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# Characteristics and outcomes of patients with chronic obstructive pulmonary disease admitted to the intensive care unit due to acute hypercapnic respiratory failure

Türkay Akbaş[1], Harun Güneş[2]

[1]Division of Intensive Care, Department of Internal Medicine, School of Medicine, Düzce University, Düzce, Türkiye
[2]Department of Emergency Medicine, School of Medicine, Balıkesir University, Balıkesir, Türkiye

**Background:** The study aimed to describe the clinical course, outcomes, and prognostic factors of chronic obstructive pulmonary disease (COPD) patients with acute hypercapnic respiratory failure.
**Methods:** This retrospective study involved patients with acute hypercapnic respiratory failure due to COPD of any cause admitted to the intensive care unit (ICU) for non-invasive or invasive mechanical ventilation (IMV) support between December 2015 and February 2020.
**Results:** One hundred patients were evaluated. The main causes of acute hypercapnic respiratory failure were bronchitis, pneumonia, and heart failure. The patients' mean Acute Physiology and Chronic Health Evaluation (APACHE) II score was 23.0±7.2, and their IMV rate was 43%. ICU, in-hospital, and 90-day mortality rates were 21%, 29%, and 39%, respectively. Non-survivors had more pneumonia, shock within the first 24 hours of admission, IMV, vasopressor use, and renal replacement therapy, along with higher APACHE II scores, lower admission albumin levels and $PaO_2/FiO_2$ ratios, and longer ICU and hospital stays than survivors. Logistic regression analysis identified APACHE II score (odds ratio [OR], 1.157; 95% confidence interval [CI], 1.017–1.317; P=0.026), admission $PaO_2/FiO_2$ ratio (OR, 0.989; 95% CI, 0.978–0.999; P=0.046), and vasopressor use (OR, 8.827; 95% CI, 1.650–47.215; P=0.011) as predictors of ICU mortality. APACHE II score (OR, 1.099; 95% CI, 1.021–1.182; P=0.011) and admission albumin level (OR, 0.169; 95% CI, 0.056–0.514; P=0.002) emerged as predictors of 90-day mortality.
**Conclusions:** APACHE II scores, the $PaO_2/FiO_2$ ratio, vasopressor use, and albumin levels are significant short-term mortality predictors in severely ill COPD patients with acute hypercapnic respiratory failure.

**Key Words:** acute hypercapnic respiratory failure; chronic obstructive pulmonary disease exacerbation; mechanical ventilation; mortality; $PaO_2/FiO_2$ ratio

**Original Article**

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**Corresponding author**
Türkay Akbaş
Division of Intensive Care, Department of Internal Medicine, School of Medicine, Düzce University, Konuralp Yerleşkesi, Beciyörükler Mevkii, Merkez, Düzce 81620, Türkiye
Tel: +90-532-238-3197
Fax: +90-380-542-12-87
Email: turkayakbas@yahoo.com



## INTRODUCTION

As a common pulmonary disease causing respiratory failure in adults, chronic obstructive pulmonary disease (COPD) is the world's fourth leading cause of death [1]. Cigarette smoking is linked to COPD in most cases, but environmental pollution also plays a role. Occupational

air pollution and smoke from household stoves are also significant contributors to the development of COPD [2]. The disease is progressive and gradually incapacitates respiratory functions in some patients. A COPD diagnosis should be made in the presence of dyspnea, chronic coughing that produces sputum, and a history of exposure to the disease's risk factors. The clinical course of COPD is interrupted by acute exacerbations which present with acute worsening of respiratory symptoms and therefore necessitates the use of additional therapy and hospital admission in severe cases. Acute exacerbations of COPD are common causes of admission to the intensive care unit (ICU), where non-invasive mechanical ventilation (NIMV) and invasive mechanical ventilation (IMV) are applied to treat acute respiratory failure [2]. Acute exacerbations of COPD constitute approximately 2% of all ICU admissions [3,4]. Previous studies have reported that the primary reason for the acute deterioration in COPD patients is not necessarily exacerbation, but that factors such as pneumonia, pulmonary edema, cardiac arrhythmias, surgery, pneumothorax, sepsis, and pulmonary embolism may also be responsible [5-7]. COPD exacerbations are a leading cause of death and morbidity. Reported in-hospital mortality associated with COPD exacerbation ranges from 11% to 32% [3,5,8,9]. However, mortality is much higher in patients requiring IMV, at 47% [4]. IMV has decreased since the early use of NIMV has been linked to lower intubation and mortality rates, and because of more rapid improvement in physiological parameters in COPD patients with acute respiratory failure due to acute exacerbations [10]. NIMV is now recommended as a first-line therapy for patients with COPD who suffer from acute hypercapnic respiratory failure [11].

