Original Article

The Effect of Risk Factors on the Clinical Course and Treatment of Older Patients with Coronavirus Disease 2019

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ABSTRACT

Introduction: Coronavirus disease 2019 (COVID-19) is known to have higher morbidity and mortality rates, parallel to the increased risk factors in the elderly. We aimed to define the risk factors related to mortality and morbidity in older patients hospitalized with COVID-19 disease in this study. **Materials and Methods:** This retrospective cross-sectional study included patients aged ≥65 years who were hospitalized with a confirmed diagnosis of COVID-19. We analyzed their demographic data, clinical findings, comorbidities, laboratory and radiologic findings, treatment protocols, and outcomes. **Results:** A total of 58 patients were included in the study. A total of eight (13.8%) patients died during the clinical follow-up and treatment, and 50 (86.2%) patients were discharged. The most common comorbidities among all patients were hypertension (HT) (69%) and diabetes mellitus (39.7%). The most common symptoms include fever (51.7%), cough (44.8%), and dyspnea (43.1%), and the most common neurologic findings were headache (27.6%) and impaired consciousness (27.6%). Intensive care unit admission was significantly higher among patients with comorbidities of HT, cerebrovascular disease, atrial fibrillation (AF), and chronic obstructive pulmonary disease. The rate of death was significantly higher in patients with a history of smoking, cerebrovascular disease, AF, and HT. Although there was a statistically significant positive correlation between the death rate and leukocyte, neutrophil, C-reactive protein, lactate dehydrogenase, D-dimer, interleukin-6, and procalcitonin levels, a negative correlation was observed in lymphocyte levels. **Conclusion:** Age-related comorbid conditions, especially HT, cerebrovascular disease, and AF, caused increased morbidity and mortality rates in older patients with COVID-19.

KEYWORDS: *Comorbidity, coronavirus disease 2019, elderly, mortality, risk factors*

INTRODUCTION

The World Health Organization (WHO) China Country Office reported the cases of pneumonia with an unknown etiology in the city of Wuhan, China, on December 31st, 2019. On January 7th, 2020, the agent was defined as a novel coronavirus that was not previously detected in humans (2019-nCoV). Later, the disease was named coronavirus disease 2019 (COVID-19). On detection of COVID-19 cases in 113 countries, except for China, in which the epidemic first broke out, the WHO declared a pandemic on March 11, 2020, considering the spread and effects of the virus.[1] COVID-19 affects all age groups but carries a significantly higher risk of morbidity and mortality in the elderly population, especially those who are more vulnerable due to underlying comorbidities, such

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as diabetes mellitus (DM), hypertension (HT), and cerebrovascular disease.[2-4]

Infections commonly have an atypical presentation in older adults. For example, fever, which is a common finding and screening method in COVID-19, may be vague in older patients; this situation may cause difficulties in the diagnosis and management of the disease.[4,5]

In patients with dementia, difficulties in the evaluation of symptoms and isolation strategies may be encountered. In older patients, the clinical presentation of COVID-19 may be wrongly perceived as exacerbation of an underlying chronic obstructive pulmonary disease (COPD) or heart failure.[4] Neurologic diseases, such as cerebrovascular disease, impaired consciousness, and epileptic seizures, which are commonly seen in older patients, may be seen as the presentation of COVID-19, causing difficulties in diagnosis.[6] Patients with neurologic symptoms should be carefully interpreted.[7]

Physiologic changes in the elderly and many age-related comorbid conditions such as heart and lung diseases, HT, DM, and dementia, multiple drug use, and living in nursing homes with exposure to an increased virus load, lead to greater risks.[4]

In the literature, insufficient reports have evaluated the effect of risk factors on the prognosis and outcomes of COVID-19 in older patients. In the face of the current pandemic, investigations on this subject have great importance in predicting morbidity and mortality rates and management of treatment protocols. In the current study, we aimed to define the morbidity- and mortality-related risk factors in older patients with COVID-19 by evaluating the demographic, clinical, laboratory, and radiologic data of the patients.

