ORIGINAL ARTICLE

Clinical Evaluation of Chronic Obstructive Pulmonary Disease Patients Hospitalized with COVID-19 Pneumonia

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Abstract

Background: Coronavirus disease 2019 (COVID-19) has been a challenging viral respiratory tract infection since 2019 and may contribute to higher mortality in patients with chronic obstructive pulmonary disease (COPD).

Methods: We analyzed the clinical data of 98 patients hospitalized with a diagnosis of COVID-19 and who had a previous diagnosis of COPD. They are grouped regarding GOLD ABCD stages, reported as follows whether in pandemic wards or intensive care units (ICU). The clinical outcomes were noted as a live hospital discharge or inhospital mortality.

Results: A total of 76 patients (77.6%) were in the pandemic wards, 22 (22.4%) were in the ICU. Around 81 (82.7%) patients survived, 17 (17.3%) were deceased. We grouped them as GOLD A and GOLD B and GLOD C, and GOLD D. Procalcitonin (PCT) level was higher and arterial oxygen partial pressure (PaO_2 in mm Hg) to fractional inspired oxygen (PaO_2/FiO_2) level was lower in the group of GOLD C and GOLD D than in GOLD A and GOLD B ($p < 0.005$). There was no statistically significant difference in inhospital mortality between these two groups ($p = 0.098$). While in the univariate model, hemoglobin (Hgb), urea, troponin, PCT, PaO_2/FiO_2, saturation%, and respiratory rate was observed to be significantly different; in the multivariate model, only a significant independent ($p < 0.05$) effect of PaO_2/FiO_2 were observed in distinguishing patients who survived or deceased.

Conclusion: Global Initiative for Chronic Obstructive Lung Disease (GOLD) ABCD groups are staging COPD patients in favor of predicting hospitalization and mortality. However, when COPD patients are hospitalized with COVID-19 pneumonia, different clinical factors and indices should be considered due to the heterogeneity and complexity of COPD.

Keywords: Chronic obstructive pulmonary disease, Coronavirus disease 2019, Mortality.

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Introduction

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is a novel coronavirus, highly transmitted through tiny droplets/aerosols or close contact.[1] The virus penetrates host cells by angiotensin-converting enzyme 2 (ACE2) receptors which are mostly present in the nasal goblet cells and type 2 alveolar cells (angiotensin II receptor type 2) that make SARS-CoV-2 infection a particular respiratory tropism.[2] COVID-19 may present as a mild viral illness but may progress to acute severe respiratory distress syndrome and death on the other side.[3] Several reports reveal that people with underlying lung disease and comorbidities like hypertension, diabetes, and obesity are prone to have severe clinical course and progression of COVID-19.[4] COPD is a long-term and treatable lung disease but is a global health problem as it is the number fourth leading cause of mortality worldwide.[5] The viral or bacterial respiratory infections may trigger exacerbations in COPD patients, which may worsen the disease. It is known that COPD is one of the strongest risk factors for getting community-acquired pneumonia which requires hospitalization.[6] As COPD is common in individuals >40 years, these COPD patients with coexisting systemic diseases and lower respiratory functional reserve may experience adverse clinical outcomes from SARS-CoV-2 infection. COVID-19 pneumonia has systemic and pulmonary disease components; these appear to be caused by endothelial and microvascular injury.[7] Although several studies have been conducted on the relationships between COPD and COVID-19 outcomes, it remains unclear. Somehow, in contrast with seasonal influenza epidemics, the negative effects of COVID-19 in COPD patients seem to be lower than expected.[8] We aimed to explore the impact of airflow limitation severity, exacerbation history, and laboratory findings of COPD patients who are hospitalized due to COVID-19 pneumonia.

