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ORIGINAL PAPER

Predictors of hospitalization in patients presenting to emergency department with an acute exacerbation of COPD – a single-center study in Turkey

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ABSTRACT

Introduction and aim. In this study, we evaluated parameters that might be associated with hospitalization in patients admitted to the emergency department (ED) with an acute exacerbation of chronic obstructive pulmonary disease (AECOPD).

Material and methods. Patients with COPD who presented to ED due to AECOPD between January 1, 2020 and December 31, 2021 were included in the study. Patient data were obtained from the hospital database. Univariable and multivariable logistic regression methods were used to identify the relationship between hospitalization and clinical parameters.

Results. The study included 237 patients divided into two groups: inpatients (n=124) and outpatients (n=113). We found significant differences between the two groups in terms of temperature, oxygen saturation, respiratory rate, C-reactive protein, white blood cell count, procalcitonin, albumin, arterial blood pH, pCO_2, and non-invasive mechanical ventilation (NIMV) requirement. Multivariable logistic regression analysis showed that body temperature [odds ratio (OR):1.62;95% confidence interval (CI):1.21–4.91; p<0.001], oxygen saturation (OR:0.73, 95% CI:0.39-0.94, p<0.001), respiratory rate (OR:1.96; 95% CI: 1.07–6.14; p<0.001), albumin (OR:0.71; 95% CI:0.41–0.93; p=0.042), procalcitonin (OR:2.93; 95% CI:1.22–4.84; p<0.001), arterial blood pH (OR:0.78; 95% CI:0.29-0.91; p=0.038), pCO_2 (OR:2.45; 95% CI:1.24–4.65; p<0.001), and NIMV requirement (OR:2.31; 95% CI:1.41–5.13; p<0.001) were the independent predictors of hospitalization.

Conclusion. Our findings may help identify patients who will require hospitalization at an early stage.

Keywords. chronic obstructive pulmonary disease, emergency department**,** hospitalization

Introduction

Chronic obstructive pulmonary disease (COPD) is a chronic inflammatory lung disease characterized by progressive, completely irreversible airflow limitation. COPD is an important cause of morbidity and mortality with its high prevalence and increasing incidence.[1] COPD is a preventable and treatable disease that presents with exacerbations.[2] Acute exacerbations negatively affect the quality of life of patients, hospitalization rates, disease progression, and mortality.[3,4]

In the Global Initiative for Chronic Obstructive Lung Disease guidelines, the acute exacerbations of COPD (AECOPD) requiring hospitalization are defined as "severe exacerbations". Mild to moderate exacerbations can usually be treated on an outpatient basis.[5] The demographic and clinical characteristics of patients play an important role in determining severe exacerbations requiring hospitalization. In addition, comorbidities, blood gas parameters, and inflammatory biomarkers are also important factors in hospitalization.[6] Airway in-

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flammation is frequently increased in AECOPD.[7] Various inflammatory markers such as, C-reactive protein (CRP), white blood cell count (WBC) have been shown to be increased in AECOPD.[8]

Aim

Due to the respiratory and systemic adverse effects of the disease, one of the most important goals of treating patients with COPD is the effective treatment and prevention of exacerbations. In an acute attack, it is extremely important to identify high-risk groups for hospitalization, especially in terms of exacerbation management, detection of conditions that require special treatment, and reducing treatment costs. Therefore, in this study, we aimed to examine the general characteristics of patients hospitalized for AECOPD and investigate parameters that might be associated with hospitalization.

Material and methods

Ethical approval

Approval for the study was obtained from the clinical research ethical committee of Aksaray University Faculty of Medicine (approval number: 2022/01-08).

Study design

This retrospective descriptive study was conducted in the emergency department (ED) of a single tertiary center in Turkey. Patients with a diagnosis of COPD who applied to the emergency department with cough, sputum and shortness of breath between January 1, 2020 and December 31, 2021 and required additional treatment were included in the study. Patients without a diagnosis of COPD, those whose records could not be reached, those who were transferred to another hospital for any reason without treatment, and those with malignancies, bronchial asthma, tuberculosis, and advanced liver or kidney failure were excluded from the study. The flowchart is shown in Figure 1.

