RESEARCH ARTICLE

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Factors Affecting Mortality and Patient Outcome in Patients with COPD Followed in The Intensive Care Unit

ABSTRACT

Objective: COPD is characterized by exacerbation and may lead to intensive care unit admission in cases such as pneumonia and sepsis. While non-invasive mechanical ventilation is the first treatment option in intensive care units, it reduces mortality and hospitalization. In our study, we aimed to determine the factors affecting mortality in patients with COPD admitted to intensive care unit.

Methods: In our study, the data of patients admitted to the intensive care unit of Bolu Izzet Baysal State Hospital with COPD were evaluated retrospectively. Duration of intensive care unit stay, APACHE II score, comorbidities, need for noninvasive mechanical ventilation, CRP albumin ratio and leukocyte lymphocyte ratio were recorded.

Results: A total of 416 patients, including 177 (42.5%) women, were included in our study. Of the patients, 107 (25.7%) (Group 1) were admitted to ICU for COPD exacerbation, 183 (44%) (Group 2) for pneumonia and 126 (30.3%) (Group 3) for sepsis. Hypertension was the most common comorbidity in 112 patients (26.9%). Mortality was higher in patients with pneumonia and sepsis than in patients with COPD exacerbation. When all patients were compared according to prognosis, age, length of ICU stay, NLR, CAR and APACHE II scores were higher in patients who died. The duration of non-invasive mechanical ventilation was higher in patients with an episode of COPD, while mortality was higher in patients receiving invasive mechanical ventilation support.

Conclusions: While pneumonia and sepsis increase mortality in patients with COPD, NIMV has a favorable prognosis in these patients with encouraging results.

Keywords: Chronic Obstructive Pulmonary Disease Exacerbation, Non Inasive Mechanical Ventilation, Intensive Care Unit, CRP to Albümin Ratio, Neutrophil to Lymphocyte Ratio.

Yoğun Bakım Ünitesinde Takip Edilen KOAH'lı Hastalarda Mortalite Ve Hasta Sonuçlarını Etkileyen Faktörler

ÖZET

Amaç: KOAH alevlenme ile karakterize olup pnömoni ve sepsis gibi durumlarda yoğun bakım ünitesine yatışa neden olabilmektedir. Non-invaziv mekanik ventilasyon yoğun bakım ünitelerinde ilk tedavi seçeneği olmakla birlikte mortaliteyi ve hastanede kalış süresini azaltmaktadır. Çalışmamızda yoğun bakım ünitesine kabul edilen KOAH'lı hastalarda mortaliteyi etkileyen faktörleri belirlemeyi amaçladık.

Gereç ve Yöntem: Çalışmamızda Bolu İzzet Baysal Devlet Hastanesi yoğun bakım ünitesine KOAH tanısı ile yatırılan hastaların verileri retrospektif olarak değerlendirildi. Yoğun bakımda kalış süresi, APACHE II skoru, komorbiditeler, noninvaziv mekanik ventilasyon ihtiyacı, CRP albumin oranı ve lökosit lenfosit oranı kaydedildi.

Bulgular: Çalışmamıza 177'si (%42,5) kadın olmak üzere toplam 416 hasta dahil edilmiştir. Hastaların 107'si (%25,7) (Grup 1) KOAH alevlenmesi, 183'ü (%44) (Grup 2) pnömoni ve 126'sı (%30,3) (Grup 3) sepsis nedeniyle YBÜ'ye kabul edilmiştir. Hipertansiyon 112 hastada (%26,9) en sık görülen komorbidite olmuştur. Mortalite, pnömoni ve sepsis hastalarında KOAH alevlenmesi olan hastalara göre daha yüksekti. Tüm hastalar prognoza göre karşılaştırıldığında, ölen hastalarda yaş, YBÜ'de kalış süresi, NLR, CAR ve APACHE II skorları daha yüksekti. Non-invaziv mekanik ventilasyon süresi KOAH atağı olan hastalarda daha yüksekken, mortalite invaziv mekanik ventilasyon desteği alan hastalarda daha yüksekti.

Sonuç: KOAH'lı hastalarda pnömoni ve sepsis mortaliteyi artırırken, NIMV bu hastalarda olumlu bir prognoza sahiptir ve cesaret verici sonuçlar vermektedir.

