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ORIGINAL RESEARCH

Clinical characteristics and outcomes of hospitalized COVID-19 patients with COPD

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ABSTRACT

Background: Although COPD is not one of the most common comorbidities in COVID-19 patients, it can be more fatal in this group. This study aimed to investigate the characteristics and prognosis of COPD patients among the population with COVID-19.

Research design and methods: Patients diagnosed with positive PCR test were included in our multicentered, retrospective study. Patients with airway obstruction (previous spirometry) were included in 'COPD group'.

Results: The prevalence of COPD in COVID-19 patients was 4.96%(53/1069). There was a significant difference between COPD and non-COPD COVID-19 patients in terms of gender, mean age, presence of dyspnea, tachypnea, tachycardia, hypoxemia and presence of pneumonia. The mortality rate was 13.2% in COPD, 7% in non-COPD patients($p = 0.092$). The significant predictors of mortality were higher age, lymphopenia ($p < 0.001$), hypoxemia ($p = 0.028$), high D-dimer level ($p = 0.011$), and presence of pneumonia ($p = 0.043$) in COVID-19 patients.

Conclusions: Our research is one of the first studies investigating characteristics of COPD patients with COVID-19 in Turkey. Although COPD patients had some poor prognostic features, there was no statistical difference between overall survival rates of two groups. Age, status of oxygenization, serum D-dimer level, lymphocyte count and pneumonia were significantly associated parameters with mortality in COVID-19.

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1. Introduction

Coronavirus disease (COVID-19), which was first detected in China in December 2019, has rapidly spread worldwide. Since December 2020, severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) has infected over 78 million people, with more than 1,700,000 deaths globally [1]. The clinical manifestations may vary from mild to severe symptoms in COVID-19 patients [1]. Patients with advanced age, male sex, obesity, or several comorbidities (including diabetes mellitus, hypertension) are known to be at increased risk for severe outcomes related to COVID-19 [2].

Chronic obstructive pulmonary disease (COPD) is a common chronic airway inflammatory disease characterized by fixed airflow limitation and persistent respiratory symptoms [3]. In 2016, the prevalence of COPD was reported as 5.8%, with approximately 3.5 million physician-diagnosed COPD cases in Turkey [4].

As COVID-19 can more easily infect older patients with comorbidities, COPD is expected to be common in this patient group as well. However, data analyzing prevalence of the COPD population in patients with COVID-19 is highly limited and contradictory. The prevalence of COPD in COVID-19 patients had been reported to be 2–3% at the beginning of pandemic, in studies from China [5,6]. Later publications revealed a higher incidence between 8–16% of preexisting COPD [7,8].

During COVID-19 pandemic, studies mostly demonstrated that COPD was related with worse outcomes. A meta-analysis reported that COPD patients were more likely to have severe disease and increased risk of mortality compared to the general population [9]. There may be a few reasons why the course of COVID-19 in COPD patients has been worse. Firstly, COPD patients tend to be older and have more comorbidities which may increase COVID-19 severity [10]. In addition, respiratory failure and hypoxemia, which are the most important causes of death in COVID-19 patients, are more common in COPD patients [11]. However, only a few data exist about the prognosis of COVID-19 patients having COPD.

Our study aimed to determine the prevalence of COPD in patients with COVID-19 and to demonstrate clinical features and outcomes in COVID-19 patients with or without COPD.

2. Patients and methods

This multicenter (four centers), retrospective cohort study included hospitalized COVID-19 patients with positive nasal and/ornasopharyngeal swabs taken using real-time PCR (RT-PCR) assay kits at four different centers between March and August 2020. Ethics committee approval for the study was obtained from the Ethics Committee of the İzmir Katip Çelebi University Atatürk Training and Research Hospital, and permission for the study was obtained from the Ministry of Health of

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the Republic of Turkey. The requirement for informed consent was waived due to the retrospective design of the study.

All enrolled patients were aged above 18 years and were confirmed as SARS-CoV-2 RNA positive based on oro-nasopharyngeal swab specimens obtained using RT-PCR assays.

Demographics, clinical, laboratory, imaging examinations, and outcome data were obtained from the digital medical records of the hospitals participating in the study. Medical history before pandemic was recorded. Patients who were previously diagnosed with COPD during their follow-up and whose ratio of forced expiratory volume in 1 s to forced vital capacity (FEV1/FVC) was below 70% in the past pulmonary function test in the hospital system were included in 'COPD patient group'. The other group without COPD was named as the 'non-COPD COVID group'.

