RESEARCH ARTICLE

Determination of predisposing factors for prolonged intensive care in patients with exacerbation of chronic obstructive pulmonary disease

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Abstract

Objective: To determine the predisposing factors for lengthy intensive care unit stay of chronic obstructive pulmonary disease patients with acute exacerbation.

Method: The retrospective study was conducted after approval from the ethics review committee of Atatürk Sanatorium Training and Research Hospital, Turkey, and comprised data from January 1, 2017, to August 31, 2022, related to acute exacerbation chronic obstructive pulmonary disease patients receiving intensive care unit treatment. Demographics, comorbidities, treatment, length of stay in hospital and in intensive care unit, and nutritional status were evaluated. Data of patients who spent <10 days in intensive care unit formed Group 1, while those having spent 10 days or more formed Group 2 for comparison purposes. Data was analysed using SPSS 22.

Results: Of the 460 patients, 366(79.6%) were in Group 1; 224(61.2%) males and 64(38.8%) females with mean age 70.81±11.57 years. There were 94(20.4%) patients in Group 2; 62(66%) males and 32(34%) females with mean age 72.38±10.88 years (p>0.05). Inotropic agent support, need for haemodialysis, timeframe of invasive mechanical ventilation, length of stay in hospital, 1-month mortality, antibiotic use, use of diuretic agent, acute physiology and chronic health evaluation-ii score, nutrition risk in the critically ill score, history of lung malignancy, and pneumonic infiltration on chest radiograph were significantly more frequenttly observed in Group 2 patients (p<0.05). Age, timeframe of invasive mechanical ventilation, and length of stay in hospital were the factors prolonging intensive care unit stay (p<0.05).

Conclusion: Higher age, longer invasive mechanical ventilation timeframe and hospital stay with acute exacerbation chronic obstructive pulmonary disease caused a prolonged stay in intensive care unit.

Keywords: Acute exacerbation of chronic obstructive pulmonary disease, Mechanical ventilation time, Prolonged intensive care stay, Prolonged hospitalisation. (JPMA 74: 1061; 2024)

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Introduction

Prolonged hospitalisation due to acute exacerbation in chronic obstructive pulmonary disease (AECOPD) patients is a common occurrence.[1] COPD is a rather common comorbid condition among patients admitted to the intensive care unit (ICU).[2]

COPD is a common cause of death, and in-hospital mortality rates ranging 11-48% have been reported.[3] Long-term stay in ICU also increases mortality.[4]

In a review that included 73 primary publications between 2006 and 2016, the majority of studies (94%) were from Europe or North America, and despite the availability of effective treatments for moderate to very severe COPD and comprehensive guidelines for their use, it was seen that COPD caused a significant economic burden on healthcare providers.[5] The cost increases with increased legth of stay (LOS) in the ICU.

Reducing the ICU stay is crucial not only for improving the outcomes of COPD patients, but also for reducing the waiting time for patients in need of ICU admission. The efficient distribution and use of ICU beds need to be optimised.[6]

To our knowledge, the causes of lengthy ICU stay in AECOPD patients have not been extensively studied. The current study was planned to fill the gap in literature by establishing the factors that make AECOPD patients more susceptible to experiencing a lengthy ICU stay.

Materials and Methods

The retrospective study was conducted after approval from the ethics review committee of Atatürk Sanatorium Training and Research Hospital, Turkey, and comprised data from January 1, 2017, to August 31, 2022, related to adult AECOPD patients of either gender having received ICU treatment. Data was retrived and screened from the hospital database. Data of patients who met AECOPD diagnostic criteria of the Global Initiative for Chronic Obstructive Lung Disease (GOLD)[7] was included. Data of patients with ICU stay <24 hours, age <18 years and those

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without an ICU admission was excluded.