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Materials and Methods

The study was conducted in a single-center tertiary hospital from March 2020 to February 2021 after the approval of the Ethics Committee. The study was carried out in compliance with the criteria of the Declaration of Helsinki. All the participants provided

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informed consent. We extracted the clinical data of 98 patients who have laboratory-confirmed SARS-CoV-2 infection and diagnosis of COVID-19 pneumonia, were admitted to the emergency room and then hospitalized and followed up either in the pandemic wards or ICU. All the patients enrolled in this study had a previous diagnosis of COPD according to GOLD Guideline criteria; which was confirmed by postbronchodilator airflow limitation; a ratio of the forced expiratory volume in the first second (FEV1) to the forced vital capacity (FVC), FEV1/FVC <0.7 using forced spirometry testing. The patients who had electronic health records of pulmonary function test (spirometry), COPD assessment test (CAT), and modified medical research council (mMRC) questionnaire scores, smoking status, exacerbation history of the previous year, and who were followed up by our chest disease outpatient department, constitute our study population. CAT and mMRC were used to measure the health status impairment and symptoms of COPD patients. We grouped the patients by combining the symptom score assessment with the patient's spirometric grading and/or risk of exacerbations regarding GOLD "combined CAT":

- GOLD A; symptoms score mMRC 0–1, CAT of <10, and exacerbation history 0 or 1 but did not need hospital admission.
- GOLD B; symptoms score mMRC of ≥2, CAT of ≥10, and exacerbation history 0 or 1 but did not need hospital admission.
- GOLD C; symptoms score mMRC 0–1, CAT of <10, and exacerbation history ≥2 or ≥1 needed hospital admission.
- GOLD D; symptoms score mMRC of ≥2, CAT of ≥10, and exacerbation history ≥2 or ≥1 needed hospital admission.

The most recent observation for each COPD patient was identified. All patients who did not meet the COPD diagnostic criteria or whose electronic data could not be extracted were excluded. Demographic features, comorbidities, vital signs, laboratory findings on the first day of admission, and clinical outcomes of the patients were all noted. For every single patient, medical records were reviewed *via* an electronic information system from hospital admission to discharge or death.

Statistics, mean, standard deviation, median lowest, highest, frequency, and ratio values were used in the descriptive statistics of the data. The distribution of variables was measured with the Kolmogorov–Smirnov test. Mann–Whitney *U* test and *t*-test were used in the analysis of independent quantitative data. Chi-squared test was used in the analysis of independent qualitative data, and Fischer's exact test was used when the Chi-squared test conditions were not met. The effect level was investigated by univariate and multivariate logistic regression. Statistical Package for the Social Sciences (SPSS) 22.0 program was used in the analysis.

Results

A total of 98 COPD patients were enrolled. The mean age of the patients was 70.2 ± 11.86 years. The number of males was dominant (68.4%). Patients were grouped into two, according to the FEV1/FVC ratio of <0.5 and the FEV1/FVC ratio of >0.5, regarding the airflow limitation. Again, the COPD composite assessment score of the patients in groups GOLD A and B were classified as mild regarding disease severity which had exacerbation history of 0 or 1 and had not been admitted to the hospital, and those in groups GOLD C and D were classified as severe who had exacerbation history of ≥2 or ≥1 but had required hospital admission. There were 57 patients with FEV1/FVC% <0.5 and 62 patients with a COPD composite assessment score of GOLD C and D that were noted as severe (Table 1). Hypertension and coronary artery disease were the

Table 1: Demographic characteristics of the patients

		*n**	*(%)*
Gender	Male	**67**	**68.4**
	Female	31	31.6
FEV1/FVC %	>0.5	41	41.8
	<0.5	57	58.2
COPD combined assessment	GOLD A and B	36	36.7
	GOLD C and D	62	63.3
Comorbidities	Hypertension	50	51.0
	Diabetes mellitus	33	33.7
	Coronary artery disease	36	36.7
	Chronic renal disease	10	10.2
	Cerebrovascular disease	4	4.1
	Malignity	7	7.1
Pandemic wards		76	77.6
ICU		22	22.4
Inhospital mortality	Deceased	17	17.3
	Survived	81	82.7
Smoking status	Smoking	24	24.5
	Nonsmoking	74	75.5
	Min–Max	*Median*	*Mean ± SD* †
Age	40–97	72.0	70.2 ± 11.86
Length of hospital stay (day)	1–148	10.0	14.3 ± 18.3

**n*, data set; †SD, standard deviation

most common chronic diseases in all COPD patients. After the diagnosis of COVID-19 with nasopharyngeal swabs in the emergency department, 76 patients were transferred to the pandemic wards, and 22 patients were transferred to the ICU according to their clinical status. The patient with the shortest hospitalization was found to be 1 day as he could not survive, and the longest hospitalization period for the patient was 148 days. Inhospital mortality was observed in 17 of 98 hospitalized patients included in the study (Table 1).