COVID-19 pneumonia was considered to be present in cases, with the thorax computed tomography (CT) report confirming the diagnosis. Radiological findings of pneumonia in the thorax CT were evaluated according to the COVID-19 pneumonia imaging classification laid out in the Radiological Society of North America Expert Consensus Statement [12].

The laboratory data in the present study included routine blood tests, such as complete blood count, biochemistry tests, blood clotting tests, and several infection-related parameters that were assessed at the time of admission. The initial values (at hospital admission) of these laboratory indices were collected for analysis in this study.

2.1. Definitions

Neutropenia is defined as an absolute neutrophil count below 2×10^9/L, and lymphopenia as blood lymphocytes lower than 1×10^9/L. Thrombocytopenia is defined as a platelet count below 150×10^9/L. The normal hemoglobin (Hb) level for males is 14–18 g/dL, and 12–16 g/dL for females. The lower Hb level is considered anemia.

An elevated transaminase level is considered to be a high serum level of alanine transaminase (>55 U/L) or aspartate transaminase (>35 U/L).

The normal serum creatinine level is considered to be 0.7–1.3 mg/dL in men and 0.6–1.1 mg/dL in women. Other biochemical parameters and their normal ranges are albumin 35–50 g/L, calcium (adjusted) 8.5–10.5 mg/dL, bilirubin (total) 0.2–1.2 mg/dL, sodium 135–145 mmol/L, potassium 3.5–-5.5 mmol/L, and lactate dehydrogenase (LDH) 220 U/L. The reference values of procalcitonin (PCT) is <0.15 ng/mL and c-reactive protein (CRP) < 0.5 mg/dL. In the present study, patients were also grouped according to their serum ferritin levels, with a cutoff of 500 ng/mL, and a D-dimer cutoff of >1000 µg/L, stated as poor prognostic criteria in the National Guidelines for COVID-19 [13].

2.2. Statistical analyses

Statistical analyses were performed using the SPSS Version 16.0. (Chicago, SPSS Inc.) software package. Baseline characteristics, including demographic data, the presence of symptoms, and radiological and laboratory findings, were summarized using descriptive statistics. The continuity correction chi-square test and a Fisher's exact test were used for the comparison of the frequency rates of the categorical variables of COPD and non-COPD patients with COVID-19. Pearson's correlation was used to assess the strength of the linear relationship between two variables. The primary outcome was mortality during hospitalization, and analyzed by the Kaplan–Meier method and a Cox-time-dependent Regression Model. Secondary outcomes included mechanical ventilation, intensive care unit admission and entubation. A p-value <0.05 was considered statistically significant.

3. Results

3.1. COPD subgroup

There were 53 patients with COPD among 1069 COVID-19 participants, with a prevalence of 4.96%. COPD subgroup consisted of 42 (79.2%) male and 11 (20.8%) female patients, with the mean age of 70.3 ± 11.4.

There were 33 (62.3%) patients who had at least one comorbidity other than COPD. Hypertension (34%) was the most common accompanying comorbidity.

Mean Body Mass Index (BMI) was 25.58 ± 4.06. There were 16 COPD patients (30.2%) with obesity according to BMI.

Median FEV1 value was 53.0 ± 16.5%. There were 5.9% mild, 52.9% moderate, 32.4% severe and 8.8% very severe COPD patients according to the spirometric classification. Thirty-five COPD patients (66%) told at least *one COPD exacerbation* in the previous year. There were 27 patients (51%) in Group D, 2 patients (3.8%) in group C, 13 patients (24.5%) in group B, and 11 patients (20.7%) in group A according to the combined assessment. Inhaled corticosteroid (ICS) treatment had been used by 40 COPD patients (75.5%).

There was a significant high requirement of noninvasive ventilation (NIV) in COPD patients with group C or D ($p = 0.049$). Relationship between prognosis and characteristics of COPD patients with COVID-19 is in (Table 1.).

3.2. Comparison of COVID-19 patients with and without COPD

There was a significant difference between COPD and non-COPD patients with COVID-19 in terms of gender ($p = 0.002$), mean age ($p < 0.001$), presence of dyspnea ($p < 0.001$), tachypnea ($p = 0.033$), tachycardia ($p = 0.009$), and hypoxemia ($p < 0.001$) at hospital admission. (Table 2) shows the features of these two groups.