This study aimed to examine the characteristics and mortality in COPD patients admitted to the ICU due to acute hypercapnic respiratory failure over 5 years. Moreover, we intended to examine the variables associated with short-term mortality in this population.

### KEY MESSAGES

- The main causes of acute hypercapnic respiratory failure in chronic obstructive pulmonary disease (COPD) patients are bronchitis, pneumonia, and heart failure.
- COPD patients with acute hypercapnic respiratory failure are admitted to the intensive care unit to have non-invasive or invasive mechanical ventilation support.
- Patients with acute hypercapnic respiratory failure still have a high in-hospital mortality rate, reaching up to 30% despite mechanical ventilation support.
- Patients with high Acute Physiology and Chronic Health Evaluation (APACHE) II scores, low $PaO_2/FiO_2$ ratios, and decreased albumin levels have a poor prognosis.

## MATERIALS AND METHODS

The study protocol was approved by the Ethics Review Board of Düzce University (No. 2022/66 dated 25.04.2022). The retrospective nature of the study waived informed consent.

Patients with COPD who experience acute hypercapnic respiratory failure for any reason admitted to a nine-bed medical ICU between December 2015 and February 2020 were retrospectively recruited to the study. Cases were defined as COPD based on previously performed pulmonary function tests in accordance with Global Initiative for Chronic Obstructive Lung Diseases criteria or a patient history with compatible physical examination findings recorded at the time of admission and the presence of chronic hypercapnia/hypoxia [2]. Exacerbation of COPD was defined as two or more of worsening of dyspnea, cough, increased sputum purulence, or increased sputum volume. All patients aged ≥40 years with known COPD admitted to the ICU because of acute hypercapnic respiratory failure, defined as pH less than 7.35, with a $PCO_2$ greater than 45 mm Hg, and who required NIMV and/or IMV support were included in the study. Exclusion criteria were a personal history of asthma, atopy and allergic disease, patients with COPD admitting for diagnosis other than acute hypercapnic respiratory failure, multi-trauma, carbon dioxide retention due to neuromuscular and cerebrovascular diseases in patients with medical histories of COPD, and death or discharge within 24 hours of admission.

The parameters documented were Acute Physiology and Chronic Health Evaluation (APACHE) II score, age, sex, comorbidities, smoking status, etiology of respiratory failure, admission laboratory tests (within the first 6 hours), admission vital signs, admission Glasgow coma score (GCS), mechanical ventilation duration and type, renal replacement therapy, vasopressor use during the ICU stay, tracheostomy procedures, length of stay (LOS) in ICU and hospital, and ICU, in-hospital and 90-day mortalities. Based on the most unfavorable values available in the ICU during the first 24 hours, the APACHE II scores were calculated. Smokers who have smoked within the past month were defined as active smokers. The net fluid balance (the balance between all fluid input and output) on the last day of the ICU stay was recorded for all patients. Data

for home-NIMV use and long-term oxygen therapy were also collected. Circulatory shock within the first 24 hours of admission was defined as a cardiovascular sequential organ failure assessment score greater than 2, with dopamine being used at a dosage higher than 5 μg/kg/min, and/or adrenalin and noradrenalin at any dosage.