Data was taken down from individual patient files related to demographics, comorbid diseases, like interstitial lung disease, pulmonary thromboembolism, lung malignancy, other malignancies, heart failure, diabetes mellitus, hypertension, cerebrovascular events, neuromuscular diseases, coronary artery disease, chronic kidney disease and Alzheimer's, Charlson Comorbidity Index Score (CCIS),[8] Glasgow Coma Scale (GCS),[9] Sequential Organ Failure Assessment (SOFA),[10] Acute Physiology and Chronic Health Evaluation-II (APACHE-II),[11] presence of sepsis, glomeruler filtration rate (GFR), need for haemodialysis (HD), history of re-admission to the ICU, timeframe of invasive/noninvasive mechanical ventilation (IMV/NIMV), use of inotropic and/or vasopressor agents, LOS hospital, LOS ICU, and 1-month mortality.

The Nutritional Risk Score-2002 (NRS)[12] and Nutrition Risk in Critically ill (NUTRIC) score[13] were used to identify the nutritional condition of the patients.

Chest X-rays (CXRs) taken on admission to the ICU were examined for pneumonic infiltration, pulmonary oedema, pleural effusion (PE), typical COPD findings or any other relevant observation.

Treatment given during ICU stay, including antibiotics, at least one dose of corticosteroid and/or at least one dose of diuretic, were recorded.

The cut-off mark to define extended ICU stay was set at 10 days. Data of patients with LOS ICU <10 days formed Group 1, and of those with LOS ICU 10 days or more formed Group 2 for comparison purposes.

Data was analysed using SPSS 22. Verifying normal distribution of continuous variables, Kolmogorov-Smirnov test was employed, and the Levene test was used to determine the homogeneity of variances. Data that followed a normal distribution was expressed as mean±standard deviation (SD), while data non-normally distributed was presented as median with interquartile range (IQR). The rest of the data was presented as frequencies and percentages. For normally distributed continuous variables, independent groups were compared using student's t-test, while non-normally distributed data was analysed using the Mann-Whitney U test. Categorical variables were compared using either the Pearson's chi-square test or Fisher's exact test. Univariate logistic regression analyses was used to explore the potential links between the risk factors and the outcomes of interest. Factors with $p<0.25$ were subjected to multivariate logistic regression analysis. P<0.05 was considered statistically significant.

Results

Of the 2,480 having had an ICU stay, 507(20.44%) had an admission diagnosis of AECOPD. Of them, 47(9.27%) were

Table-1: Intergroup comparison of demographic and clinical characteristics.

	Group 1 (n=366) [n (%)]	**Group 2** (n=94) [n (%)]	***p*-value**
Mean Age (year)	70.81±11.57	72.38±10.88	0.234
<50	12 (3.3)	-	0.203
50-74	214 (58.5)	56 (59.6)	
>74	140 (38.3)	38 (40.4)	
Gender			
Male	224(61.2)	62(66.0)	0.396
Female	64(38.8)	32(34.0)	
Inotropic agent Support			
No	302(82.5)	44(46.8)	<0.001***
Yes	64(17.5)	50(53.2)	
Malignancy			
No	338 (92.3)	82 (87.2)	0.116
Yes	28 (7.7)	12 (12.8)	
Haemodialysis			
No	356 (97.3)	86 (91.5)	0.016*
Yes	10 (2.7)	8 (8.5)	
Re-admission to ICU			
No	266 (72.7)	60 (63.8)	0,092
Yes	100 (27.3)	34 (36.2)	
Length of stay hospital, med(IQR) (day)	12 (12)	29(19)	<0.001***
1-Month Mortality			
No	266 (72.7)	46 (48.9)	<0.001***
Yes	100 (27.3)	48 (51.1)	
Steroid Use			
No	202 (55.2)	62 (66.0)	0.060
Yes	164 (44.8)	32 (34.0)	
Antibiotic Use			
No	98 (26.8)	12 (12.8)	0.005**
Yes	268 (73.2)	82 (87.2)	
Diuretic Use			
No	120 (32.8)	16 (17.0)	0.003**
Yes	246 (67.2)	78 (83.0)	
APACHE II, med(IQR)	20(8)	22 (11)	0.003**
GKS, med(IQR)	14(2)	14(4)	0.059
CCIS, med(IQR)	6 (3)	6(2)	0.182
GFR, med(IQR)	77 (49)	70(52)	0.909
SOFA-sepsis, med(IQR)	6 (2)	5(2)	0.564
NRS -2002, med(IQR)	5 (1)	5(1)	0.351
NUTRIC Skor, med(IQR)	5 (3)	5(2)	0.035*
Invasive MV Duration, med(IQR) (day)	0 (1)	8(16)	<0.001***
MV (there may be >1 in a patient)			
No	88 (24.0%)	-	<0.001***
Yes	278 (76.0)	94 (100.0%)	
Noninvasive	196 (53.6)	46(48.9)	0.424
Intubated	118(32.2)	60(63.8)	<0.001***
Tracheostomy	4 (1.1)	12(12.8)	<0.001***