Lymphopenia ($p = 0.041$), anemia, hypoalbuminemia, and hyponatremia (all $p < 0.001$) were significantly more common in the COPD group than the non-COPD group. There were significantly more patients with elevated levels of LDH ($p = 0.032$), PCT ($p = 0.040$), D-dimer (> 1000 µg/L), and CRP ($p < 0.001$) in the COPD patients with COVID-19. The rate of COPD patients with COVID-19 pneumonia and having multifocal involvements according to thorax CT was significantly higher than that of non-COPD COVID-19 patients ($p < 0.001$ and $p = 0.040$, respectively). (Table 3) presents the numerous

Table 1. Relationship between prognosis and characteristics of COPD patients with COVID-19.

Features		Survivors (n = 46) n, %	Non-survivors (n = 7) n, %	p value	Requirement of NIV (n = 13) n, %	No requirement of NIV (n = 40) n, %	p value	Admission to ICU (n = 9) n, %	No Admission to ICU (n = 44) n, %	p value
Gender	**male**	38, 82.6%	4, 57.1%	0.071	10, 77%	32, 80%	0.354	6, 66.7%	36, 81.8%	0.177
	female	8, 17.4%	3, 42.9%		3, 23%	8, 20%		3, 33.3%	8, 18.2%	
Hypertension	**present**	16, 34.8%	2, 28.6%	0.492	6, 46.2%	12, 30%	0.112	5, 55.6%	13, 29.5%	0.088
	not	30, 65.2%	5, 71.4%		7, 53.8%	28, 70%		4, 44.4%	31, 71.5%	
Obesity	**present**	11, 23.9%	2, 28.6%	0.738	3, 23.1%	10, 25%	0.504	2, 28.6%	11, 25%	0.644
	not	35, 76.1%	5, 71.4%		10, 66.9%	30, 75%		7, 71.4%	33, 75%	
Spirometric classification	**FEV1>%50**	26, 56.5%	5, 71.4%	0.536	8, 62.5%	23, 57.5%	0.627	4, 44.4%	27, 61.4%	0.388
	FEV1<%50	20, 43.5%	2, 28.6%		5, 37.5%	17, 42.5%		5, 55.6%	17, 38.6%	
Combined classification	**group A-B**	22, 47.8%	2, 28.6%	0.321	3, 23%	31, 52.5%	**0.049***	4, 44.4%	22, 45.5%	0.526
	group C-D	24, 52.2%	5, 71.4%		10, 77%	19, 47.5%		5, 55.6%	24, 54.5%	
Usage of ICS	**yes**	34, 73.9%	6, 85.7%	0.203	10, 77%	30, 75%	0.621	6, 66.7%	34, 77.3%	0.343
	no	12, 26.1%	1, 14.3%		3, 23%	10, 25%		3, 33.3%	10, 22.7%	

COVID-19: Coronavirus disease 2019, COPD: Chronic obstructive pulmonary disease, NIV: Non-invazive ventilation, ICU: intensive care unit, FEV1: forced expiratory volume in one second, ICS: Inhaled corticosteroid.
* statistically significant

Table 2. Features of COPD and non-COPD in COVID-19 patients.

Features		COPD group (n = 53) (n, %)	Non-COPD group (n = 1016) (n, %)	p value
Gender	**M**ale	42 (79.2%)	**592** (58.3%)	0.052
	Female	11(20.8%)	424 (41.7%)	
Age (mean)		70.3 ± 11.4	54.5 ± 18.2	**<0.001***
Overweight	**Yes**	13 (24.5%)	254 (25%)	0.658
(BMI>	**No**	40 (75.5%)	762 (75%)	
Comorbidities <other than COPD>	**Present**	33 (18.9%)	498 (49%)	0.715
	Not present	20 (81.1%)	518 (51%)	
HT	**Present**	17 (32.1%)	245 (24.1%)	0.189
	Not present	36 (67.9%)	771 (75.9%)	
Presenting symptoms and vital signs		**COPD group (n = 53) (n, %)**	**Non-COPD group (n = 1016) (n, %)**	**p value**
Fever	**Present**	18 (34%)	498 (49%)	0.108
	Not present	35 (66%)	518 (51%)	
Cough	**Present**	38 (71.7%)	711 (70%)	0.796
	Not present	15 (28.3%)	305 (30%)	
Dyspnea	**Present**	43 (81.1%)	264 (26%)	**<0.001***
	Not present	10 (18.9%)	752 (74%)	
Tachypnea	**Present**	15 (28.3%)	142 (14%)	**0.033***
	Not present	38 (71.7%)	874 (86%)	
Tachycardia	**Present**	16 (30.2%)	122 (12%)	**0.009***
	Not present	37 (69.8%)	894 (88%)	
Hypotension	**Present**	3 (5.7%)	45 (4.4%)	0.821
	Not present	50 (94.3%)	971 (95.6%)	
Hypoxemia	**Present**	23 (43.4%)	207 (20.4%)	**<0.001***
	Not present	30 (56.6%)	809 (79.6%)	