A total of 24 patients were currently smoking. The mean duration of hospital stay in the active smokers was 26.6 days, which was longer than the nonsmoker group with 10.3 days, and was found statistically significant ($p = 0.005$) (data not shown).

No statistically significant difference was noted between the mean age, gender distribution, and chronic diseases of the patients in the group presented as (GOLD A and B), and the group presented as (GOLD C and D) ($p > 0.05$). A statistically significant difference was found between the hematological parameters PCT level and PaO_2/FiO_2 ($p < 0.005$). In the group of GOLD C and D, the PCT level was high, and PaO_2/FiO_2 level was low. Although both groups had lymphopenia, there was no statistical difference between the groups. No statistically significant difference was found in inhospital mortality between these two groups ($p = 0.098$, 8.3, and 22.6%, respectively) (Table 2).

We compared the sociodemographic, clinical, and hematological parameters of patients who were deceased after follow-up and treatment or were discharged. There was no statistical difference between the deceased and survivor groups in terms of age and chronic diseases. But their vital signs, like fever, saturation%, and respiratory rate, were statistically significantly different at the time of admission to the emergency department ($p < 0.05$). Moreover, we found a statistically significant difference between these groups for hematological parameters such as Hgb, urea, PaO_2/FiO_2, PCT, and troponin levels ($p < 0.05$) (Table 3).

In the univariate model, a significant ($p < 0.05$) effect of the distribution of vital and hematological parameters such as Hgb, urea, troponin, PCT, PaO_2/FiO_2, saturation%, and respiratory rate was observed in distinguishing patients who survived or deceased. In the multivariate model, only a significant independent ($p < 0.05$) effect of PaO_2/FiO_2 was observed in distinguishing patients with and without inhospital mortality (Table 4).

Receiver operating curve (ROC) analysis was performed to show the usability of PaO_2/FiO_2 in predicting mortality in

Table 2: Laboratory findings, length of hospital stay, and inhospital mortality of the COPD patients according to GOLD stages

		GOLD A and B (n:36)		*GOLD C and D (n:62)*			
		Mean ± SD	*Median*	*Mean ± SD*	*Median*	*p-value*	
Age		69.94 ± 13.46	71.0	70.37 ± 10.93	72.0	0.889	**m**
Hgb		12.7 ± 2.42	12.6	12.1 ± 2.29	11.8	0.252	**m**
Lymphocyte		1.74 ±1.56	1.21	1.46 ± 1.17	1.11	0.393	**m**
NLR		6.63 ± 5.71	5.11	12.05 ± 18.04	6.64	0.148	**m**
CRP		77.3 ± 70.4	55.5	111.8 ± 86.2	109.5	0.066	**m**
Glucose		151.4 ± 65.7	131.0	142.3 ± 53.1	130.0	0.749	**m**
Urea		50.3 ± 46.9	37.5	57.6 ± 36.4	48.0	0.075	**m**
PO_2		82.3 ± 9.5	85.0	80.0 ± 12.3	81.5	0.376	**t**
PaO_2/FiO_2		248.9 ± 59.4	246.0	208.1 ± 36.8	210.0	0.001	**t**
PCO_2		44.5 ± 9.6	43.5	47.7 ± 11.7	44.0	0.229	**m**
Lactate		1.89 ± 0.9	1.65	1.77 ± 0.68	1.63	0.232	**m**
PCT		0.28 ± 0.51	0.13	2.99 ± 13.27	0.23	0.014	**m**
Ferritin		327.1 ± 402.3	193.0	324.0 ± 433.0	127.5	0.894	**m**
D-dimer		1672.4 ± 3367.2	771.5	1657.0 ± 1780.8	1045.0	0.072	**m**
Troponin		43.5 ± 60.0	13.5	60.0 ± 183.9	20.0	0.244	**m**
Length of hospital stay (days)		12.8 ± 15.4	8.0	15.2 ± 19.8	10.0	0.211	m
		n (%)		*n* (%)			
Gender	Male	27 (75%)		40 (64.5%)		0.395	χ^2
	Female	9 (25%)		22 (35.5%)			
Comorbidities	HT	21(58.3%)		29 (46.8%)		0.371	χ^2
	DM	14 (38.9%)		19 (30.6%)		0.541	χ^2
	CAD	11(30.6%)		25 (40.3%)		0.454	χ^2
	CRD	2 (5.6%)		8 (12.9%)		0.317	χ^2
	CVD	1(2.8%)		3 (4.8%)		1.000	χ^2
	Malignity	5 (13.9%)		2 (3.2%)		0.096	χ^2
Inhospital mortality		3 (8.3%)		14 (22.6%)		0.098	χ^2