All patients had inhaled $\beta_2$-agonist and ipratropium bromide at least four times a day, with antibiotics if the patients had increased sputum or sputum purulence, infiltration on radiological images, or presence of any other infection. Corticosteroid was ordered for 5 days in those patients whose exacerbations were due to inflammation/infection [2]. All patients received H2-receptor antagonist, and prophylactic doses of low molecular weight heparin during their ICU stay, except in case of atrial fibrillation and pulmonary embolism when full dose low molecular weight heparin therapy was ordered. Thoracic computed tomography and/or chest X-rays were performed on all patients before or after ICU admission. Data from the first admission were used in case of more than one admission. A 3-month follow-up of all patients admitted to the ICU was performed by reviewing clinical records, telephone contacts, or death registration records in order to detect out-of-hospital mortality. The study's primary outcome measure was to determine ICU, in-hospital, and 90-day mortality rates and mortality predictors. The secondary outcome was to evaluate the differences between survivors and non-survivors.

All patients received either NIMV and/or IMV in the ICU. The attending physicians in the emergency, pulmonary, or intensive care units decided the types of mechanical ventilation to use. NIMV was generally used first. IMV was employed for cases with hemodynamic instability, deep coma (GCS <8), life-threatening gas exchange abnormalities, inability to manage secretion, and a failed NIMV trial. A continuous regimen of NIMV was initially prescribed based on the tolerance of the patient and the values of the arterial blood gas. Once arterial pH exceeded 7.35 and the patient was stable, NIMV was blocked for 1 hour. If no change was observed in pH and the patient tolerated this 1-hour block, the block time was increased progressively to 2, 3, and 4 hours. The patient was successfully weaned from NIMV when he was taking 4-hour blocks with clinical stability and a pH greater than 7.35. All NIMV was administered with bi-level positive airway pressure. Weaning from IMV commenced once the patient initiated spontaneous breathing through a progressive reduction in pressure support ventilation. Patients generally received NIMV after endotracheal extubation, and NIMV tapering was performed in line with the protocol described above. Since all patients received oxygen support during ICU admission, all admission laboratory measurements were performed under supplemental oxygen, and the $PO_2/FiO_2$ ratio was therefore used instead of $PO_2$. Oral feeding was started in patients capable of tolerating 2-hour blocks. If oral feeding was not expected to be commenced within 3 days, enteral feeding was initiated via nasogastric tube. Patients undergoing endotracheal intubation received enteral feeding within the first 24 hours of intubation. Parenteral feeding was undertaken in case of gastrointestinal contraindications to enteral feeding.

### Statistical Analysis

Descriptive data were reported as mean with standard deviation or median with interquartile range (IQR, 25%–75%). For normally distributed variables, the Student t-test was used, while for non-normally distributed variables, the Mann-Whitney U-test was used, and for categorical variables, the chi-square or Fisher's exact test was used. Independent predictors of ICU and 90-day mortalities were identified using logistic regression analysis. Variables yielding P-values <0.100 at univariate testing between survivors and non-survivors were included in forward stepwise-logistic regression analysis. An analysis of the APACHE II score's predictive ability for ICU mortality was conducted using receiver operating characteristic (ROC) curve analysis, which calculated the area under the curve (AUROC), sensitivity, and specificity. The odds ratio (OR) and AUROC curve were reported with a 95% confidence interval (CI). It was considered statistically significant when the p value was less than 0.05. IBM SPSS ver. 23 software (IBM Corp.) was used for statistical analysis.

## RESULTS

One hundred nineteen patients were evaluated and 19 patients were excluded from the study; four patients had a history of asthma, three patients died within the first 24 hours of admission, 10 patients had pneumonia without carbon dioxide retention, and two patients had a recent cerebrovascular accident and were intubated due to hypercapnia (Figure 1). One hundred patients with COPD (age, 71.6±9.1 years; 59 male [59%], 41 female [41%]) with acute hypercapnic respiratory failure were included in the study. The smoking rate was 64%, at 68±44 pack-years, and the remaining participants were exposed to indoor/outdoor air pollution, such as stoves for domestic heating, passive smoking exposure, and using