Anahtar Kelimeler: Kronik Obstrüktif Akciğer Hastalığı Alevlenmesi, Noninaziv Mekanik Ventilasyon, Yoğun Bakım Ünitesi, CRP Albümin Oranı, Nötrofil Lenfosit Oranı.

INTRODUCTION

Chronic obstructive pulmonary disease (COPD) is a progressive disease caused by inflammation in the airways, with acute deterioration in lung function and respiratory symptoms, often requiring hospitalization. Although COPD is among the leading causes of morbidity in the world, it is the third most common cause of death in terms of the frequency of causes of death (1).

Since COPD frequently progresses with exacerbations, it causes a significant socioeconomic burden on patients and their relatives (2). Although mortality rates associated with COPD exacerbation vary in various studies, rates ranging between 11% and 32% have been reported (3-7). However, the need for mechanical ventilation is increasing in COPD patients with acute exacerbation (4-8).

Community-acquired pneumonia is one of the most common infectious diseases seen worldwide and ranks 8th among the leading causes of death in the world. Age, male gender, smoking and presence of comorbid diseases have been shown to increase mortality in pneumonia patients.

In COPD patients with pneumonia, mortality rates vary from study to study. Some studies have shown that the presence of pneumonia increases morbidity and mortality, while others have not found a statistically significant difference. The use of noninvasive mechanical ventilation (NIMV) significantly reduces the need for invasive mechanical ventilation in patients with acute exacerbation of COPD. However, the accompaniment of conditions such as pneumonia, ARDS, pulmonary embolism, extrapulmonary sepsis in COPD exacerbation increases the need for invasive mechanical ventilation (4,12).

Sepsis is a dysregulated host response to infection and causes life-threatening organ dysfunction. Underlying comorbidities, corticosteroid use, anticholinergic drug use, smoking history and impaired barrier function in the respiratory tract have been shown to be risk factors for sepsis in patients with COPD (12,13).

The aim of our study was to investigate the mortality difference between patients admitted to the intensive care unit (ICU) due to COPD exacerbation and patients with COPD and concomitant pneumonia or patients hospitalized in the ICU due to COPD and concomitant extrapulmonary sepsis and the factors affecting the course of the disease.

MATERIAL AND METHODS

Data of 416 patients with COPD in Adult ICUs of Bolu Izzet Baysal State Hospital between January 2018 and December 2020 were retrospectively analyzed. Age, gender, duration of ICU stay, comorbidities, discharge status, types of respiratory support, neutrophil lymphocyte ratios (NLR), CRP albumin ratios (CAR), APACHE II scores and ICU hospitalization diagnoses were recorded. Patients were divided into 3 groups according to their hospitalization diagnoses: COPD exacerbation patients with respiratory failure and no signs of infection were divided into group l, COPD+pneumonia patients with respiratory failure according to imaging method and infection parameters were divided into group ll, and COPD+sepsis patients according to infection parameters, hemodynamic instability and culture growth were divided into group lll. Patients with missing data, patients under 18 years of age and patients with Covid-19 were excluded from the study. Bolu İzzet Baysal University Clinical Research Ethics Committee approval was obtained for the study (decision no: 2021/282, date: 21,12,2021).

Results were presented as mean ± SD. SPSS 18.0 package program was used to evaluate the data. $P<0.05$ values were considered significant. Pearson Chi-Square and Fisher's Exact test were used for comparison. Mann-Whitney U analysis with Bonferroni correction was performed to find out which groups were responsible for the differences. Kruskal Wallis H analysis was used in groups that did not show normal distribution.

RESULTS

A total of 416 patients, including 177 (42.5%) women, were included in our study. Of the patients, 107 (25.7%) (Group 1) were admitted to ICU for COPDexacerbation, 183 (44%) (Group 2) for pneumonia and 126 (30.3%) (Group 3) for sepsis. The most common comorbidity was hypertension (HT) in 112 patients (26.9%), followed by diabetes mellitus (DM), heart disease (CH) and malignancy. The mortality rate of the patients included in our study was 39.2%. Of the patients admitted to the ICU, 134 (32.2%) were treated with NIMV only, 48 patients were intubated at the time of ICU admission, and 234 patients were treated with IMV because they were treated with NIMV at the time of ICU admission and failed. The mean age of the patients included in the study was 74.73 (±11.11) years and the mean length of ICU stay was 12.52 (±12.94) days. The characteristics of the patients at admission and follow-up are shown in Table 1.