CAD, coronary artery disease; CRD, chronic kidney disease; CRP, C-reactive protein; CVD, cerebrovascular diseases; DM, diabetes mellitus; Hgb, hemoglobin; HT, hypertension; m, Mann–Whitney *U* test; NLR, neutrophil/lymphocyte ratio; PaO_2/FiO_2, arterial oxygen partial pressure (PaO_2 in mm Hg) to fractional inspired oxygen (FiO_2); PCT, procalcitonin; PCO_2, arterial carbon dioxide partial pressure; PO_2, arterial oxygen partial pressure; t, *t*-test; χ^2, Chi-squared test

Table 3: Comparison of vital signs, laboratory findings, and demographic characteristics of survivors and nonsurvivors

		Inhospital mortality (n:17)		*Survived (n:81)*			
		Mean ± SD	*Median*	*Mean ± SD*	*Median*	*p*-value	
Age		74.76 ± 11.74	74.0	69.26 ± 11.73	72.0	0.291	m
Systolic blood pressure (mm Hg)*		123.50 ± 31.9	120	123.32 ± 17.8	120	0.528	m
Diastolic blood pressure (mm Hg)*		70.0 ± 16.0	72.5	75.0 ± 9.8	77.0	0.327	m
Heart Rate (beats/min)*		99.0 ± 15.4	100	93.9 ± 16.3	90.0	0.282	m
Vital findings fever temperature (degrees C)*		37.4 ± 0.72	37.3	36.9 ± 0.53	37.0	**0.031**	**m**
SpO_2 (percentage)*		83.9 ± 15.2	90.5	92.2 ± 5.49	94.0	**0.002**	**m**
Respiratory rate (breaths/min)*		28.0 ± 7.7	29.5	18.4 ± 5.0	16.0	**0.000**	**m**
Hgb		11.2 ± 2.61	10.8	12.53 ± 2.22	12.5	**0.016**	m
Hct		35.87 ± 8.92	33.5	38.79 ± 6.59	38.8	**0.059**	m
Urea		86.53 ± 65.9	56.0	48.27 ± 29.39	48.0	**0.001**	m
PaO_2/FiO_2		171.5 ± 29.3	176.0	234.7 ± 46.7	232	**0.001**	m
PCT		3.30 ± 7.8	0.91	1.71 ± 11.1	0.14	**0.003**	**m**
Troponin		179.4 ± 331.8	50	27.6 ± 62.7	13	**0.000**	m
			n	*n*			
Comorbidities	HT		9 (18%)	41 (82%)		0.862	χ^2
	DM		6 (18.2%)	27 (81.8%)		0.876	χ^2
	CAD		7 (19.4%)	29 (80.6%)		0.454	χ^2
	CRD		1 (10%)	9 (90%)		0.451	χ^2
	CVD		0 (0%)	4 (100%)		0.461	χ^2
	Malignity		1 (14.3%)	6 (85.7%)		0.650	χ^2
Pandemic wards			1 (1.3%)	75 (98.75%)		**0.000**	χ^2
ICU			16 (27.3%)	6 (72.7%)			