Materials and Methods

In this retrospective cross-sectional study, the study population was defined as patients with COVID-19 aged ≥65 years. The study was conducted in a tertiary center and the medical records of the patients who were admitted to the COVID-19 clinic between March 2020 and June 2020 were retrospectively evaluated. The inclusion criteria were the presence of COVID-19 clinical findings, which were confirmed with laboratory tests. Nasal and pharyngeal swabs were obtained for severe acute respiratory syndrome coronavirus 2 virus analysis and COVID-19 positivity was diagnosed using the real-time reverse transcriptase-polymerase chain reaction. A body temperature of ≥37.4°C was accepted as fever.

The study was approved by the Turkish Ministry of Health (2020-05-07T02-23-01) and the Ethics Committee of the University of Health Sciences Gülhane Training and Research Hospital (14.05.2020/2020-195) and was conducted according to the principles of the declaration of Helsinki.

The following data were obtained from the included patients: Age, sex, habits such as smoking or alcohol consumption, COVID-19 time-related clinical symptoms, comorbidities, laboratory parameters (hemoglobin, leukocyte, lymphocyte, neutrophil, C-reactive protein (CRP), procalcitonin, lactate dehydrogenase (LDH), interleukin-6 (IL-6), and D-dimer levels, radiologic data, treatments given, complications, length of hospital stay (LOS), and discharge status (cured/exitus). All parameters were statistically analyzed, and the endpoint, and morbidity-and mortality-related risk factors were defined.

Treatments

First-line treatment (favipiravir and low-molecular-weight heparin [LMWH]), second-line treatment (steroids, tocilizumab, plasma, intravenous immune globulin treatments), and third-line treatment (intensive care support).

Statistical analysis

Statistical analysis was performed using the Statistical Package for the Social Sciences (SPSS) software version. 22.0 (SPSS Inc., Chicago, IL, US). The continuous variables were expressed as the mean ± standard deviation and median (first and third quartiles) according to the distribution. Numbers and percentages were used for the categorical variables. Normality tests for the distribution were performed using the Kolmogorov − Smirnov test for the numerical data. For normally distributed continuous data, an independent samples *t*-test was performed. For parameters with nonnormal distribution, a nonparametric *t*-test (Mann–Whitney U) was performed. The Chi-square test was used for the analysis of categorical variables. Pearson's correlation test was used to analyze the relationship between the variables. Multiple linear regression analysis was performed to determine the independent predictors of LOS. Table 1 shows the correlations among the variables in this study. As shown in Table 1, no inter-construct correlations exceed the recommended threshold of 0.7 indicating the lack of multicollienarity in the research model.[8] $P < 0.05$ was considered statistically significant.

Results

A total of 58 patients who met the inclusion criteria were included in the study. Approximately two-thirds of

Table 1: Correlation between the variables

	Cerebrovascular disease		COPD		Psychosis		Dementia		D-dimer	
	r	*P**	*r*	*P**	*r*	*P**	*r*	*P**	*r*	*P**
Total length of hospital stay	0.491	<0.001	0.356	0.006	0.259	0.049	0.322	0.014	0.345	0.008
Cerebrovascular disease			−0.013	0.925	−0.100	0.455	0.280	0.033	0.273	0.038
COPD					0.391	0.002	−0.137	0.304	0.169	0.205
Psychosis							−0.087	0.518	−0.121	0.366
Dementia									−0.106	0.426

*Pearson correlation test was performed to show the multicollinearity correlation between the variables in the research model.
COPD: Chronic obstructive pulmonary disease

the patients (n = 38, 65.5%) were overweight or obese. Eleven (19%) patients had a history of smoking and 50 (86.2%) had at least one chronic disease [Table 2]. The most common chronic diseases were HT (n = 40, 69%) and DM (n = 23, 39.7%) [Table 2].

At least one symptom was recorded for 82.2% (n = 48) of the patients. The most common symptoms were fever (n = 30, 51.7%), cough (n = 26, 44.8%), and dyspnea (n = 25, 43.1%) [Table 3]. Headache (27.6%) and impaired consciousness (27.6%) were the most common neurologic findings [Table 3].

Approximately half of the patients (n = 31, 53.4%) developed complications during the follow-up, the most common of which were secondary infections (n = 24, 41.4%) [Table 3].