IQR: Interquartile range, APACHE II: Acute Physiology and Chronic Health Evaluation-2, GKS: Glasgow Coma Scale, CCIS: Charlson Comorbidity Index, GFR: Glomerular filtration rate, SOFA: Sequential organ failure assessment, NRS: Nutritional Risk Screening, NUTRIC: Nutrition Risk in the Critically ill, MV: Mechanical ventilation; P-*<0.05, **<0.01 and ***<0.001 were statistically significant.

excluded for having ICU stay <24 hours. The study sample as such stood at 460(90.72%) with mean LOS ICU 6.63±7.9 days. There were 366(79.6%) patients in Group 1; 224(61.2%) males and 64(38.8%) females with mean age 70.81±11.57 years. There were 94(20.4%) patients in Group 2; 62(66%) males and 32(34%) females with mean age 72.38±10.88 years (p>0.05).

Table-2: Intergroup comparison of comorbidity profile.

	Group 1 (n=366) [n (%)]	Group 2 (n=94) [n (%)]	*p*-value
Comorbidity			
No	100 (27.3)	24 (25.5)	0.727
Yes	266 (72.7)	70 (74.5)	
Interstitial lung disease	10 (2.7)	-	0.225
Pulmonary thromboembolism	12 (3.3)	2 (2.1)	0.745
Lung malignancy	8 (2.2)	8 (8.5)	0.007
Other malignancies	18 (4.9)	4 (4.3)	0.999
Heart failure	80 (21.9)	16 (17.0)	0.303
Diabetes mellitus	70 (19.1)	12 (12.8)	0.151
Hypertension	112 (30.6)	20 (21.3)	0.075
Cerebrovascular events	18 (4.9)	4 (4.3)	0.999
Neuromuscular diseases	2 (0.5)	-	0.999
Coronary artery disease	22 (6.0)	4 (4.3)	0.511
Chronic kidney disease	16 (4.4)	4 (4.3)	0.999
Alzheimer's	22(6.0)	2(2.1)	0.192

Table-3: Intergroup comparison of chest X-(CXR) findings.

	Group 1 (n=366) [n (%)]	Group 2 (n=94) [n (%)]	*p*-value
Chest X-ray Findings			
No	31(16.9)	4 (4.3)	0.002**
Yes	304 (83.1)	90 (95.7)	
Pneumonic Infiltration	172 (47.0)	74 (78.7)	<0.001***
Pulmonary oedema	10 (2.7)	2 (2.1)	0.999
Pulmonary effusion	92 (25.1)	32 (34.0)	0.083
Typical COPD findings	80 (21.9)	20 (21.3)	0.903
Other findings	34 (9.3)	10 (10.6)	0.692

COPD: Chronic obstructive pulmonary disease; *p-<0.05, **p<0.01 and ***p<0.001 were statistically significant; Note: CXR findings may have been more than one in a patient.

Inotropic agent support, need for HD, use and duration of IMV, LOS hospital, 1-month mortality, antibiotic use, use of diuretic agent, APACHE-II score, NUTRIC score, history of lung malignancy, and pneumonic infiltration on CXR were significantly more frequently observed in Group 2 patients compared to Group 1 (Table 1).

LOS ICU was longer in patients with lung malignancies (p=0.007). There was no significant correlation between other comorbidities and LOS ICU (Table 2).