CAD, coronary artery disease; CRD, chronic renal disease; CVD, cerebrovascular diseases; DM, diabetes mellitus; Hct, hematocrit; Hgb, hemoglobin; HT, hypertension; m, Mann–Whitney *U* test; PCT, procalcitonin; PaO_2/FiO_2, ratio of arterial oxygen partial pressure (PaO_2 in mm Hg) to fractional inspired oxygen (FiO_2); SpO_2 (percentage), oxygen saturation; t, *t*-test; χ^2, Chi-squared test

Table 4: Univariate and multivariate analysis of laboratory findings of nonsurvivors

	Univariate model					*Multivariate model*				
Inhospital mortality	*OR*	*95% CI*			*p-value*	*OR*	*95% CI*			*p-value*
Respiratory rate	0.163	1.082	–	1.279	**0.000**					
Saturation of oxygen	–0.088	0.863	–	0.972	**0.004**					
PaO_2/FiO_2	–0.042	0.938	–	0.978	**0.000**	0.039	0.935	–	0.991	**0.010**
Hbg	–0.263	0.601	–	0.984	**0.037**					
Urea	0.020	1.006	–	1.034	**0.005**					
PCT	0.011	0.939	–	1.052	0.588					
Troponin	0.007	0.999	–	1.015	0.084					
CRP	0.005	0.998	–	1.011	0.140					
Ferritin	0.001	1.000	–	1.002	0.099					
D-dimer	0.006	1.000	–	1.010	0.065					

CI, confidence interval; forward LR, logistic regression; nagelkerke R^2, 0.72; OR, odds ratio

COVID-19-positive COPD patients and it was found to have a high significance in predicting mortality (area under the curve—0.89, $p < 0.005$, 95%GA—0.837–0.960). We found the associated PaO_2/FiO_2 value of <199.5, with sensitivity and specificity of 94 and 79%, respectively (Fig. 1).

Discussion

In our study, no significant age, gender, comorbidity, or length of hospital stay difference were noted between patients of COPD who were grouped as GOLD C and D and GOLD A and B, hospitalized with COVID-19. Although Pellicori et al. defined three variables—age, sex, and duration of hospital stay as predictive of mortality in patients with COPD exacerbation after hospitalization, our results are not in line with this.[9] Some reports suggest that COVID-19 may lead to an increased risk for exacerbation and worsen the condition of COPD, where some researchers have tried to explain the underlying mechanisms of how the virulence of SARS-CoV-2 impacts COPD exacerbation.[10] Moreover, we found no significant difference between these GOLD/ABCD groups for inhospital mortality.

We aimed to analyze the characteristics of hospitalization and the risk of survival in COPD patients who are hospitalized with the diagnosis of COVID-19 pneumonia. Pneumonia significantly contributes to more days of hospitalization in COPD patients, along with respiratory outcomes.[6] Several studies reveal that hospital admission with pneumonia has higher mortality rates than admission with an exacerbation of COPD.[11]

During the COVID-19 outbreak, the main concern is based on our knowledge that patients with COPD are prone to respiratory exacerbations, which are triggered by viral respiratory infections.[5] In this present study, 22.4% of patients were transferred to the ICU and the mortality rate was 17.3%. Based on the currently available literature, there is no higher prevalence and severity of COVID-19 in patients with COPD, as anticipated.[12]

As smoking has a negative impact on the respiratory system by decreasing lung function, and active smokers are known to be susceptible to more severe viral respiratory tract infections, the association between smoking and COVID-19 is widely investigated. But the reports have some controversies. The prevalence of active smokers >15 years of age is 31.2% in Turkey, according to the latest updated data, and 24.5% of our participants in the study were active smokers, which is less than the ratio seen in Turkish society.[13] In this present study, the length of hospital stay was found to be significantly longer for the smokers than the nonsmokers ($p = 0.005$), different from Chousein et al. study results, in which they noted no difference between smokers and nonsmokers.[14]