When we compared the patients according to their hospitalization diagnoses, there was no difference in terms of gender in all three groups, while mortality was significantly higher in group 2 and group 3. When we compared comorbidities, we found that patients with DM were significantly more in group 3. While NIMV success was higher in group 1, more IMV support was required in group 2 and group 3. Comparison of all 3 groups in terms of gender, mortality, comorbidity and respiratory support is shown in Table 2.

Table 1. Characteristics of Cases in Intensive Care Admission and Follow-up

		n	%
Tanı	Group 1	107	25.7
	Group 2	183	44.0
	Group 3	126	30.3
Discharge status	Discharged	253	60.8
	Deceased	163	39.2
Gender	Female	177	42.5
	Male	239	57.5
Comorbidities	HT	112	26.9
	DM	86	20.7
	CD	51	12.3
	Malignancy	32	7.7
Only NIMV		134	32.2
Only lMV		48	11.5
NIMV+lMV		234	56.3
		Mean.±SD	(Min.-Max.)
Age		74.73±11.11	(18-100)
Length of Stay		12.52±12.94	(3-88)
NLR		16.82±19.76	(1-330)
CAR		27.06±25.54	(1-155)
APACHE II		21.38±6.6	(6-38)

NLR: Neutrophil to lymphocyte ratio, CAR: CRP to Albumin ratio, HT: Hypertension, DM: Diabetes mellitus, Cardiac disease, NIMV Non inavasive mechanical ventilation, IMV: Invasive mechanical ventilation

Table 2. Distribution of gender, discharge, comorbidity, NIMV and IMV rates according to groups

		Group 1		Group 2		Group 3		p
		n	%	n	%	n	%	
Gender	Male	59	55.1	102	55.7	78	61.9	0.478
	Female	48	44.9	81	44.3	48	38.1	
Discharge status	Deceased	23	21.5	87	47.5	53	42.1	***0.000***
	Discharged	84	78.5	96	52.5	73	57.9	
Comorbidity		35	32.7	54	29.5	59	46.8	***0.006***
HT		25	23.4	45	24.6	42	33.3	0.148
DM		21	19.6	26	14.2	39	31	***0.002***
CD		14	13.1	19	10.4	18	14.3	0.563
Malignancy		5	4.7	15	8.2	12	9.5	0.362
NIMV		51	47.7	43	23.5	40	31.7	***0.000***
IMV		5	4.7	21	11.5	22	17.5	***0.010***

Pearson Chi-Square

When the relationship between the mortality status of the patients in our study and all 3 groups was analyzed, no relationship was found with gender, while the presence of comorbidity was found to significantly affect mortality. When the three groups were analyzed separately, the presence of DM and HT in group 1 and the presence of all comorbidities in group 2 were associated with mortality. In group 3, comorbidities were not associated with mortality. The comorbidity-mortality relationship in all 3 groups is shown in Table 3.

When the characteristics of the patients according to the groups were analyzed, no significant difference was found in terms of age and length of ICU stay. Group 1 had longer NIMV support, which was associated with benefiting from NIMV and being persistent. While NLR was higher in Group 3, CAR was significantly different in all three groups. APACHE II scores were significantly lower in group 1. The relationship between NIMV, NLR, CAR, APACHE II and length of hospitalization according to the groups is shown in Table 4.