The clinical data of the patients were obtained from the hospital's electronic database and by retrospectively screening the patient files. The patients' age, gender, vital signs (temperature, blood pressure, respiratory rate and oxygen saturation), comorbid diseases (coronary artery disease, diabetes mellitus and hypertension), laboratory parameters, NIMV and invasive mechanical ventilation (IMV) requirements, intensive care unit admission, and in-hospital mortality rates were recorded. The clinical diagnosis, treatment, and follow-up of the patients were provided according to international standard guidelines.[5]Acute respiratory failure, sudden worsening of dyspnea at rest, high respiratory rate, severe symptoms such as decreased oxygen saturation, confusion, drowsiness, onset of new physical symptoms (e.g. cyanosis, peripheral edema), failure to respond to medical therapy, presence of serious comorbidities, inadequate home support was determined as the criteria for hospitalization. Discharge criteria were defined as mild to moderate AECOPD that improved with treatment according to the guideline.[5] NIMV (Non-invasive mechanical ventilation) indications included respiratory acidosis ($pCO_2 \geq 45$ mmHg and arterial pH≤7.35), severe dyspnea with use of accessory respiratory muscles, and persistent hypoxemia despite supplemental oxygen therapy. IMV indications included status post-respiratory or cardiac arrest, diminished consciousness, psychomotor agitation inadequately controlled by sedation, massive aspiration or persistent vomiting, persistent inability to remove respiratory secretions, severe hemodynamic instability without response to fluids and vasoactive drugs, severe ventricular or supraventricular arrhythmias, life-threatening hypoxemia in patients unable to tolerate NIMV.[5] The effects of the patients' clinical parameters on hospitalization were evaluated.

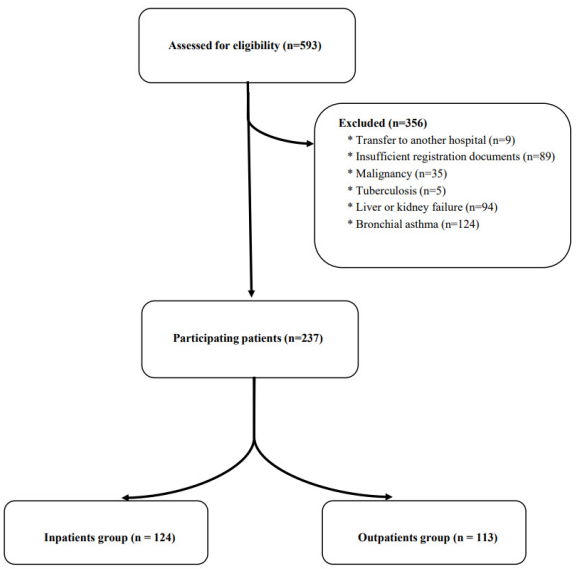

Fig. 1. Recruitment process flowchart

Statistical analysis

SPSS v. 22.0 (SPSS Inc, Chicago, IL, USA) was used for the statistical analysis of the data obtained from the study. Numerical variables were expressed as mean ± standard deviation or median (25–75% quartiles) and qualitative variables as numbers and percentages. The conformity of the results to the normal distribution was checked with the Kolmogorov-Smirnov test. The chi-square test was used to determine whether there was a difference between the groups in terms of qualitative variables. Student's t-test was used to compare normally distributed data between the two groups, and Mann-Whitney U test was used to compare non-normally distributed data. The univariable and multivariable logistic regression analyses were undertaken to determine the relationship between hospitalization and possible clinical variables (Body temperature, oxygen saturation, respiratory rate, white blood cell, albumin, procalcitonin, C-reactive protein, arterial blood pH,

pCO_2, NIMV requirement). The multivariable logistic regression analysis was applied to the variables with a p value of <0.05 in the univariable logistic regression analysis. p<0.05 was considered statistically significant.