COVID-19: Coronavirus disease 2019, COPD: Chronic obstructive pulmonary disease, HT: hypertansion, * statistically significant

differences in the laboratory and radiological findings of COVID-19 patients with or without COPD.

The mortality rate was 13.2% in COPD and 7% in non-COPD patients (p = 0.092). The usage of NIV was significantly higher in COVID-19 patients with COPD (p = 0.001). The subgroup, including COPD patients with hypoxemia at hospital admission, had significantly higher rates of mortality (p < 0.001). (Table 4) demonstrates the prognosis of patients with COVID-19.

On multivariable Cox regression analysis, significant predictors of mortality were higher age, lymphopenia (p < 0.001), hypoxemia (p = 0.028), high D-dimer level (p = 0.011), and presence of pneumonia (p = 0.043) in patients with COVID-19 (Table 5).

Kaplan-Meier analysis showed no significant difference between overall survival rates of COVID-19 patients with or without COPD (H 1.878; 95% CI 0.811–4.346, p = 0.141).

4. Discussion

This is a multicentered, retrospective cohort study exploring the features of COPD patients in hospitalized COVID-19 population. Our data confirmed that approximately 5% of patients with SARS-CoV-2 were diagnosed with COPD. There were some demographic, symptomatic, laboratory and radiological differences between COPD and non-COPD patients with COVID-19. Although COPD patients with COVID-19 had some poor prognostic features, there was no statistical difference between overall survival rates of COVID-19 patients with or without COPD. Significant predictors of mortality were high age, hypoxemia and presence of pneumonia in patients with COVID-19.

Our study revealed the prevalence of COPD in patients with COVID-19 as 4.96%. Different results have been recorded about COPD prevalence in a population infected with SARS-CoV-2 according to COVID-19 studies worldwide. The incidence of COPD has been reported between 2% and 16% in several studies [5,8]. Our results about prevalence appear to be reliable since we accepted a confirmed diagnosis using a previous obstructive spirometric pattern (FEV1/FVC <70%) and not by a personal statement.

In our study, patients with COPD had male dominance when compared with non-COPD patients with COVID-19. Males were more likely to smoke and have an emphysema-predominant phenotype than females, which may explain COPD is more common in men [14]. Besides, patients with COVID-19 are most commonly males, as SARS-CoV-2 infection is through ACE2 receptor, which is expressed at higher levels in men than in women [15].

Dyspnea and cough were the most commonly observed symptoms on admission in our cohort of COPD patients. The most common clinical findings at the onset of illness were fever, cough, and fatigue in patients with COVID-19 [16]. COVID-19 pneumonia usually manifests with a sudden onset of fever and productive cough [17]. As COPD is a disease of the airways, respiratory symptoms such as cough and shortness of breath are frequent.

Low lymphocyte count and high D-dimer level in blood were the laboratory parameters significantly associated with mortality in COVID-19. Lymphopenia on admission has been associated with poor outcomes in patients with COVID-19. *Attaway et al*. found an increased rate of COVID-19 positivity in the COPD cohort with a lower absolute lymphocyte count [18]. D-dimer, with a cutoff of > 1000 µg/L, is stated as poor

Table 3. Laboratory and radiological findings of COVID-19 patients according to the presence of COPD.