Table 3. Distribution of gender, comorbidity, NIMV, and IMV rates according to the discharge status in all cases and groups

		Discharged		Deceased		p
		n	%	n	%	
All cases						
Cinsiyet	Male	154	60.9	85	52.1	0.079
	Female	99	39.1	78	47.9	
Comorbidity		75	29.6	73	44.8	***0.002***
HT		50	19.8	62	38.0	***0.000***
DM		38	15.0	48	29.4	***0.000***
CD		21	8.3	30	18.4	***0.002***
Malignancy		10	4.0	22	13.5	***0.000***
Group 1						
Gender	Male	50	59.5	9	39.1	0.081
	Female	34	40.5	14	60.9	
Comorbidity		22	26.2	13	56.5	***0.006***
HT		16	19.0	9	39.1	***0.044***
DM		10	11.9	11	47.8	***0.000***
CD		8	9.5	6	26.1	0.073
Malignancy		3	3.6	2	8.7	0.292
Group 2						
Gender	Male	55	57.3	47	54.0	0.657
	Female	41	42.7	40	46.0	
Comorbidity		18	18.8	36	41.4	***0.001***
HT		13	13.5	32	36.8	***0.000***
DM		9	9.4	17	19.5	***0.049***
CD		5	5.2	14	16.1	***0.016***
Malignancy		4	4.2	11	12.6	***0.037***
Group 3						
Gender	Male	49	67.1	29	54.7	0.157
	Female	24	32.9	24	45.3	
Comorbidity		35	47.9	24	45.3	0.768
HT		21	28.8	21	39.6	0.202
DM		19	26.0	20	37.7	0.160
CD		8	11.0	10	18.9	0.210
Malignancy		3	4.1	9	17.0	***0.015***

Pearson Chi-Square, Fisher's Exact test

Table 4. Mean distribution of age, hospitalization duration, NIMV days, NLR, CAR, and APACHE II scores according to the groups

	Group 1		Group 2		Group 3		p
	Mean.±SD	Median (Min.-Max.)	Mean.±SD	Median (Min.-Max.)	Mean.±SD	Median (Min.-Max.)	
Age	73.72±10.33	75 (46-92)	76.04±11.42	78 (18-100)	73.67±11.18	75,5 (22-95)	0.060
Length of Stay	11.17±11.69	7 (3-68)	12.84±12.6	8 (3-86)	13.21±14.36	8 (3-88)	0.192
NIMV day	3.68±2.31	3 (0-11)	2.85±2.2	2 (1-12)	3.05±2.13	2 (1-9)	***0.001***
NLR	15.39±31.62	10 (1-330)	15.23±11.28	12 (1-70)	20.36±15.67	17 (3-90)	***<0.001***
CAR	7.26±9.28	4 (1-60)	31±25.37	30 (1-155)	38.15±25.95	35 (2-150)	***<0.001***
APACHE II	19.55±5.84	18 (10-35)	21.92±7.08	22 (6-38)	22.15±6.21	20 (10-37)	***0.002***

Kruskal Wallis H analizi
NLR: Neutrophil to lymphocyte ratio, CAR: CRP to Albumin ratio

When all patients were compared according to discharge status, age, ICU length of stay, NLR, CAR and APACHE II scores were significantly higher in patients who exited. In surviving patients, the duration of NIMV was significantly higher. The relationship between mortality and variables is shown in Table 5.

Table 5. Mean distribution of age, hospitalization duration, NIV days, NLR, CAR, and APACHE II scores according to the discharge status

	Discharge status				p
	Discharged		Deceased		
	Mean.±SD	Median (Min.-Max.)	Mean.±SD	Median (Min.-Max.)	
Age	73.47±11.06	75 (18-96)	76.69±10.93	79 (41-100)	***0.002***
Length of Stay	9.51±9.06	6 (3-55)	17.2±16.27	12 (3-88)	***0.002***
NIMV day	3.38±2.35	2 (1-12)	21.6±11.82	2 (0-11)	***0.000***
NLR	15.64±22.23	11 (1-330)	18.66±15.03	14 (1-90)	***0.010***
CAR	19.97±19.49	11 (1-150)	38.06±29.67	35 (1-155)	***0.000***
APACHE II	18.55±5.23	18 (6-35)	25.79±6.08	27 (7-38)	***0.000***

Mann Whitney U analizi
NLR: Neutrophil to lymphocyte ratio, CAR: CRP to Albumin ratio