LOS ICU was longer in patients with clinical findings on the CXR compared to those with normal findings (p=0.002), and the rate of pneumonic infiltration on CXR was higher in Group 2 compared to Group 1 (p<0.001) (Table 3).

Univariate logistic regression analysis showed that inotropic agent support, need for HD, IMV duration, LOS hospital, antibiotic use, diuretic use, high APACHE-II score, low NUTRIC score, and abnormal CXR findings were significantly associated with prolonged ICU stay (p<0.25). Multivariate logistic regression analysis showed that age, IMV duration, and LOS hospital were the factors prolonging ICU stay (Table 4).

Discussion

In the current study, 94(20.4%) of 460 patients admitted due to AECOPD had a long LOS ICU, with old age, lengthy IMV duration and LOS hospital were the factors that could cause prolonged ICU stay in these patients.

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Table-4: Univariate and multivariate logistic regression analysis.

	Univariate Logistic Regression					Multivariate Logistic Regression				
	Wald	OR	%95 CI	for OR	*p*-value	Wald	OR	%95 CI	for OR	*p*-value
Age (year)	1.415	1.012	0.992	1.033	0.234	5.825	1.041	1.008	1.076	0.016
Gender	0.718	0.814	0.506	1.310	0.397					
Inotropic agent support	45.737	5.362	3.362	8.724	<0.001	1.009	0.646	0.276	1.515	0.315
Need for hemodialysis	5.988	3.312	1.269	8.641	0.014	0.011	0.918	0.183	4.594	0.917
MV Duration	60.813	1.527	1.373	1.698	<0.001	42.630	1.571	1.372	1.799	<0.001
Length of Hospitalization	61.302	1.078	1.058	1.099	<0.001	27.319	1.067	1.042	1.094	<0.001
Antibiotic Use	7.662	2.499	1.306	4.779	0.006	0.246	0.800	0.331	1.932	0.620
Diuretic Use	8.555	2.378	1.331	4.249	0.003	0.025	1.064	0.494	2.293	0.874
Comorbidity	0.122	1.096	0.654	1.840	0.727					
APACHE II	5.440	1.037	1.006	1.070	0.020	0.049	0.994	0.942	1.049	0.824
SOFA score	0.013	1.006	0.911	1.111	0.908					
NUTRIC Score	4.020	0.866	0.753	0.997	0.045	2.287	0.850	0.689	1.049	0.130
MV need	0.001	-	-	-	0.996					
Chest X-ray finding	8.275	4.589	1.625	12.958	0.004	2.514	3.269	0.756	14.133	0.113
Constant	-	-	-	-	-	15.395	0.001			0.001

Wald: Test statistics.OR: Odds radio. CI: Confidence interval. Statistically significant p-values are in bold.

patients with LOS ICU at least 30 days who had a mean age of 66.93±19.85 years.[4] Older age had an effect on the probability of hospitalisation and LOS ICU in COPD patients.[14] Advanced age, co-morbidities, and socioeconomic deprivation are common factors associated with prolonged stay.[15] In the current study the mean age did not significantly differ in the two groups. However, multivariate logistic regression analysis indicated that the increase in age increased LOS ICU. While there is a correlation between age and increased mortality rates and a longer ICU stay, the ultimate outcome depends largely on the severity of the disease and other factors.

In a study with 3,925 patients, the mean LOS ICU was 10.2 days.[16] In a study comprising data from 1,150 centers in 88 countries, the mean ICU stay was 10 days.[17] In another study with 242 AECOPD ICU patients, the ICU stay was of 10 days or more.[18] In this study, the average length of stay in ICU was 6.63±7.9 days, which is lower than the literature. This situation has been attributed to the presence of a team experienced in pulmonary diseases, as our hospital used to be a specialty hospital for chest diseases.