In a study conducted by United Kingdom researchers, the number of COPD exacerbations during the previous year was shown to be associated with increased subsequent mortality rates.[15] In early cohorts, it was shown that GOLD A had the best survival, GOLD D had the worst, and GOLD B and C had in-between hospitalization outcomes in terms of COPD exacerbation.[16] However, in the GOLD 2019 classification, groups B and D had the worst mortality, which mentioned the importance of the burden of symptoms, and thereby some criticism arose on this GOLD staging score.[17] COPD is a heterogenous disease; the results of COPD studies suggest that comorbidities, clinical phenotypes such as emphysema or chronic bronchitis, and some different indexes should be included in staging the severity of COPD.[18] It must be taken into consideration that the main goal of the COPD classifications, which are built on symptom scores and history of exacerbation, is conceived to guide clinical management and not enough to predict future exacerbations, hospitalizations, or death.[5]

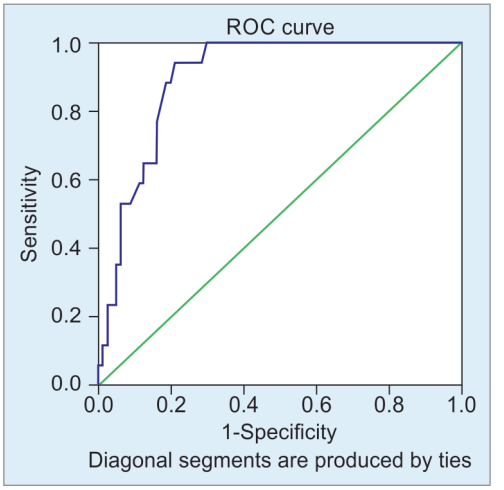


Fig. 1: ROC analysis of PaO_2/FiO_2 for mortality

Hypertension and coronary artery diseases are the most common comorbidities in our study, which is not surprising, as GOLD guidelines state cardiovascular diseases as particularly accompanying diseases with COPD.[5]

The group of GOLD C and D had increased levels of PCT and lower levels of PaO_2/FiO_2 than the group of GOLD A and B. It is hard for COPD patients to early detect SARS-CoV-2 infection, as they have similar symptoms like cough and breathlessness before, which may result in the progression of the disease. The lung is inevitably the major target organ invaded by SARS-CoV-2. Pneumonia caused by SARS-CoV-2 infection could be the responsible mechanism of viral infection-induced exacerbation in COPD patients. Hence, even if a symptomatic or asymptomatic COVID-19 patient, pneumonia is commonly present and observed as the disease progresses.[3] The systematic review made by Gerayeli et al. reported COPD as a risk factor for hospitalization, ICU admission, and mortality in patients with COVID-19, although previous studies reveal different results about the association of COPD and COVID-19 clinical outcomes.[19] One possible explanation for this is; ACE2 is highly expressed in the lower respiratory tract of COPD patients, favoring the severity of COVID-19.[20] While SARS-CoV-2 infection may cause acute respiratory distress syndrome (ARDS) and several COVID-19 patients present with hypoxia and respiratory failure, the most frequently used oxygenation index PaO_2/FiO_2 is investigated as a predictor of mortality.[21] COPD is a comorbidity that itself may cause respiratory failure also. COVID-19 pneumonia seems to be generated by pulmonary exudations through endothelial injury.[7] In the capillary bed, the widespread microvascular coagulation and alveolar edema reduce ventilation and perfusion, which appear to cause COVID-19 hypoxemia.[22] The ventilation/perfusion mismatching causes hypoxic pulmonary vasoconstriction and intrapulmonary shunting of blood. This shunting diverts blood to areas with debilitated gas exchange and reduces arterial oxygen saturation via arteriovenous admixture and the severity of the shunt may predict adverse clinical outcomes, longer duration of hospital stay, and mortality.[23] Hypoxemia is a major indicator of hospitalization with COVID-19. As COPD patients have impaired ventilation due to small airway disease and have diminished respiratory reserves, this intrapulmonary shunting worsens hypoxemia.[24] Hypoxic pulmonary vasoconstriction increases

the risk for thrombus formation in COPD patients.[5] Pulmonary thromboembolism is a hallmark of severe COVID-19 and the increased susceptibility of COPD patients to thromboembolic events may be much worsened by COVID-19.[25] In postmortem COVID-19 autopsies, histopathological findings are hyaline membranes in the alveoli and inflammatory cells in the interstitium and alveoli which are seen in ARDS.[26] PaO_2/FiO_2 ratio is the index which is used to classify the severity of ARDS according to the Berlin criteria.[27] Santus et al. reported that impairment in PaO_2/FiO_2 ratio is associated with an increased risk of inhospital mortality.[28] Similarly, Gu et al. defined PaO_2/FiO_2 as an independent risk factor for death in their study cohort of COVID-19 patients requiring intensive care.[29]