DISCUSSION

COPD is a progressive chronic disease that affects the respiratory system, reduces lung function, and frequently requires hospitalization. When the etiology of hospital admission in patients with severe COPD is analyzed, the most common etiology is COPD exacerbation, followed by pneumonia. The etiology of respiratory failure cannot be determined in 21% of patients (13). In COPD patients, pneumonia has been shown to prolong hospital stay, increase the need for mechanical ventilation, and increase mortality and ICU hospitalization rate (14). Sepsis is a state of dysregulated response to infection with poor long-term patient outcomes, high mortality, high frequency of hospital readmission, and impaired quality of life. Bacterial infections are common in COPD patients, either respiratory or non-respiratory. Underlying comorbidities, corticosteroid use, anticholinergic drug use, smoking history, and impaired barrier function in the respiratory tract have been shown as factors (12,13). In our study, 25.7% patients were followed up due to COPD exacerbation, 44% due to COPD and pneumonia, and 30.3% due to COPD and sepsis. While a mortality rate of 21.5% was found in our patients in the COPD exacerbation group, this rate was lower than in other COPD patients hospitalized with pneumonia or sepsis.

When the factors affecting mortality were evaluated, the duration of ICU stay and mean age were similar between the groups. The mortality rate was found to be higher in patients with comorbidities in terms of comorbidities, and the frequency of comorbidities was higher in group 2 and group 3, where mortality was higher in group 2 and group 3 with pneumonia or sepsis. In particular, it was found that the presence of DM significantly increased mortality and APACHE II scores of COPD patients with sepsis and pneumonia were higher.

In a study, ICU mortality rate was 9% and hospital mortality rate was 17% in patients admitted with COPD exacerbation. Another study found that the mortality rate of patients with a diagnosis of pneumonia and COPD who were followed up in the ICU (30.1%) was higher than those hospitalized for COPD alone (21.4%) (15,16).

Survival was found to be significantly correlated with APACHE II score and presence of active malignancy in ICU patients (16). In our study, the presence of malignancy did not have a significant effect on survival among the 3 groups. However, APACHE II value was found to be significantly lower in patients hospitalized with a diagnosis of COPD exacerbation and mortality was also found to be significantly lower in this group. It was observed that dyspnea and tachypnea developed more frequently in patients hospitalized in the ICU for pneumonia in the presence of male gender, advanced age and smoking. In these patients, the duration of ICU stay was found to be longer and the need for NIMV was also higher. In a 2018 study, hospital mortality of patients hospitalized with COPD and concomitant pneumonia was 8.3% and the 60-day mortality rate of the same group was reported as 12.6% (17). In another study, the 30-day mortality rate was found to be 8.4% in patients diagnosed with COPD and pneumonia, but it was also reported that no mortality difference was found between patients diagnosed with pneumonia alone and patients with COPD (16).

In a study by Keenan et al. it was reported that mortality was higher in patients with a diagnosis of COPD and comorbidities, while in another study by Patil et al. mortality was found to be higher in patients with cardiovascular disease (18,19). In our study, the presence of DM was found to be the most important reason increasing mortality.

Gadre et al. found that the mean number of days of hospitalization due to COPD was 20.7 days and the need for ICU developed in 14.3% of patients (15). In our study, the duration of ICU stay due to COPD exacerbation was found to be 11.17 days. However, no significant difference was found between the ICU length of stay in patients with pneumonia or extrapulmonary sepsis.

In the literature, there is no significant consistency between the ICU mortality rates of

COPD patients. However, there is a consensus that the presence of comorbidity, APACHE II elevation, age, and length of ICU stay affect mortality and morbidity. In addition, not only the ICU follow-up of the patients, but also their post-discharge care, treatment status and measures to be taken to prevent the disease have an effect on mortality and morbidity. In addition, other factors affecting mortality and morbidity include nutritional status of the patient, frequency of hospitalization, smoking status, and changes in lung reserve (10-21).

In the treatment of COPD exacerbation, NIMV is one of the proven methods because it reduces hypoventilation and corrects hypoxemia. In addition, it has been shown to reduce respiratory muscle fatigue by decreasing respiratory workload, decrease airway resistance, provide recruitment of collapsed alveoli and decrease dynamic hyperinflation with applied positive pressure (22,23). It has been found that respiratory acidosis regresses with the use of NIMV and the need for invasive mechanical ventilation decreases even in patients with severe acidosis.(10, 24)

Dai et al. reported that the need for NIMV, ICU admission and APACHE II score were higher in COPD patients admitted to ICU due to pneumonia compared to patients who developed only COPD exacerbation. It was reported that NIMV was associated with 60-day mortality and decreased the rate of intubation. In patients who failed NIMV ventilation and were intubated, the mortality rate reached 50% (17,25).