The mean age of the 16 (27.6%) patients who developed impaired consciousness was significantly higher (P = 0.024). Impaired consciousness was significantly more common among patients with cerebrovascular disease and dementia (P < 0.001 and P = 0.006, respectively).

LMWH and favipiravir as anti-viral therapy were initiated in all patients as the first-line treatment. The second-line treatment was initiated in seven (12.1%) patients and 14 (24.1%) patients required third-line treatment, which was intensive care support [Table 3]. The rate of patients with HT who needed third-line treatment was significantly higher when compared with those who did not (P = 0.027). In patients with cerebrovascular disease, the rates of patients who needed second-line (P = 0.033) and third-line treatments (P < 0.001) were significantly higher compared with patients without cerebrovascular disease. Patients with COPD (P = 0.002) and atrial fibrillation (AF) (P = 0.002) had significantly higher rates of needing third-line treatment.

Eight (13.8%) patients died during the clinical follow-up and treatment and 50 (86.2%) were discharged [Table 4]. In terms of the mean age, no statistically significant difference was observed between the patients who died (77.50 ± 5.95 years) and those who were discharged (72.4 ± 7.38 years) (P = 0.073).

Table 2: Characteristics of older patients diagnosed with coronavirus disease 2019 infection (n=58)

Descriptive features	*n* (%)
Sex	
Female	35 (60.3)
Male	23 (39.7)
Body mass index	
Normal	20 (34.5)
Overweight	25 (43.1)
Obese	13 (22.4)
Smoking	
No	47 (81.0)
Yes	11 (19.0)
Chronic diseases	
Hypertension	40 (69.0)
Diabetes	23 (39.7)
Coronary artery disease	14 (24.1)
Cerebrovascular disease	9 (15.5)
Chronic obstructive pulmonary disease	7 (12.1)
Atrial fibrillation	7 (12.1)
Dementia	7 (12.1)
Hyperlipidemia	6 (10.3)
Psychosis	3 (5.2)
Epilepsy	3 (5.2)
Hypothyroidism	3 (5.2)
Chronic kidney disease	2 (3.4)

An evaluation of the comorbid conditions revealed that the chronic diseases that affected the prognosis were HT, cerebrovascular disease, and AF. Twenty percent of the patients with HT died; all patients without HT were discharged (P = 0.041). The rate of death was also significantly higher in patients with cerebrovascular disease (P < 0.001), in patients with AF (P < 0.001), and in patients who smoked (P = 0.035) [Table 4].

The mean LOS was 15.64 ± 6.38 (range, 6–36) days. The duration of hospital stay had a significantly positive but weak correlation with increasing age (r = 0.276, P = 0.036).

Table 3: Distribution of symptoms and complications and treatments received by elderly patients with coronavirus disease 2019 infection (*n*=58)

	n (%)
Signs and symptoms	
Temperature	30 (51.7)
Cough	26 (44.8)
Shortness of breath	25 (43.1)
Chest pain	3 (5.2)
Neurologic symptoms	
Impaired consciousness	16 (27.6)
Headache	16 (27.6)
Myalgia	9 (15.5)
Loss of smell	8 (13.8)
Loss of taste	6 (10.3)
Stroke	3 (5.2)
Complications	
Secondary infection	24 (41.4)
Impaired consciousness	16 (27.6)
Respiratory failure	15 (25.9)
Electrolyte disturbance	14 (24.1)
Hypotension	8 (13.8)
Heart failure	6 (10.3)
Acute kidney failure	7 (12.1)
Thrombocytopenia	3 (5.2)
Treatments	
First-line treatment (favipiravir and LMWH treatment)	58 (100.0)
Second-line treatment (one of the steroid, tocilizumab, plasma, IVIG treatments)	7 (12.1)
Tocilizumab	4 (6.9)
Steroid treatment	2 (3.4)
Plasma treatment	2 (3.4)
IVIG treatment	1 (1.7)
Third-line treatment (intensive care support)	14 (24.1)

LMWH: Low-molecular-weight heparin, IVIG: Intravenous immune globulin

Table 4: Analysis of discharge and death rates of older patients with coronavirus disease 2019 infection (*n*=58)