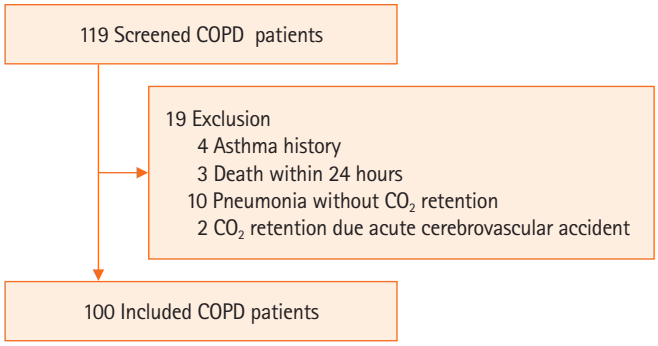


**Figure 1.** Recruitment diagram of chronic obstructive pulmonary disease (COPD) patients with acute hypercarbic respiratory failure.

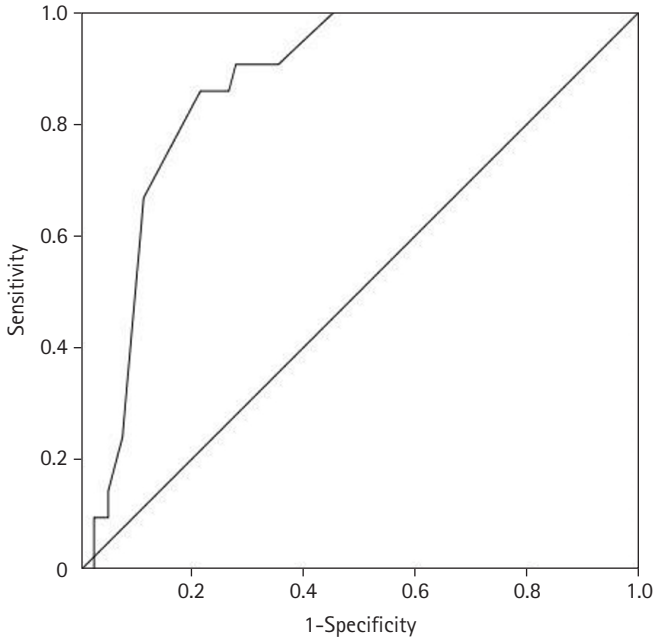


**Figure 2.** Receiver operating characteristic (ROC) analysis curve for the determination of intensive care unit mortality for chronic obstructive pulmonary disease patients with acute hypercapnic respiratory failure. Area under the ROC for Acute Physiology and Chronic Health Evaluation (APACHE) II score was 0.866 (95% confidence interval, 0.793–0.938; P<0.001) with sensitivity of 86% and specificity of 79%.

tandoor ovens for baking. Rates for long-term oxygen therapy and NIMV use at home were 51% and 39%, respectively. The causes of acute hypercapnic respiratory failure were bronchitis (46%), pneumonia (31%), heart failure (11%), surgery (7%), treatment non-compliance (2%), urosepsis (2%), and pulmonary embolism (1%). Fifty-one patients (51%) were admitted to the ICU from the wards and 49% from the emergency department. The mean GCS value was 11.7±3.9, and median ICU and hospital LOS were 6 days (IQR, 4–11 days) and 11 days (IQR, 7–16 days), respectively. Female patients were older (74.7±7.8 vs. 69.5±9.4 years, P=0.004), with lower smoking rates (14.6% vs. 89.8%, P<0.001) but greater exposure to indoor/outdoor air pollution (78% vs. 6.8%, P<0.001) than the men. Other parameters were similar between the genders.