Results

During the study, 593 patients were evaluated for eligibility. 356 patients were excluded from the study. A total of 237 patients who met the criteria were included in the study. The patients were divided into two groups: inpatients (n=124) and outpatients (n=113). The mean age of the patients was 70.7±9.2 years, 77.2% (n=183) were men, and 22.8% (n=54) were women. The most common comorbidity was hypertension (77.2%). In ED, 2.1% of the patients were treated with IMV and 11.8% with NIMV. Of all the patients, 6.8% were admitted to the intensive care unit (n=16), and the in-hospital mortality rate was 3.4% (n = 8). Table 1 shows the demographic data and clinical characteristics of the patients who presented to ED due to AECOPD.

Table 1. Demographic data and clinical characteristics of the study population (n=237)*

Variable	
Age, years, mean ± SD	70.7 ± 9.2
Male, n (%)	183 (77.2%)
Vital signs at presentation to ED	
Systolic blood pressure, mmHg, median (25th–75th percentile)	135 (126–150)
Diastolic blood pressure, mmHg, median (25th–75th percentile)	80 (80–90)
Body temperature, (°C), median (25th–75th percentile)	36.7 (36.5–36.9)
Oxygen saturation, (%), median (25th–75th percentile)	85 (75–88)
Respiratory rate, per/minute, median (25th–75th percentile)	29 (26–34)
Hypertension, n (%)	157(66.2%)
Diabetes mellitus, n (%)	38 (16.0%)
Heart disease, n (%)	95 (40.1%)
Hemoglobin, g/dL, mean ± SD	14.2±2.2
White blood cell, x10^9/L, median (25th–75th percentile)	10.2 (7.9–12.4)
Glucose, mg/dL, median (25th–75th percentile)	127 (104–155)
Creatinine, mg/dL, median (25th–75th percentile)	0.80 (0.63–1.01)
Albumin, g/dL, median (25th–75th percentile)	37.3 (34.2–40.0)
Procalcitonin, ng/mL, median (25th–75th percentile)	0.06 (0.03–0.14)
C–reactive protein, mg/dL, median (25th–75th percentile)	18 (7.3–78.4)
Lactate/albumin ratio, median (25th–75th percentile)	0.04 (0.03–0.06)
Arterial blood pH, median (25th–75th percentile)	7.34 (7.30–7.39)
pCO_2, mmHg, median (25th–75th percentile)	54 (47–66)
Arterial blood lactate, mmol/L, median (25th–75th percentile)	1.7(1.2–2.3)
Invasive MV requirement, n (%)	5 (2.1%)
Non–invasive MV requirement, n (%)	28 (11.8%)
ICU admission, n (%)	16 (6.8%)
In–hospital mortality, n (%)	8 (3.4%)

* Data are presented as mean ± standard deviation, median (25%–75% percentiles), or n (%); ED – emergency department; MV – mechanical ventilation; ICU – intensive care unit; pCO_2 – partial pressure of carbon dioxide

When the vital signs were examined, a statistically significant difference was found between the two groups in terms of respiratory rate, oxygen saturation, and body temperature (p<0.05). There were statistically significant differences in the WBC, albumin, procalcitonin, and CRP parameters between the inpatient and outpatient groups (p=0.02; p=0.011, p<0.001, and p<0.001, respectively). In addition, the arterial partial pressure of carbon dioxide (pCO_2) value was significantly higher in the inpatient group (p < 0.001). The laboratory parameters and clinical characteristics of the groups are given in Table 2.