		Discharge and death rates		
	n	Discharge (*n*=50; 86.2)	Death (*n*=8; 13.8), *n* (%)	*P**
Smoking	11	7 (63.6)	4 (36.4)	0.035
Diabetes	23	18 (78.3)	5 (21.7)	0.155
Hypertension	40	32 (80)	8 (20.0)	0.041
Cerebrovascular disease	9	4 (44.4)	5 (55.6)	<0.001
Coronary artery disease	14	10 (71.4)	4 (28.6)	0.066
Atrial fibrillation	7	3 (42.9)	4 (57.1)	<0.001
Hyperlipidemia	6	6 (100.0)	-	0.301
COPD	7	6 (85.7)	1 (14.3)	0.968
Dementia	7	5 (71.4)	2 (28.6)	0.227
Psychosis	3	3 (100.0)	-	0.477
Epilepsy	3	2 (66.7)	1 (33.3)	0.313
Hypothyroidism	3	2 (66.7)	1 (33.3)	0.313
Chronic kidney disease	2	2 (100.0)	-	0.565

*Chi-square test, $P<0.05$ value was considered significant. COPD: Chronic obstructive pulmonary disease

The mean LOS was significantly longer in patients with comorbidities of cerebrovascular disease ($P < 0.001$), COPD ($P = 0.016$), dementia ($P = 0.016$), and psychosis ($P = 0.029$) [Table 5].

Multiple linear regression analysis was performed to assess the independent predictors of LOS [Table 6]. It were found that cerebrovascular disease ($\beta = 0.361$, $P = 0.001$), COPD ($\beta = 0.258$, $P = 0.020$), psychosis (β

Table 5: Analysis of the total length of stay of older patients with coronavirus disease 2019 infection (*n*=58)

	Total length of hospital stay		*P**
	n	Median (quartiles)	
Smoking			
Yes	11	11 (8-22)	0.151
No	47	14 (12-19)	
Diabetes			
Yes	23	15 (11-19)	0.981
No	35	14 (12-20)	
Hypertension			
Yes	40	14.5 (11.25-19.75)	0.879
No	18	12.5 (11.75-17.25)	
Cerebrovascular disease			
Yes	9	22 (18-27)	<0.001
No	49	12 (11-16)	
Coronary artery disease			
Yes	14	15 (11-21.25)	0.648
No	44	13 (11.25-18.50)	
Atrial fibrillation			
Yes	7	22 (11–25)	0.100
No	51	14 (12–17)	
Hyperlipidemia			
Yes	6	14 (11.75-21)	0.748
No	52	14 (11.25-19)	
COPD			
Yes	7	23 (19–25)	0.016
No	51	13 (11–16)	
Dementia			
Yes	7	21 (14-22)	0.016
No	51	12 (11-17)	
Psychosis			
Yes	3	24 (19--)	0.029
No	55	14 (11-17)	
Epilepsy			
Yes	3	16 (14--)	0.298
No	55	14 (11-19)	
Hypothyroidism			
Yes	3	10 (9--)	0.458
No	55	14 (12-19)	
Chronic kidney disease			
Yes	2	18 (12--)	0.534
No	56	14 (11.25-19)	

*Mann-Whitney *U* test, *P*<0.05 value was considered significant.
COPD: Chronic obstructive pulmonary disease

= 0.253, P = 0.021), dementia (β = 0.307, P = 0.004), and D-dimer levels (β = 0.266, P = 0.014) were the independent predictor of LOS [Table 6].

A positive and moderate correlation was observed between D-dimer values and age (r = 0.273, P = 0.038).

When the correlation between the total LOS and blood parameters of the patients was examined, a statistically significant positive and moderate correlation was found between the LOS and D-dimer levels (r = 0.345, P = 0.008). Similarly, there was a positive and moderate statistically significant correlation with IL-6 levels (r = 0.368, P = 0.004). There was no significant difference between total LOS and other blood parameters [Table 7].

In addition, when the correlation between the death and discharge status of the patients and the blood parameters was examined, a statistically significant positive and moderate correlation was seen between the death rate and leukocyte (r = 0.585, P < 0.001), neutrophil (r = 0.639, P < 0.001), and CRP (r = 0.538, P < 0.001) levels [Figure 1]. Similarly, there was a positive and moderate statistically significant correlation with LDH (r = 0.336, P = 0.010), D-dimer (r = 0.369, P = 0.004), IL-6 (r = 0.393, P = 0.002), and procalcitonin (r = 0.412, P = 0.004) levels. A statistically significant negative and moderate correlation was found between the death rate and lymphocyte levels (r = −0.332, P = 0.011) [Table 7].