IMV was applied to 43% of the patients for a median of 3 days (IQR, 1–13 days) and NIMV to 90% for a median of 3 days (IQR, 2–4). Ten patients (10%) received only IMV during their ICU stays, seven of whom died. Two patients underwent tracheostomy due to prolonged IMV. ICU, in-hospital, and 90-day mortality rates were 21%, 29% and 39%, respectively. The mean APACHE II score was 23.0±7.2, and the mortality predicted by APACHE II was 46.5%±21.8%, higher than the actual ICU mortality. APACHE II had an AUROC of 0.866 (95% CI, 0.793–0.938; P<0.001) (Figure 2). In the prediction of ICU mortality, APACHE II probability of death had a sensitivity of 86% and a specificity of 79%. The cut-off point for APACHE II in predicting mortality was 26. A higher percentage of non-survivors had APACHE II scores ≥26 than survivors (85.7% vs. 24.6%, P<0.001).

Non-survivors exhibited higher rates of pneumonia, IMV, shock within the first 24 hours of admission, vasopressor use and renal replacement therapy, higher APACHE II scores, but lower GCS than survivors (Table 1). Non-survivors also had lower admission $PO_2/FiO_2$ ratios and albumin levels, but higher admission heart rates than surviving patients (Table 2). Non-survivors had higher net fluid balances (10,760 ml [4,378–16,915] vs. 1,280 ml [−465 to 3,410], P<0.001) and noradrenalin infusion dosages (1.29±0.66 μg/kg/min vs. 0.30±0.25 μg/kg/min, P<0.001), longer noradrenalin infusion times (14 days [IQR, 4–19] vs. 2 days [IQR, 2–5], P=0.026), and extended IMV (8 days [IQR, 2–20] vs. 2 days [IQR, 1–8], P=0.044) than survivors. Mortality rates were higher in the patients admitted to the ICU from the wards than in those admitted from the emergency department (33.3% vs. 8.2%; P=0.002). Forward logistic regression analysis identified APACHE II scores (OR, 1.157; 95% CI, 1.017–1.317; P=0.026), admission $PaO_2/FiO_2$ ratio (OR, 0.989; 95% CI, 0.978–0.999; P=0.046) and vasopressor use during ICU stay (OR, 8.827; 95% CI, 1.650–47.215; P=0.011) as significant prognostic factors for ICU mortality (Hosmer-Lemeshow: $\chi^2$, 6.205; df, 8; P=0.624). APACHE II scores (OR, 1.099; 95% CI, 1.021–1.182; P=0.011) and admission albumin levels (OR, 0.169; 95% CI, 0.056–0.514; P=0.002) emerged solely as independent risk factors for 90-day mortality (Hosmer-Lemeshow: $\chi^2$, 5.994; df, 8; P=0.648)

**Table 1.** Characteristics and outcomes of survivors and non-survivors[a]

| Parameter | Survivor (n=79) | Non-survivor (n=21) | P-value |
|---|---|---|---|
| Age (yr) | 70.7±9.1 | 74.9±8.9 | 0.071 |
| Male | 47 (59.5) | 12 (57.1) | 0.846 |
| Smoking | 48 (60.8) | 11 (52.4) | 0.488 |
| Active smoking | 22 (27.8) | 2 (9.5) | 0.093 |
| Indoor/outdoor pollution[b] | 26 (32.9) | 10 (47.6) | 0.212 |
| Long-term $O_2$ therapy | 40 (50.6) | 11 (52.4) | 0.887 |
| Home-NIMV use | 32 (40.5) | 7 (33.3) | 0.549 |
| Comorbidity | | | |
| Hypertension | 50 (63.3) | 14 (66.7) | 0.776 |
| Heart failure | 42 (53.2) | 10 (47.6) | 0.651 |
| Ischemic heart disease | 21 (26.6) | 6 (28.6) | 0.855 |
| Atrial fibrillation | 18 (22.8) | 9 (42.9) | 0.066 |
| Diabetes mellitus | 22 (27.8) | 7 (33.3) | 0.622 |
| CKD (stage 2–5) | 14 (17.7) | 6 (28.6) | 0.269 |
| Cerebrovascular disease | 7 (8.9) | 5 (23.8) | 0.122 |
| Tuberculosis | 8 (10.1) | 2 (9.5) | 0.935 |
| Cancer[c] | 3 (3.8) | 6 (28.6) | <0.001 |
| Cause of respiratory failure[d] | | | |
| Acute COPD exacerbation | | | |
| Bronchitis | 37 (46.8) | 9 (42.9) | 0.596 |
| Non-compliance with therapy | 2 (2.5) | 0 | 1.000 |
| Pneumonia | 19 (24.1) | 12 (57.1) | 0.004 |
| Heart failure | 11 (13.9) | 0 | 0.365 |
| Surgery | 7 (8.9) | 0 | 0.340 |
| Urosepsis | 2 (2.5) | 0 | 1.000 |
| Pulmonary embolism | 1 (1.3) | 0 | 1.000 |
| APACHE II score | 21.2±6.9 | 29.5±3.8 | <0.001 |
| GCS | 12.1±3.8 | 10.1±3.6 | 0.010 |
| IMV | 25 (31.6) | 18 (85.7) | <0.001 |
| NIMV | 76 (96.2) | 14 (66.7) | 0.001 |
| Shock[e] | 13 (16.5) | 12 (57.1) | <0.001 |
| Renal replacement therapy[f] | 2 (2.5) | 7 (33.3) | <0.001 |
| Vasopressor[g] | 16 (20.3) | 18 (85.7) | <0.001 |
| ICU stay (day) | 6 (4–9) | 14 (4–26) | 0.006 |
| Hospital stay (day) | 10 (7–14) | 15 (10–28) | 0.044 |