Table 2. Comparison of the demographic and clinical characteristics between the outpatient and inpatient groups*

Variable	Inpatients (n=124)	Outpatients (n=113)	p
Age, years, mean ± SD	71.0±9.3	70.4±9.2	0.725
Male, n (%)	96 (77.4%)	87 (77.0%)	0.937
Vital signs at presentation to ED			
Systolic blood pressure, mmHg, median (25th–75th percentile)	140 (125–157)	130 (125–140)	0.168
Diastolic blood pressure, mmHg, median (25th–75th percentile)	80 (80–90)	80 (75–85)	0.170
Body temperature, °C, median (25th–75th percentile)	36.8 (36.5–37.0)	36.7 (36.5–36–8)	<0.001
Oxygen saturation, %, median (25th–75th percentile)	79 (67–85)	88 (85–90)	<0.001
Respiratory rate, per/minute, median (25th–75th percentile)	32 (28–35)	28 (25–30)	<0.001
Hypertension, n (%)	89 (71.8%)	68 (60.2%)	0.059
Diabetes mellitus, n (%)	21 (16.9%)	17 (15.0%)	0.692
Heart disease, n (%)	54 (43.5%)	41 (36.3%)	0.254
Hemoglobin, g/dL, mean ± SD	14.5 ± 2.4	13.9 ± 2.0	0.051
White blood cell, x10^9/L, median (25th–75th percentile)	10.6 (8.3–13.5)	9.8 (7.7–11.8)	0.020
Glucose, mg/dL, median (25th–75th percentile)	130 (110–165)	119 (100–151)	0.096
Creatinine, mg/dL, median (25th–75th percentile)	0.78 (0.61–0.99)	0.81 (0.66–1.02)	0.268
Albumin, g/dL, median (25th–75th percentile)	36.4 (33.4–38.9)	37.6 (35.7–41.0)	0.011
Procalcitonin, ng/mL, median (25th–75th percentile)	0.08 (0.04–0.17)	0.04 (0.02–0.09)	<0.001
C–reactive protein, mg/dL, median (25th–75th percentile)	35.6 (10.9–116.7)	11.6 (3.6–43.6)	<0.001
Lactate/albumin ratio, median (25th–75th percentile)	0.04 (0.03–0.07)	0.04 (0.03–0.05)	0.237
Arterial blood pH, median (25th–75th percentile)	7.34 (7.29–7.39)	7.36 (7.31–7.40)	0.015
pCO_2, mmHg, median (25th–75th percentile)	60.5 (49–73)	51.0 (45–58)	<0.001
Arterial blood lactate, mmol/L, median (25th–75th percentile)	1.75 (1.2–2.6)	1.70 (1.2–2.3)	0.264
Invasive MV requirement, n (%)	5 (4.0%)	0	0.038
Non–invasive MV requirement, n (%)	27 (21.8%)	1 (0.9%)	<0.001
ICU admission, n (%)	16 (12.9%)	0	<0.001
In–hospital mortality, n (%)	8 (6.5%)	0	<0.001

* Data are presented as mean ± standard deviation, median (25%–75% percentiles), or n (%); ED – emergency department; MV – mechanical ventilation; ICU – intensive care unit; pCO_2 – partial pressure of carbon dioxide

Univariable and multivariable logistic regression analyses were used on the statistically significant parameters. The multivariable logistic regression analysis revealed that body temperature [odds ratio (OR): 1.62; 95% confidence interval (CI): 1.21–4.91; p<0.001], oxygen saturation (OR: 0.73; 95% CI: 0.39–0.94; p<0.001), respiratory rate (OR: 1.96; 95% CI: 1.07–6.14; p<0.001), albumin (OR: 0.71; 95% CI: 0.41–0.93; p=0.042), procalcitonin (OR: 2.93; 95% CI: 1.22–4.84; p<0.001), arterial blood pH (OR: 0.78, 95% CI: 0.29–0.91, p=0.038), pCO2 (OR: 2.45; 95% CI: 1.24–4.65; p<0.001), and NIMV requirement (OR: 2.31; 95% CI: 1.41–5.13; p<0.001) were the independent predictors of hospitalization (Table 3).