Discussion

The COVID-19 pandemic has affected the population in many ways. The disease affects individuals in different ways. Older people with comorbid conditions are especially vulnerable to this disease. In some studies, senility has been associated with morbidity and mortality.[2-4] The clinical features in the elderly that might be associated with COVID-19-related deaths are still a matter of concern. In the current study, older patients with COVID-19 were evaluated in terms of demographic, clinical, and laboratory features, and mortality-related risk factors were defined.

Studies have reported that the most common comorbidities among patients with COVID-19 were HT, DM, cardiovascular diseases, and cerebrovascular diseases.[9] Angiotensin-converting enzyme (ACE) inhibitors and angiotensin receptor blockers are commonly used in older patients with diabetic or hypertensive disorders, both for the treatment of HT and for the prevention of ischemic heart disease. It is known that human pathogenic coronaviruses bind to target cells through ACE 2 receptors.[10-12] ACE 2 expression increases in patients with Type 1 and 2 diabetes who are treated with ACE inhibitors and ARBs, and upregulation of ACE 2 occurs in patients with HT who are treated with ACE 2 blockers or ARBs.[12] ACE 2 may also be increased by thiazolidinediones.[13] Therefore, increased ACE 2 expression may ease COVID-19 infections.[14] Moreover, patients with diabetes also carry a higher risk of infection due to decreased neutrophil function.[15] In a meta-analysis of 1576 patients, Yang *et al*. reported the most common comorbidities as HT (21.1%) and

Table 6: Multiple linear regression analysis for the predictor of long hospital stay

	Unstandardized coefficients		Standardized coefficients		*P*
	B	SE	*B*	*t*	
Total length of hospital stay (R^2=0.525)					
Cerebrovascular disease	6.312	1.836	0.361	3.438	0.001
COPD	5.022	2.084	0.258	2.410	0.020
Dementia	5.962	1.986	0.307	3.002	0.004
Psychosis	7.231	3.039	0.253	2.380	0.021
D-dimer	1.559	0.613	0.266	2.543	0.014

SE: Standard error; *B*: Unstandardized regression coefficient; β: Standardized β coefficient, COPD: Chronic obstructive pulmonary disease, SE: Standard error

Table 7: The correlation between the total length of hospital stay, the death and discharge status, and the blood parameters older patients diagnosed with coronavirus disease 2019 infection

	Total length of hospital stay		Death	
	r	*P**	*r*	*P**
Leukocyte (*n*=58)	−0.088	0.513	0.585	<0.001
Neutrophil (*n*=58)	−0.073	0.588	0.639	<0.001
Lymphocyte (*n*=58)	−0.243	0.066	−0.332	0.011
Platelets (*n*=58)	−0.169	0.204	−0.140	0.294
Hemoglobin (*n*=58)	0.118	0.377	0.134	0.314
LDH (*n*=58)	−0.005	0.971	0.336	0.010
CRP (*n*=57)	0.005	0.973	0.538	<0.001
D-dimer (*n*=58)	0.345	0.008	0.369	0.004
IL 6 (*n*=58)	0.368	0.004	0.393	0.002
Procalcitonin (*n*=47)	0.097	0.518	0.412	0.004

*Pearson correlation test. LDH: Lactate dehydrogenase, CRP: C-reactive protein, IL-6: Interleukin-6

DM (9.7%),[16] consistent with our study (60.0% and 39.7%, respectively). The increased prevalence of HT and DM in our study is related to the increased age of the study population (≥65 years), in which HT and DM are more commonly seen compared with younger populations.