Gadre et al. found that the rate of invasive mechanical ventilation was lower and the duration of mechanical ventilation was shorter in patients admitted to the ICU due to COPD exacerbationcompared to patients hospitalized in the ICU for other reasons. They stated that pneumonia was the most common cause of clinical deterioration in COPD patients requiring IMV. In the same study, mortality rates were found to be 25% in patients requiring invasive mechanical ventilation and this rate was similar to ICU mortality rates. When COPD patients requiring IMV for other reasons were excluded, they stated that the epidemiology and outcomes of COPD patients could not be fully specified. They explained this situation as COPD being a comorbidity in ICU intubated patients and not the main reason for intubation (15).

There is a reluctance to apply invasive mechanical ventilation in clinicians who follow patients admitted to ICU with a diagnosis of COPD exacerbation. This may be due to the fear that if these patients are intubated, they may not be weaned from the mechanical ventilator for a long time or at all. It has been shown in a study that COPD patients who developed respiratory failure due to other causes and who underwent invasive mechanical ventilation were weaned from the mechanical ventilator for up to 3 days with the application of intermittent spontaneous breathing studies and sedation holidays, and that this period was even shorter in patients who were intubated only because of COPD exacerbation (15). In our study, the rate of NIMV application in patients with a diagnosis of COPD exacerbation only was found to be significantly higher than in COPD patient groups with pneumonia or sepsis. Similar to the aforementioned study, the reason for the insistence on NIMV was the clinician's belief that patients could not be weaned from invasive mechanical ventilation. We also think that this is due to the fact that non-COPD patients do not respond well to NIMV and need IMV support quickly.

In our study, 47.7% of our patients hospitalized with a diagnosis of COPD exacerbation received NIMV and only 4.7% needed invasive mechanical ventilation. 78.5% of these patients were discharged. On the other hand, the need for invasive mechanical ventilation was found to be higher in patients with pneumonia and sepsis.

Chronic inflammation and malnutrition are frequently seen in COPD patients. Therefore, it is thought that CAR may be used as a mortality marker in COPD patients admitted to ICU. In a study by Cırık et al. in which 235 COPD patients were evaluated, it was reported that CAR, APACHE II, duration of mechanical ventilation, WBC, CRP values were higher in patients who died compared to survivors. It has been reported that APACHE II, WBC, CRP and CAR can be used effectively in determining 30-day mortality(26). In other studies, it has been reported that CAR can be used as a mortality marker in critically ill patients with sepsis or septic shock who are followed up with parenteral nutrition (28). In our study, age, ICU length of stay, CAR, NLR and APACHE II values were found to be significantly higher in patients with exitus compared to survivors.

There are studies showing that high NLR in COPD patients is associated with exacerbation and is also an independent risk factor in determining mortality (6-8). NLR is thought to be a new inflammatory marker for the evaluation of inflammation in COPD patients because it is cheap, rapid and easily measurable. In our study, NLR value was found to be significantly higher in patients with exitus. We think that NLR can be used effectively in the evaluation of inflammation and mortality in COPD patients.

The limitations of our study include the fact that it was a single-center, retropective study, functional status, nutritional status, frequency of hospitalization, and smoking status of the patients before hospitalization were not known.

CONCLUSION

COPD is a costly disease that does not only progress exacerbation, and the presence of comorbidities and/or infection can worsen the condition, requiring hospitalization and ICU admission. Sometimes, although COPD is not the

reason for hospitalization, its presence as a comorbidity increases mortality or morbidity. We think that it is indisputably important to know that NIMV reduces the duration of hospitalization, duration of mechanical ventilation and mortality in these patients and to plan NIMV in patient management. Detection of pneumonia or sepsis in COPD patients are important factors that increase the need for invasive mechanical ventilation. Comorbidities such as DM and elevated APACHE II were also found to be factors increasing mortality. We think that the use of markers such as NLR and CAR will be useful in the evaluation of inflammation, detection of exacerbation and evaluation of mortality.

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