Values are presented as mean±standard deviation, number (%), or median (interquartile range).
NIMV: non-invasive mechanical ventilation; CKD: chronic kidney disease; COPD: chronic obstructive pulmonary disease; APACHE: Acute Physiology and Chronic Health Evaluation; GCS: Glasgow coma score; IMV: invasive mechanical ventilation; ICU: intensive care unit.
a) The survivors and non-survivors were grouped by intensive care mortality; b) Indoor/outdoor pollution included using stoves for domestic heating, passive smoking exposure, and using tandoor ovens for baking; c) This involved lung (n=5), colon (n=1), tongue (n=1), thyroid (n=1) and renal cell (n=1) cancers; d) All patients had acute hypercapnic respiratory failure on admission to the ICU; e) Septic shock patients within 24 hours of admission were included; f) This comprised all patients receiving renal replacement therapy during their ICU stays; g) The parameter included all patients receiving vasopressor infusion during their ICU stays.

**Table 2.** Vital signs and laboratory parameters of survivors and non-survivors on admission to the intensive care unit[a]

| Parameter | Survivor (n=79) | Non-survivor (n=21) | P-value |
|---|---|---|---|
| Systolic blood pressure (mm Hg) | 129.0±23.4 | 120.5±24.3 | 0.151 |
| Diastolic blood pressure (mm Hg) | 67.8±15.2 | 61.3±12.6 | 0.095 |
| Respiratory rate (/min) | 23.7±4.9 | 25.3±4.8 | 0.162 |
| Heart rate (/min) | 97.4±22.6 | 111.7±25.1 | 0.027 |
| Creatinine (mg/dl) | 1.35±1.20 | 1.88±1.77 | 0.106 |
| Albumin (g/dl) | 3.4±0.6 | 2.7±0.5 | <0.001 |
| White blood cell ($\times 10^3$/L) | 14.4±9.8 | 15.4±8.8 | 0.679 |
| Hemoglobin (g/dl) | 13.2±9.4 | 11.3±1.7 | 0.076 |
| C-reactive protein (mg/dl) | 6.2 (1.7–11.1) | 10.6 (5.7–17.1) | 0.033 |
| Alanine aminotransferase (U/L) | 15.5 (10.8–24.3) | 17.5 (8.6–26.6) | 0.246 |
| Aspartate aminotransferase (U/L) | 21.9 (16.0–36.9) | 22.2 (15.7–33.7) | 0.321 |
| pH | 7.263±0.069 | 7.246±0.123 | 0.358 |
| $PCO_2$ (mm Hg) | 67.6±17.7 | 62.3±13.6 | 0.259 |
| $HCO_3$ (mEq/L) | 26.0±5.9 | 23.8±7.2 | 0.208 |
| $PaO_2/FiO_2$ (mm Hg) | 222.3±93.0 | 163.3±91.3 | 0.015 |
| Lactate (mmol/L) | 1.3 (1.0–2.1) | 1.8 (1.1–2.2) | 0.198 |

Values are presented as mean±standard deviation or median (interquartile range).
a) The survivors and non-survivors were grouped by intensive care unit mortality.