The typical findings of COVID-19 infection were fever, cough, dyspnea, and tiredness. In a meta-analysis by Rodriguez-Morales *et al*., the most common symptoms were fever (88.7%), cough (57.6%), and dyspnea (45.6%),[17] which were corroborated by our study (51.0%, 44.8%, and 43.1%, respectively). In our study, it was observed to be lower fever level when compared with the meta-analyses. This could be related to our study population consisting of older patients in whom the infection may be atypical and the fever response may be uncertain.[5]

Although there is evidence of the relationship between COVID-19 and its effects on the nervous system,[18] it is difficult to define how several neurologic findings are related to the pathophysiology of the disease. It is yet unclear whether the neurologic findings are a result of viral infection or indirectly caused by mechanisms such as hypoxia, sepsis or multi-organ failure. A possible mechanism is the alveolar inflammation and edema caused by the coronavirus, leading to hypoxia, which causes increased brain blood flow and increased intracranial pressure, resulting in several neurologic findings and symptoms, including headache and coma.[6] Headache was the most common symptom found in the study by Karadaş *et al*., which evaluated neurologic symptoms of 239 patients.[6] Our evaluation of neurologic findings identified headache and impaired consciousness as the most common symptoms in older patients with COVID-19. Moreover, impaired consciousness was more common among patients with cerebrovascular disease, dementia, and older ages. Patients with comorbid conditions, especially neurologic diseases, and older patients with acute respiratory symptoms are at a higher risk for impaired consciousness. This situation can be related to the impaired cognition in the older population. Therefore, prospective studies are needed to investigate cognitive functions.

In a meta-analysis by Rod *et al*., which evaluated 17 studies, increasing age, D-dimer levels, and the presence of DM were the most significant risk factors for the severity of COVID-19.[19] In our study, we found a correlation between increasing patient age, LOS, and the death rate, and higher D-dimer values.

It is believed that the proinflammatory mechanisms during COVID-19 infection lead to increased clotting and disruption in vasomotor activity, which increases the risk for stroke and worsens the conditions of patients with cerebrovascular disease.[20] Further, recent studies reported that COVID-19 acted on ACE 2 functional receptors, which have been implicated in severe cerebrovascular events, including stroke, in patients with risk factors for cerebrovascular diseases, such as smoking or diabetes.[21-24] Choi *et al*. demonstrated that smoking or the presence of diabetes increased ACE 2 expression in ischemic brains and vessels in