Laboratory findings		COVID-19 patients with COPD (n = 53) (n,%)	COVID-19 patients without COPD (n = 1016) (n,%)	p value
Neutropenia	**Present**	6 (2.5%)	37 (6%)	0.052
	Not present	236 (97.5%)	581 (94%)	
Lymphopenia	**Present**	14 (26.4%)	160 (15.8%)	**0.041***
	Not present	39 (73.6%)	856 (84.2%)	
Thrombocytopenia	**Present**	10 (18.9%)	172 (16.9%)	0.715
	Not present	43 (81.1%)	844 (83.1%)	
Anemia	**Present**	15 (27.8%)	102 (10.1%)	**<0.001***
	Not present	38 (72.2%)	914 (89.9%)	
Elevated aminotransferase levels	**Present**	18 (34%)	275 (27.1%)	0.273
	Not present	35 (66%)	741 (72.9%)	
High serum creatinine level	**Present**	12 (23.5%)	149 (14.6%)	0.081
	Not present	41 (76.5%)	867 (85.4%)	
Hypoalbuminemia	**Present**	23 (43.4%)	207 (20.4%)	**<0.001***
	Not present	30 (56.6%)	809 (79.6%)	
Hyponatremia	**Present**	23 (43.4%)	222 (21.9%)	**<0.001***
	Not present	30 (56.6%)	794 (78.1%)	
High serum LDH level	**Present**	30 (56.6%)	432 (42.5%)	**0.032***
	Not present	23 (43.4%)	584 (57.5%)	
High CRP level	**Present**	49 (92.5%)	703 (69.2%)	**<0.001***
	Not present	4 (7.5%)	313 (30.1%)	
High Procalcitonin level	**Present**	27 (51.2%)	210 (20.7%)	**0.040***
	Not present	26 (48.8%)	806 (79.3%)	
Serum Ferritin Level (> 500 ng/mL)	**Present**	12 (22.7%)	127 (12.5%)	0.067
	Not present	41 (77.3%)	889 (89.9%)	
Serum D-dimer Level (> 1000 µg/L)	**Present**	16 (30.4%)	127 (12.5%)	**<0.001***
	Not present	37 (69.6%)	889 (87.2%)	
Radiological CT findings	**Yes**	47 (88.5%)	839 (82.6%)	**<0.001***
	No	6 (1.5%)	177 (17.4%)	
Presence of pneumonia				
Multifocal involvement	**Yes**	12 (96.7%)	835 (82.2%)	**0.040***
	No	45 (3.3%)	181 (16.7%)	
Ground-glass opacities	**Yes**	46 (86.7%)	994 (97.8%)	0.518
	No	7 (13.3%)	22 (2.2%)	
Peripheral lesions (only)	**Yes**	40 (76.7%)	660 (65%)	0.682
	No	13 (23.3%)	356 (35%)	
Bilateral involvement	**Yes**	39 (90.9%)	833 (82%)	0.444
	No	14 (9.1%)	183 (18%)	

COVID-19: coronavirus disease, LDH: lactate dehydrogenase, CRP: c-reactive protein, CT: computed tomography, * statistically significant

Table 4. Prognosis of COVID-19 patients with and without COPD.

Features		COPD group (n = 53) (n, %)	Non-COPD group (n = 1016) (n, %)	p value
Admission to the internal care unit	**Yes**	9 (79.2%)	115 (58.3%)	0.186
	No	44(20.8%)	901 (41.7%)	
Length of hospital stay (days)		10.06 ± 4.04	11.05 ± 5.42	0.291
Usage of NIMV	**Yes**	13 (18.9%)	92 (49%)	**0.001***
	No	40 (81.1%)	924 (51%)	
Intubation history	**Yes**	8 (34%)	89 (49%)	0.102
	No	45 (66%)	927 (51%)	
Mortality	**Yes**	7 (71.7%)	71 (70%)	0.092
	No	46 (28.3%)	945 (30%)	

COVID-19: coronavirus disease, COPD: chronic obstructive pulmonary disease, NIV: noninvasive ventilation
* statistically significant

Table 5. Risk of death (OR and 95% CI) in COVID-19 patients adjusted by covariates in models of logistic regression multivariate analyses.

Variable	β	SE	Wald	Sig.	Exp(β)	95.0% CI for Exp(β)	
						Lower	Upper
Age	0.038	0.010	15.084	**<0.001***	1.039	1.019	1.059
Hypoxemia	0.687	0.313	4.804	**0.028***	1.987	1.076	3.672
Presence of pneumonia	1.474	1.028	2.059	**0.048**	4.369	0.583	32.731
High D-dimer level	0.749	0.295	6.432	**0.011***	2.115	1.185	3.772
Lymphopenia	1.103	0.276	15.963	**<0.001***	3.013	1.754	5.175

Variables included in the model: COPD, Age, Gender, Hypoxemia, Presence of pneumonia, High D-dimer level (> 1000 µg/L), lymphopenia (<1 × 10^9/L).
COVID-19: coronavirus disease, COPD: chronic obstructive lung diseases, CI: confidence interval, OR: odds ratio
* statistically significant
# at hospital admission

prognostic criteria in the Turkish National Guideline for COVID-19 [8]. Since COPD and COVID-19 are chronic diseases with inflammatory processes and characterized by a hypercoagulable state, D-dimer levels may be higher in both situations.