Table 3. Predictors of hospitalization as determined by the univariable and multivariable logistic regression analyses*

Variables	Univariable logistic regression		Multivariable logistic regression	
	OR (95% CI)	p	OR (95% CI)	p
Body temperature, °C	1.41 (1.09–3.66)	<0.001	1.13 (1.03-4.77)	<0.001
Oxygen saturation, %	0.61 (0.44–0.92)	<0.001	0.73 (0.39–0.94)	<0.001
Respiratory rate	1.82 (1.13–5.17)	<0.001	1.96 (1.07–6.14)	<0.001
White blood cell, x10^9/L	1.76 (1.55–3.97)	0.023		
Albumin, g/dL	0.64 (0.43–0.89)	0.012	0.71 (0.41–0.93)	0.042
Procalcitonin, ng/mL	2.51 (1.26–3.32)	<0.001	2.93 (1.22–4.84)	<0.001
C-reactive protein	1.33 (1.15–3.25)	<0.001		
Arterial blood pH	0.71 (0.26–0.82)	0.015	0.78 (0.29–0.91)	0.038
pCO_2	2.23 (1.39–3.89)	<0.001	2.45 (1.24–4.65)	<0.001
Non-invasive MV requirement	2.01 (1.38–4.33)	<0.001	2.31 (1.41–5.13)	<0.001

* OR – odds ratio; CI – confidence interval; MV – mechanical ventilation, pCO_2 – partial pressure of carbon dioxide

Discussion

In this study, we investigated parameters that could affect the hospitalization of patients who presented to ED due to AECOPD. On completion of the study, body temperature, oxygen saturation, respiratory rate, arterial blood pH, pCO_2, albumin, procalcitonin, and NIMV requirement were identified as factors determining hospitalization.

The effect of age and gender on hospitalization remains controversial. Previous studies have showed that the rates of AECOPD and hospitalization are higher in women because they are more sensitive to external factors. The increase in women's exposure to tobacco and biomass in the last 15 years has increased the frequency of COPD. In addition, some theories have been put forward to explain the sensitivity of women to these substances. Some of these theories are estrogen effect, impaired gas exchange in the lungs and small bronchi.[9-11] Similarly, Antonela et al. showed that male gender was a higher risk factor for COPD-related morbidity and mortality.[12] In contrast, recent studies have shown no statistically significant difference between genders in terms of hospitalization rates.[13,14] There are also researchers reporting that the length of hospital stay in COPD increases as patient age increases.[15,16] In the current study, no significant difference was found between the inpatient and outpatient groups in relation to age and gender. Therefore, we consider that gender or age alone is not sufficient to determine hospitalization and discrepancies between studies are also related to regional and cultural differences.

Fever shows the severity of the clinical manifestations of the infection causing the exacerbation and supports the decision for hospitalization.[17] Similar to Lieberman et al., we found fever to be an important clinical finding for making the hospitalization decision in patients who presented to ED with AECOPD.[17] Another cardinal symptom of COPD, dyspnea, is the most common reason for referral to ED. Increasing dyspnea is an indicator of hypoxemia and causes hypercapnia.[18,19] In our study, the pCO_2 value was significantly higher in the inpatients, which is consistent with the literature. Hypercapnia is an important indicator of emerging respiratory failure and predicts hospitalization requirement.[18]

Respiratory rate can be easily measured with non-invasive methods and information about the severity of the disease can be obtained. In studies, it has been shown that respiratory rate is 18-20 per minute in patients admitted to ED with AECOPD and treated as an outpatient, while it is >24 in inpatients.[20] In another study, it was stated that respiratory rate <24 breaths per minute is mild AECOPD and outpatient treatment is sufficient.[21] In our study, Tseng et al. similar to his study, it was shown that the respiratory rate was statistically significantly higher in hospitalized patients.[22]