APACHE II score, one of the scoring systems commonly used in ICU in terms of mortality, morbidity and prognosis, has been found effective in predicting LOS ICU.[19] The APACHE-II score is frequently used as a marker of mortality in AECOPD patients.[20] Additionally, malnutrition is common and associated with high mortality rates in patients with COPD due to pathophysiological changes, systemic inflammation, anorexia, inadequate energy intake and/or increased energy expenditure.[21] As malnourished patients are at a high risk of complications during their hospitalisation, LOS hospital also increases.[22] The current study observed that high APACHE-II score and low NUTRIC score may be the factors prolonging ICU stay in COPD patients.

The current study noted that patients who required IMV had a longer LOS ICU compared to those who did not require such intervention. For patients undergoing IMV, adequate enteral nutrition is provided according to the caloric deficit calculated daily. Makhoul et al. determined that most of the patients with an APACHE-II score of around 24 needed IMV. Consistent with the findings in the literature, the current study found a significant positive correlation between APACHE II score and the need for IMV, indicating that patients with a higher APACHE II score were more likely to require IMV during their ICU stay.[18] In a study done in Australia and New Zealand, it was observed that 20% AECOPD patients in ICUs required IMV.[23] In the current study, patients with a prolonged ICU hospitalisation had significantly higher rates of IMV ($p<0.001$) and longer IMV duration ($p<0.001$) compared to those who had an ICU stay of <10 days. Also, it was found that the need for long-term IMV may cause a prolonged ICU stay. With these findings, the importance of daily extubation trials and follow-up in IMV in the shortest possible time is understood. Patients who stayed in the general ward for a long time before being admitted to the ICU were more likely to stay in the ICU for a longer time and mortality.[24] The current study also found that the increased LOS hospital was one of the factors affecting the prolongation of LOS ICU. The LOS hospital may also have been affected by LOS ICU. There were patients who were were admitted to the ICU directly from an external centre or emergency, and required monitoring in the ICU for a long time. Providing purposeful interventions, such as early mobilisation, can reduce LOS hospital.

Upper or lower respiratory tract infection is considered to be one of the primary factors linked to an elevated risk of acute exacerbation of COPD.[18] A meta-analysis also showed that bacterial infections were an important risk factor for AECOPD.[25] In an observational study, in-hospital antibiotic use among patients with severe AECOPD was associated with a longer hospital stay.[26] The current study noted that patients with abnormal CXR during ICU stay had a longer duration of LOS ICU. Prolonged ICU hospitalisation was significantly higher in patients with pneumonic infiltrates and receiving antibiotics.

In a study in Turkey, the need for renal replacement therapy and the use of inotropic, vasopressor agents were found to be predictive factors for prolonged ICU stay.[27] In a large-scale study involving 16,018 patients from 13 countries in Europe, diuretic use was found to be one of the patient and care process factors with the highest impact on increased LOS hospital.[28] In the current study, it was seen that the need for inotropic agent support, diuretic agent use, and HD for prolonged ICU hospitalisation in AECOPD patients were significantly higher. In COPD patients, attention should be paid to fluid resuscitation and drug support appropriate to haemodynamics.

One of the other important factors that increase the frequency of hospitalisation is the presence of different diseases. A common and often fatal complication of COPD is lung cancer.[29] The main cause of lung cancer patients requiring ICU treatment is acute respiratory failure. One of the causes of acute respiratory failure is an acute exacerbation of COPD.[30] In the current study, when the patients' co-morbidities other than COPD were examined, it was found that LOS ICU was longer in patients with lung malignancies. The prolonged hospitalisation was not significantly associated with the comorbidity of other diseases.

The current study had limitations owing to its retrospective design. Depending on the socioeconomic status of COPD patients, LOS hospital may be longer. Prolonged hospitalisation can lead to an increased risk of nosocomial infections and may also elevate the likelihood of being admitted to the ICU. The current study lacked information on the socioeconomic status of patients.

Conclusion

Higher age, longer IMV duration and extended LOS hospital were found to be the predisposing factors that could cause prolonged ICU stay in AECOPD patients.

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MD, GED, MT, HS: All of the authors declare that they have all participated in the design, execution and analysis of the paper and that they have approved the final version.