Our results showed that patients with COPD were associated with worse prognosis (as determined by higher rates of NIV requirement and mortality). The presence of COPD was significantly associated with an increased risk of adverse outcomes among patients with COVID-19 in previous studies [19]. *Zhao et al*. revealed a 4.4-fold increased risk of severe COVID-19 and poor outcomes in COPD patients with COPD [20]. As patients with COPD have lower basal lung functions, abnormal lung structures, and weak immune systems owing to pathologic changes such as emphysema and chronic inflammation of the airways, infection by SARS-CoV2 may result in a poor prognosis [21].

The requirement of NIV was significantly higher in the COPD group than the non-COPD group in our study. It was reported that 5% of patients infected by SARS-CoV2 required ventilatory support during their hospitalization [22]. *Xiao et al*. revealed a 16% requirement of NIV support in COVID-19 patients with chronic respiratory diseases [19]. NIV is suggested in COPD patients (having COVID-19) with acute hypoxemic respiratory failure if oxygen therapy fails [23]. As patients with COPD have a higher risk of developing a severe COVID-19 disease requiring oxygen therapy, the need for mechanical ventilator support also becomes higher in this group.

There was a higher mortality rate in COVID-19 patients with COPD (13.2% vs. 7%); however, preexisting COPD was not a risk factor for death according to the Kaplan Meier and Cox regression analysis. COPD was considered as a risk factor for death in patients with severe COVID-19 [15]. *Attaway et al*. revealed no significant difference in-hospital mortality risk of COPD patients with COVID-19 when compared with non-COPD ones [18]. However, there have been some studies that demonstrated a tendency to higher mortality in COVID-19 patients with COPD [24]. Our results demonstrated that initially, hypoxemic patients with COPD were more likely to die during hospitalization owing to COVID-19, which supports the study by *He et al* [15].

One of the significant predictors of mortality was higher age in patients with COVID-19, according to our results. Several studies approved high age as a risk factor for COVID-19 related mortality [25,26]. *Graziani et al*. demonstrated that patients with COPD and COVID-19 (with the mean age of 75) had significantly higher risk or mortality than their non-COPD participants with the mean age of 66 [27]. National Guideline for COVID-19 issued by Scientific Advisory Board on Coronavirus affiliated with the Turkish Health Ministry recommended to hospitalize and monitor patients with COVID-19 aged above 50 years, owing to a high risk of severe disease and complications such as mortality [8]. Therefore, elderly patients need careful observation and early intervention to prevent the poor prognosis of COVID-19.

Our study showed that hypoxemia, which was significantly higher in the COPD group, was also observed as a dependent risk factor of mortality in all patients with COVID-19. COPD is a chronic airway disease characterized by the destruction of lung tissues; therefore, hypoxemia may be a common clinical finding in patients with COPD. SARS-CoV-2 can cause serious damage to the respiratory system, particularly with the development of pneumonia. Severe hypoxemia affected most of the patients with COVID-19 who were admitted to critical care, which makes it an important predictor of mortality in critically ill patients [28]. Therefore, clinicians should be more cautious in initially hypoxemic patients infected with SARS-CoV-2, particularly those with preexisting chronic lung disease, owing to the possibility of a poor prognosis.

Most COPD patients with COVID-19 were found to have pneumonia (generally with multifocal lung involvement) statistically higher than those in the non-COPD group, which was also demonstrated as a predictor for high mortality in both groups. COPD patients have an increased risk of severe and extensive pneumonia when they develop COVID-19, which may be related to poor underlying lung capacity or increased expression of ACE-2 receptors in small airways [29]. Non-pneumonia COVID-19 predominantly occurred among young adults with mild clinical symptoms and without underlying conditions [30]. *Melendi et al*. showed that most COVID-19 patients without pneumonia did not develop critical disease or die during hospitalization; however, 4% had a severe disease during follow-up [31]. A significantly good prognosis was observed in COVID-19 patients without pneumonia, similar to our study; however, unfavorable clinical progression may develop even among this group.