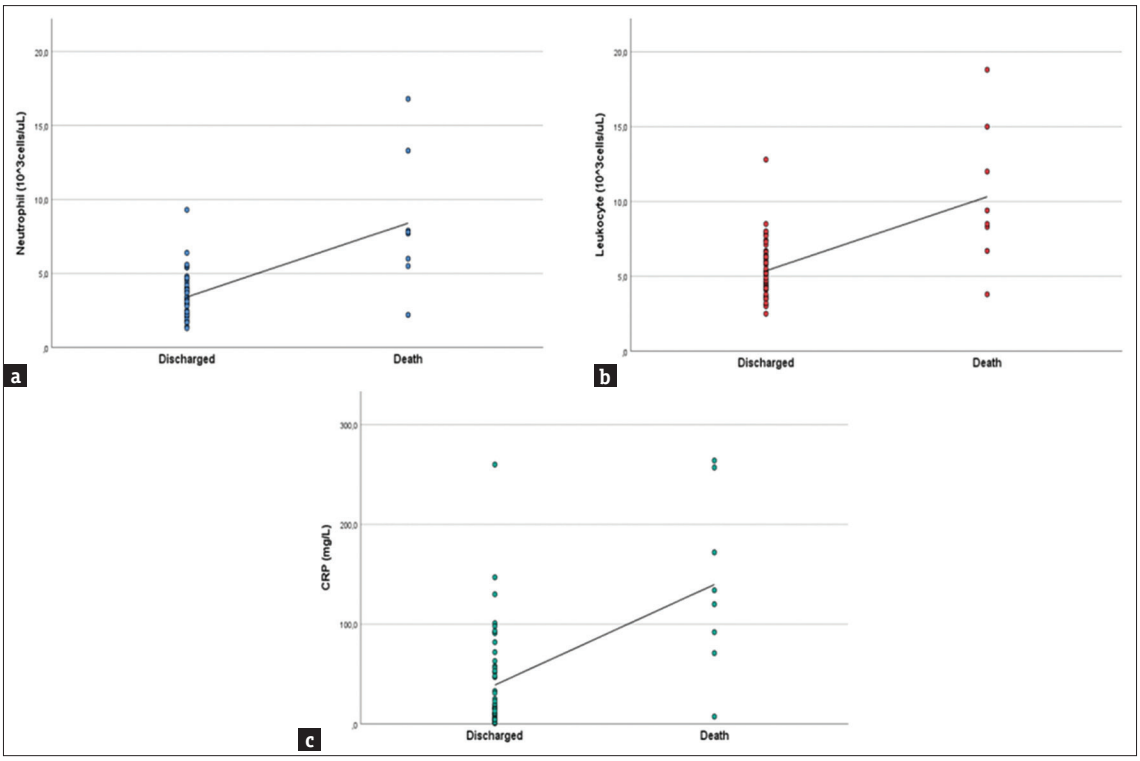

Figure 1: Graphics of significant moderate correlations neutrophil/death (a), leukocytes/death (b), C-reactive protein/death (c) in older patients with coronavirus disease 2019 infection

rats, which reduced the defense against the virus that causes COVID-19.[24] The authors reported that in patients with stroke or a history of stroke, ACE 2 levels could increase and cause vulnerability for COVID-19. In our study, the rate of intensive care unit (ICU) admission and/or death rates was significantly higher in patients with cerebrovascular disease. The increase in COVID-19 sensitivity due to ACE 2 expression in this patient group and the high D-dimer levels associated with severe disease may have caused an increase in the severity of the disease.[19,24] Consistently, a previous meta-analysis revealed an important correlation between previously diagnosed cerebrovascular disease and increased mortality, and emphasized the relationship between ICU admission and the need for mechanical ventilation.[25]

AF causes a loss in atrioventricular synchronization, which decreases the duration of diastolic filling, and, as a result, causes a decrease in cardiac output. This decrease in cardiac output aggravates tissue hypoxia in patients with COVID-19. Furthermore, the agents that are used in the treatment of AF, especially sotalol, propafenone, and nonselective β-blockers, may cause bronchospasm.[26] Phelps *et al*. detected moderately increased risk among 75-year-old women with AF, which was a determinant for severe COVID-19 infection when compared with patients without comorbidities.[27] In our study, we found a significant increase in rates of admission to the ICU and mortality in patients with AF and HT.

LOS increased with age and in patients with comorbidities, such as cerebrovascular disease, COPD, psychosis, and dementia. Our findings suggest that comorbidities such as cerebrovascular disease, COPD, psychosis, and dementia have higher clinical importance in predicting LOS in older patients with COVID-19.

Our study was limited by its retrospective design, being a single-center study, and the limited number of patients. Although many risk factors were adjusted for in the linear regression analysis, the probability of residual confounding from uncalculated covariates cannot be excluded. Other limitations are the lack of correct expression of some symptoms in older patients in relation to comorbid conditions such as age-related frailty, dementia, and cerebrovascular disease.

Conclusion

An evaluation of the data of older patients with COVID-19 revealed many risk factors that defined the severity of the disease. Increased morbidity and mortality were detected and associated with some underlying comorbidities. HT, cerebrovascular disease, and AF were the main factors that affected the prognosis of these patients. Cerebrovascular disease, COPD,

psychosis, dementia, and D-dimer levels have higher clinical importance in predicting LOS. Hospital LOS and D-dimer levels were positively correlated with increasing age.

In the older population, which is more vulnerable to COVID-19, defining morbidity and mortality-related risk factors are essential for the follow-up and management of the disease. To draw attention to the importance of this issue, multicentral prospective studies with a large number of patients are needed.

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Conflicts of interest

There are no conflicts of interest.