Procalcitonin (PCT) is a biomarker used to assess bacterial infection and the progression of the disease and also guide antibiotic treatment in sepsis and severe respiratory infections.[30] However, as the hyperinflammatory response is a fact in severe SARS-CoV-2 infection, a cytokine storm may cause an inflammatory cascade, and PCT may rise due to this mechanism in COVID-19 patients.[31] Therefore, a high-level of PCT at the time of admission may indicate an inflammatory state in patients for whom early intensive treatment may be offered. In our study, PCT levels distinguishing both COVID-19 patients with COPD who survived or not and as well as the groups of COPD patients according to disease severity as GOLD C and D and GOLD A and B. Kumar et al. mentioned the predictive accuracy of PCT for mortality and severity of the disease in COVID-19 patients in their meta-analyzes.[32] The prognostic impact of PCT in these patients is explained by bacterial superinfections; however, new researches suggest that PCT levels may rise in severe respiratory infections even if there is no bacterial infection.[33] To our knowledge, most COPD patients are characterized by ongoing immune dysfunction and having colonizing bacteria in the airways during the stable phase, which may, in turn, cause secondary bacterial infections after viral respiratory tract infections.[5] This may explain the mechanism of bacterial coinfections seen in COPD patients with COVID-19. On the contrary, Ergan et al. used PCT as a predictor for bacterial COPD exacerbation and reported high PCT levels, which might relate to a higher mortality rate in ICU patients hospitalized with COPD exacerbation.[34] In our study, at hospital admission, fever, % saturation of oxygen, respiratory rate, blood urea level, troponin, and PCT were found to be significantly higher, Hgb, and PaO_2/FiO_2 ratio was lower in the patients who were deceased than in the ones who survived. This was in line with the published literature. Likewise, Du et al. mentioned hypertension, troponin, and PaO_2/FiO_2, as the predictive variables of mortality in COVID-19 patients in the early days of the pandemic.[35] Sartini et al. demonstrated that % saturation of oxygen is <94%, PaO_2/FiO_2 ratio < 300, were strongly associated with poor outcomes.[36] Importantly, in our study cohort, among the variables analyzed (respiratory rate, saturation O_2%, PaO_2/FiO_2, Hgb, urea, PCT, troponin, CRP, ferritin, and D-dimer), PaO_2/FiO_2 ratio was the best independent predictive biomarker for mortality, similar with the work done by Sinatti et al.[21]

In fact, while the univariate analysis in our sample showed that respiratory rate, oxygen saturation%, PaO_2/FiO_2, Hgb, urea, PCT, troponin, CRP, ferritin, and D-dimer increase the inhospital-mortality of COVID-19 patients with COPD; the multivariate analysis revealed that it was PaO_2/FiO_2 ratio itself was the cause of mortality.

Besides, there was no meaningful interpretation between the more severe patients of COPD with increased rates of exacerbation, and the milder ones, depending on the mortality.

We have several limitations—it is a retrospective study and the example size is small according to the missing information of many COPD patients who are followed up by the outpatient clinic of our hospital, so they were excluded from the study.

Conclusion

In a cohort of 98 hospitalized COVID-19 patients with COPD, who are staged according to GOLD/ ABCD classification, PCT levels, and PaO_2/FiO_2 ratio were found to be significantly different when we compared groups GOLD A and B and GOLD C and D. There were no significant age, gender, comorbidity, length of hospital stay, and inhospital-mortality difference noted between these groups. More studies with large cohorts are warranted to clarify the interlocking questions about COVID-19 and COPD relations as COPD incidence is increasing all around the world with a large socioeconomic burden, and also growing evidence points to us that new outbreaks of respiratory infections are possible in the future.

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