. Early use of non-invasive ventilation for acute exacerbations of chronic obstructive pulmonary disease on general respiratory wards: a multicentre randomised controlled trial. Lancet. 2000;355:1931-5.
20. Chandra D, Stamm JA, Taylor B, et al. Outcomes of noninvasive ventilation for acute exacerbations of chronic obstructive pulmonary disease in the United States, 1998-2008. Am J Respir Crit Care Med. 2012;185:152-9.
21. Global Initiative for Chronic Obstructive Lung Disease. Global Strategy for the Diagnosis, Management, and Prevention of Chronic Obstructive Pulmonary Disease: 2025 Report. GOLD; 2024. Available from: https://goldcopd.org/2025-gold-report/
22. Akbaş T, Güneş H. Characteristics and outcomes of patients with chronic obstructive pulmonary disease admitted to the intensive care unit due to acute hypercapnic respiratory failure. Acute Crit Care. 2023;38:49-56.
23. Abualhamael SA, Alasmi AT, Alqurayqiri AF, et al. Role of non-invasive ventilation (NIV) in managing acute exacerbations of chronic obstructive pulmonary disease (COPD): a systematic review. Cureus. 2024;16:e67418.
24. Balkan B, Kaya E, Gokoglu G, Balkan AO, Yilmaz G. Management strategies for hypercapnic respiratory failure in chronic obstructive pulmonary disease (COPD): a case-based discussion. Cureus. 2025;17:e84717.
25. Jiang X, Li J, Ju J, Ding H, Yang S. Construction and validation of a machine learning-based risk prediction model for invasive mechanical ventilation in AECOPD patients complicated with respiratory failure. Int J Med Inform. 2026;208:106244.