This study has some limitations. First, the baseline characteristics of patient groups were not equal numerically. Additionally, the sample size is limited for comparison.

Second, the COPD group had a higher mean age, which may affect the comparisons of study endpoints. Third, being a retrospective study is another handicap. A prospective cohort study with an equal number of COVID-19 patients with and without COPD is still required.

5. Conclusion

Our research is a multicentered, retrospective cohort study, which was one of the first to investigate the prevalence and characteristics of COVID-19 patients with COPD in Turkey. COPD is not one of the most common comorbidities in patients with COVID-19; however, COVID-19 can have worse prognosis in this patient group. Although COPD patients with COVID-19 had some poor prognostic features, there was no significant difference between overall survival rates of COVID-19 patients with or without COPD. Significant predictors of mortality were high age, hypoxemia, high serum D-dimer level, low lymphocyte count and presence of pneumonia in hospitalized patients with COVID-19.

Author contributions

OT: conception and design, analysis and interpretation of the data; the drafting of the paper and the final approval of the version to be published.

BAY, PAT, AM: revising critically for intellectual content.

Declaration of interest

The authors have no relevant affiliations or financial involvement with any organization or entity with a financial interest in or financial conflict with the subject matter or materials discussed in the manuscript. This includes employment, consultancies, honoraria, stock ownership or options, expert testimony, grants or patents received or pending, or royalties.

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References

1. Coronavirus Worldometer. [cited 2020 Dec 23]. Available from: www.worldometers.info/coronavirus/Date
2. Guan WJ, Ni ZY, Hu Y, et al. China medical treatment expert group for Covid-19. Clinical characteristics of coronavirus disease 2019 in China. N Engl J Med. 2020 Feb 28;382(18):1708–1720.
3. Global strategy for the diagnosis. Management and prevention of chronic obstructive pulmonary disease, Global initiative for chronic obstructive lung disease (GOLD). 2020. Available from: http://www.goldcopd.org/. Cited 2020 Oct 20.
4. Özdemir T, Demirci NY, Kiliç H, et al. An epidemiologic study of physician-diagnosed chronic obstructive pulmonary disease in the Turkish population: COPDTURKEY-1. Turk J Med Sci. 2020 Feb 13;50 (1):132–140.
5. Wang D, Hu B, Hu C, et al. Clinical characteristics of 138 hospitalized patients with 2019 novel coronavirus–infected pneumonia in Wuhan, China. JAMA. 2020;323(11):1061–1069. http://dx.doi.org/10.1001/jama.2020.1585
6. Guan W, Liang W, Zhao Y, et al. Comorbidity and its impact on 1590 patients with Covid-19 in China: a nationwide analysis. Eur Respir J. 2020;55(5):2000547.
7. Signes-Costa J, Núñez-Gil IJ, Soriano JB, et al. HOPE COVID-19 investigators. Prevalence and 30-Day mortality in hospitalized patients with Covid-19 and prior lung diseases. Arch Bronconeumol. 2020 Dec 16:S0300–2896(20)30535–4. Epub ahead of print. PMID: 33423874; PMCID: PMC7744014. DOI:10.1016/j.arbres.2020.11.012
8. Onder G, Rezza G, Brusaferro S. Case-fatality rate and characteristics of patients dying in relation to COVID-19 in Italy. JAMA. 2020. DOI:10.1001/jama.2020.4683
9. Zhang JJ, Dong X, Cao YY, et al. Clinical characteristics of 140 patients infected with SARS-CoV-2 in Wuhan, China. Allergy. 2020;75(7):1730–1741. Epub 2020/02/23PubMed PMID:32077115
10. Alqahtani JS, Oyelade T, Aldhahir AM, et al. Prevalence, severity and mortality associated with COPD and smoking in patients with COVID-19: a rapid systematic review and meta-analysis. PLoS ONE. 2020;15(5):e0233147. Epub 2020/05/12PubMed PMID:32392262
11. Edis EÇ. Chronic pulmonary diseases and COVID-19. Turk Thorac J. 2020;21(5):345–349.
12. Simpson S, Kay FU, Abbara S, et al. Radiological society of North America expert consensus statement on reporting chest CT findings related to COVID-19. Endorsed by the society of thoracic radiology, the American College of Radiology, and RSNA - secondary publication. J Thorac Imaging. 2020 Jul;35(4):219–227.
13. COVID-19 Guideline: management of Severe Pneumonia, ARDS, Sepsis and Septic Shock [online]. Ministry of Health, Turkey. [cited 2020 Nov 2]. Available from: https://covid19bilgi.saglik.gov.tr/tr/
14. Jain NK, Thakkar MS, Jain N, et al. Chronic obstructive pulmonary disease: does gender really matter? Lung India. 2011;28(4):258–262.
15. He Y, Xie M, Zhao J, et al. Clinical characteristics and outcomes of patients with severe COVID-19 and Chronic Obstructive Pulmonary Disease (COPD). Med Sci Monit. 2020 Sep;4(26):e927212. PMID: 32883943; PMCID: PMC7491229.
16. Zhang J, Wang X, Jia X, et al. Risk factors for disease severity, unimprovement, and mortality in COVID-19 patients in Wuhan, China. Clin Microbiol Infect. 2020;26(6):767–772.
17. Li X, Xu S, Yu M, et al. Risk factors for severity and mortality in adult COVID-19 inpatients in Wuhan. J Allergy Clin Immunol. 2020;146 (1):110–118.
18. Attaway A, Hatipoğlu U. Management of patients with COPD during the COVID-19 pandemic. Cleve Clin J Med. 2020 Jul 17. DOI:10.3949/ccjm.87a.ccc007. Epub ahead of print. PMID: 32393594.
19. Xiao WW, Xu J, Shi L, et al. Is chronic obstructive pulmonary disease an independent predictor for adverse outcomes in coronavirus disease 2019 patients? Eur Rev Med Pharmacol Sci. 2020 Nov;24 (21):11421–11427. PMID: 33215464.
20. Zhao Q, Meng M, Kumar R, et al. The impact of COPD and smoking history on the severity of Covid-19: a systemic review and meta-analysis. J Med Virol. 2020 Apr 15; https://doi:10.1002/jmv.2588 92(10): 1915–1921
21. Wu F, Zhou Y, Wang Z, et al. Medical treatment expert group for COPD and COVID-19. Clinical characteristics of COVID-19 infection in chronic obstructive pulmonary disease: a multicenter, retrospective, observational study. J Thorac Dis. 2020 May;12(5):1811–1823. PMID: 32642086; PMCID: PMC7330323.
22. Simons SO, Hurst JR, Miravitlles M, et al. Caring for patients with COPD and COVID-19: a viewpoint to spark discussion. Thorax. 2020