With increasing age, the number of COPD exacerbations and mortality rate increase as a result of the deterioration of respiratory function and the increasing incidence of comorbid diseases. Similar to our study, Raherison et al. found the most common comorbid disease to be hypertension in their cohort.[23] Infectious factors, especially increased airway inflammation are the most critical factors triggering a COPD attack. As a result, changes are observed in infectious parameters in the blood.[24] In a recent study, procalcitonin levels were shown to predict the hospitalization and prognosis of patients.[8] In another study, the authors reported a significant relationship between procalcitonin levels and disease severity and NIMV requirement in patients with AECOPD followed up in the intensive care unit.[25] CRP is a highly sensitive indicator of inflammation but cannot always be used to distinguish between bacterial and non-bacterial inflammation. In a meta-analysis that included 12 studies comparing procalcitonin and CRP levels in the diagnosis of bacterial infection in hospitalized patients, the former was found to be more useful than the latter in differentiating bacterial infection from other non-infectious causes

of systemic inflammation.[26] In addition, high procalcitonin and CRP values in COPD exacerbations have been suggested to be significant predictors of short-term (one-month) and long-term (two-year) mortality.[27] Albumin is a negative acute phase protein that decreases in inflammatory conditions, and hypoalbuminemia is associated with chronic diseases. It has been showed that albumin plays an important role in the prognosis of COPD cases accompanied by comorbidities.[28] In the present study, we found a statistically significant difference in the albumin and procalcitonin values between the inpatients and outpatients with AECOPD.

Arterial blood gas parameters are important to evaluate patients with AECOPD and determine their mechanical ventilation and hospitalization requirements. In the literature, it has been reported that the pH value in blood gas has a critical prognostic importance.[29] Respiratory acidosis in arterial blood gas and an increased pCO_2 level in AECOPD indicate the need for intensive care, NIMV, or IMV.[30] It has been observed that at the time of their presentation to the hospital, patients with COPD require mechanical ventilator therapy during exacerbation periods when respiratory acidosis becomes more evident.[31]

Study limitations

This study has certain limitations. First, due to the retrospective and single-center design of the study, the data were limited to the records that we were able to access from the hospital database. In addition, the single-center study design inherent carries risks of bias. Second, some patients had recurrent presentations during the study period, but only the data from their first visit were taken into consideration. Lastly, the measured blood parameters were obtained only at the time of the patients' presentation to ED, and changes in these biomarkers during follow-up were not examined. Despite these limitations, we consider that the results of this study are important in terms of guiding future research on this subject.

Conclusion

We determined that body temperature, oxygen saturation, respiratory rate, arterial blood pH, pCO_2, albumin, procalcitonin, and NIMV requirement were associated with hospitalization in patients with AECOPD. Our findings suggest that the hospitalization requirement is associated with parameters indicating the severity of the disease. It should be kept in mind that COPD attacks will be more severe in these patients, and therefore they may require hospitalization at any time.

Declarations

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Author contributions

Conceptualization, T.S.M. and E.T.S.; Methodology, T.S.M.; Software, T.S.M.; Validation, T.S.M. and E.T.S.; Formal Analysis, E.T.S.; Investigation, T.S.M.; Resources, T.S.M..; Data Curation, T.S.M.; Writing – Original Draft Preparation, T.S.M. and E.T.S.; Writing – Review & Editing, T.S.M.; Visualization, T.S.M. and E.T.S..; Supervision, T.S.M.; Project Administration, T.S.M.; Funding Acquisition, T.S.M.

Conflicts of interest

No conflict of interest was declared by the authors.

Data availability

The datasets used and/or analyzed during the current study are open from the corresponding author on reasonable request.

Ethics approval

All subjects gave their informed consent for inclusion before they participated in the study. This study protocol was approved by Clinical Research Ethical Committee of Aksaray University Faculty of Medicine with a protocol number of 2022/01-08 and conducted in accordance with the Declaration of Helsinki and Good Clinical Practices.

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