## DISCUSSION

All consecutive patients with COPD admitted to the ICU due to acute hypercapnic respiratory failure for mechanical ventilation support were included in this study. ICU, in-hospital, and 90-day mortality rates were 21%, 29% and 39%, respectively. Non-survivors had greater rates of pneumonia, shock within the first 24 hours of admission, IMV, vasopressor use and renal replacement therapy, received more fluid, stayed longer in the ICU and the hospital, and had higher APACHE II scores but lower admission albumin and $PaO_2/FiO_2$ values than survivors. Logistic regression analysis identified APACHE II scores, admission $PO_2/FiO_2$ ratio, and vasopressor use as significant ICU mortality predictors, and APACHE II scores and admission albumin levels as significant 90-day mortality predictors.

Consistent with the previous literature, the leading causes of acute hypercapnic respiratory failure in COPD patients in this study were acute COPD exacerbation, pneumonia, and heart failure. Afessa et al. [6] reported that 58% of patients were diagnosed with acute COPD exacerbation, followed, in order of

prevalence, by pneumonia (23%) and cardiovascular diseases (10%). Pincelli et al. [12] reported that 45.8% of patients had an acute COPD exacerbation, 33.3% had pneumonia, and 12.5% had cardiovascular events. Ucgun et al.'s prospective study [7], including COPD patients, revealed COPD exacerbation (49.9%), pneumonia-sepsis (29.2%), and cardiac failure (15.9%) as the main three reasons for acute hypercapnic respiratory failure. A study of 1016 patients by Connors et al. [5] reported that the main reasons for acute respiratory failure in severe COPD were infection (51.3%) and heart failure (25.7%), followed by arrhythmias (4.8%) and lung cancers (3.3%). Several studies excluded COPD patients who had respiratory failure due to pneumonia, heart failure, pulmonary embolism, and other known conditions [3,8,13,14]. Reported studies with such exclusions were likely to have a low mortality rate in the ICU because they typically included patients who suffered from a reversible, self-limited, and treatment-responsive acute respiratory failure induced by an exacerbation of bronchitis. The reported mortality rates in these studies were between 6% and 14% [3,4,8,13,14]. Studies including patients with pneumonia, heart failure, pulmonary embolism, and other known causes, together with acute exacerbation of bronchitis, have reported high ICU mortality rates, as also seen in the present study. ICU mortality rate increased to 25% in these studies [7,9,12].

The severity of illness measured by APACHE II scores in COPD patients with acute respiratory failure has been found to be associated with mortality, with non-survivors registering higher APACHE II scores than survivors, as also in our cases [6,7,13,15]. APACHE II scores have also been reported as an independent predictor of ICU, in-hospital, and 90-day mortality in COPD patients [6,8,13,15]. In addition, Rivera-Fernández et al. [9] identified APACHE III as a significant predictor of 6-year mortality. Afessa et al. [6] reported that the AUROC for the APACHE II-predicted mortality exhibited good performance, with a value of 0.748. In the current study, the AUROC for APACHE II-predicted mortality was 0.866, with a sensitivity of 79% and specificity of 84%, and this exhibited very good performance in discriminating survivors from non-survivors. The ICU mortality rate in the present study was 21%, lower than the APACHE II-predicted mortality rate of 46%. Similarly to the present research, several studies have shown that the actual mortality rate of critically ill COPD patients with acute respiratory failure was lower than the APACHE II-predicted mortality rate [6,13,14]. This is most probably due to the components of the APACHE II score. This involves scores from three physiological parameters of the respiratory system (breaths per minute, pH, and $PaO_2$). APACHE II also involves scores from the previous health status in which the presence of severe COPD adds additional five points to the score. Since severe COPD patients are usually hypoxic or on the borderline of hypoxia with hypercapnia in daily life, a deterioration in the clinic can result in severe decrements in pH and $PaO_2$, and therefore, APACHE II scores are calculated high in these patients. Therefore, the exclusion of one of the blood gas parameters (pH or $PaO_2$) from APACHE II score in critically ill COPD patients with acute respiratory failure could limit the gap between the APACHE II-predicted mortality and actual mortality.