Dec;7512:1035–1039. PMID: 32878969; PMCID: PMC7474898 Epub 2020 Sep 2.
23. Lim JP, Low KYH, Lin NJJ, et al. Predictors for development of critical illness amongst older adults with COVID-19: beyond age to age-associated factors. Arch Gerontol Geriatr. 2021 Dec;24 (94):104331. Epub ahead of print. PMID: 33476755; PMCID: PMC7834606.
24. Zhou F, Yu T, Du R, et al. Clinical course and risk factors for mortality of adult inpatients with COVID-19 in Wuhan, China: a retrospective cohort study. Lancet. 2020;395 (10229):1054–1062.
25. Turan O, Mirici A. Chronic obstructive pulmonary disease and COVID-19. Eurasian J Pulmonol. 2020;22(Suppl 4):56–60.
26. Kang SJ, Jung SI. Age-related morbidity and mortality among patients with COVID-19. Infect Chemother. 2020;52(2):154–164.
27. Graziani D, Soriano JB, Del Rio-Bermudez C, et al. Characteristics and Prognosis of COVID-19 in Patients with COPD. J Clin Med. 2020 Oct 12;9(10):3259.
28. Mellado-Artigas R, Ferreyro BL, Angriman F, *et al*. High-flow nasal oxygen in patients with COVID-19-associated acute respiratory failure. Crit Care. 2021;25(1):58. DOI: 10.1186/s13054-021-03469-w
29. Leung JM, Niikura M, Yang CWT, et al. COVID-19 and COPD. Eur Respir J. 2020 Aug 13;56(2):2002108. PMID: 32817205; PMCID: PMC7424116.
30. Huang C, Wang Y, Li X, et al. Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. The Lancet. 2020;395 (10223):497–506.
31. Melendi SE, Pérez MM, Salas CE, et al. COVID-19 with and without pneumonia: clinical outcomes in the internal medicine ward. Medicina (B Aires). Aires B. 2020; 80(Suppl 6): 56–64. English. PMID: 33481734