The current study identified admission serum albumin levels as a 90-day mortality predictor. This is compatible with the previous literature. Connor et al.'s prospective study [5] identified serum albumin measured within the first 24 hours of admission as an in-hospital mortality predictor in severe COPD patients with acute exacerbation. Admission albumin levels were also described as an ICU mortality predictor in Ai-Ping et al.'s retrospective study [13] of critically ill COPD patients with acute respiratory failure. Critical illness generally has an acute phase response which causes low serum albumin levels, either by changing the distribution of albumin between intravascular and extravascular compartments or by altering the synthesis and degradation of albumin [16]. The serum albumin level is a good indicator of the severity of a disease, and hypoalbuminemia is generally associated with poorer outcomes in critically ill patients [17].

The admission $PaO_2/FiO_2$ ratio also emerged as an important ICU mortality predictor in this study. Connors et al. [5] identified the $PO_2/FiO_2$ ratio as one of the hospital mortality predictors in multivariate logistic regression analysis in COPD patients with acute exacerbation. Other authors have analyzed the effect of $PaO_2$ on mortality, but not that of the $PaO_2/FiO_2$ ratio, and have not observed any relationship between mortality and $PaO_2$ [4,7,13,14]. The $PaO_2/FiO_2$ ratio is a quantitative index of the severity of lung disease used in cases with acute respiratory distress syndrome and demonstrates problems in the pulmonary gas exchange system [18]. Abnormalities in gas exchange in diseased lungs may stem from shunting of blood through unventilated vessels, non-uniform distribution of ventilation or perfusion, or both, throughout the lungs, and diffusion abnormality of $O_2$ exchange across the alveoli walls [19]. More than one mechanism may be involved in lung diseases, and the lower the $PaO_2/FiO_2$ ratio, the more severe the lung injury [18]. The initial $PaO_2/FiO_2$ ratio is a known mortali-

ty marker in critically ill patients with acute respiratory distress syndrome [20].

There are several limitations to this research. First, it constitutes a single-centre study with a short number of cases, and our findings may not apply to the general population. Additionally, potentially important prognostic factors, such as pulmonary function tests, outpatient medications and daily living activities, were not included. Finally, complications associated with mechanical ventilation, such as pneumothorax and ventilator-associated pneumonia, which are significant causes of morbidity and even mortality, were not investigated.

In conclusion, the findings of this study showed that in ICU admissions for COPD patients with acute hypercapnic respiratory failure for any reason, the patients had high disease severity scores. In addition, nearly half of our patients required IMV, and one-fifth died in the ICU. The rates of pneumonia, IMV, vasopressor use and renal replacement therapy were higher in non-survivors than in the survivors. Additionally, non-survivors had high APACHE II scores, lengthy ICU and hospital stays, and low $PaO_2/FiO_2$ ratios and albumin levels. APACHE II scores, vasopressor use, and the $PaO_2/FiO_2$ ratios emerged as predictors for ICU mortality, and also APACHE II scores and serum albumin levels appeared as predictors for the 90-day mortality.

## CONFLICT OF INTEREST

No potential conflict of interest relevant to this article was reported.

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## ORCID

Türkay Akbaş https://orcid.org/0000-0002-2150-6866
Harun Güneş https://orcid.org/0000-0003-4899-828X

## AUTHOR CONTRIBUTIONS

Conceptualization: all authors. Data curation: all authors. Formal analysis: all authors. Methodology: all authors. Project administration: TA. Visualization: TA. Writing–original draft: all authors. Writing–review & editing: all authors.

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