References

1. Republic of Turkey Ministry of Health. COVID-19 (SARS-CoV-2 Enfeksiyonu) Genel Bilgiler, Epidemiyoloji ve Tanı, Scientific Advisory Board Study [e-pub]; 2020. Available from: https://covid19.saglik.gov.tr/Eklenti/39551/0/covid-19rehberigenelbilgilerepidemiyolojivetanipdf.pdf. [Last accessed on 2020 Dec 07].
2. Liu K, Chen Y, Lin R, Han K. Clinical features of COVID-19 in elderly patients: A comparison with young and middle-aged patients. J Infect 2020;80:e14-8.
3. Wang D, Hu B, Hu C, Zhu F, Liu X, Zhang J, *et al.* Clinical characteristics of 138 hospitalized patients with 2019 novel coronavirus-infected pneumonia in Wuhan, China. JAMA 2020;323:1061-9.
4. Nikolich-Zugich J, Knox KS, Rios CT, Natt B, Bhattacharya D, Fain MJ. SARS-CoV-2 and COVID-19 in older adults: What we may expect regarding pathogenesis, immune responses, and outcomes. Geroscience 2020;42:505-14.
5. High KP, Bradley SF, Gravenstein S, Mehr DR, Quagliarello VJ, Richards C, *et al.* Clinical practice guideline for the evaluation of fever and infection in older adult residents of long-term care facilities: 2008 update by the Infectious Diseases Society of America. J Am Geriatr Soc 2009;57:375-94.
6. Karadaş Ö, Öztürk B, Sonkaya AR. A prospective clinical study of detailed neurological manifestations in patients with COVID-19. Neurol Sci 2020;41:1991-5.
7. Baysal Kirac L, Uysal H. COVID-19 associate neurological complications. Neurol Sci Neurophysiol 2020;37:1-3.
8. Belsley DA, Kuh E, Welsch RE. Regression Diagnostics: Identifying Influential Data and Sources of Collinearity. Vol. 571. John Wiley & Sons, Hoboken, USA, 2005.
9. Li B, Yang J, Zhao F, Zhi L, Wang X, Liu L, *et al.* Prevalence and impact of cardiovascular metabolic diseases on COVID-19 in China. Clin Res Cardiol 2020;109:531-8.
10. Li W, Moore MJ, Vasilieva N, Sui J, Wong SK, Berne MA, *et al.* Angiotensin-converting enzyme 2 is a functional receptor for the SARS coronavirus. Nature 2003;426:450-4.
11. Kuhn JH, Li W, Choe H, Farzan M. Angiotensin-converting enzyme 2: A functional receptor for SARS coronavirus. Cell Mol Life Sci 2004;61:2738-43.
12. Wan Y, Shang J, Graham R, Baric RS, Li F. Receptor recognition by the novel coronavirus from Wuhan: An analysis based on decade-long structural studies of SARS coronavirus. J Virol 2020;94:e00127-20.
13. Li XC, Zhang J, Zhuo JL. The vasoprotective axes of the renin-angiotensin system: Physiological relevance and therapeutic implications in cardiovascular, hypertensive and kidney diseases. Pharmacol Res 2017;125:21-38.
14. Fang L, Karakiulakis G, Roth M. Are patients with hypertension and diabetes mellitus at increased risk for COVID-19 infection? Lancet Respir Med 2020;8:e21.
15. Ma RC, Holt RI. COVID-19 and diabetes. Diabet Med 2020;37:723-5.
16. Yang J, Zheng Y, Gou X, Pu K, Chen Z, Guo Q, *et al.* Prevalence of comorbidities and its effects in patients infected with SARS-CoV-2: A systematic review and meta-analysis. Int J Infect Dis 2020;94:91-5.
17. Rodriguez-Morales AJ, Cardona-Ospina JA, Gutiérrez-Ocampo E, Villamizar-Peña R, Holguin-Rivera Y, Escalera-Antezana JP, *et al.* Clinical, laboratory and imaging features of COVID-19: A systematic review and meta-analysis. Travel Med Infect Dis 2020;34:101623.
18. Ng Kee Kwong KC, Mehta PR, Shukla G, Mehta AR. COVID-19, SARS and MERS: A neurological perspective. J Clin Neurosci 2020;77:13-6.
19. Rod JE, Oviedo-Trespalacios O, Cortes-Ramirez J. A brief-review of the risk factors for covid-19 severity. Rev Saude Publica 2020;54:60.
20. Sonkaya AR, Öztrk B, Karadaş Ö. Cerebral hemodynamic alterations in patients with covid-19. Turk J Med Sci 2021;51:435-9.
21. Archie SR, Cucullo L. Cerebrovascular and neurological dysfunction under the threat of COVID-19: Is there a comorbid role for smoking and vaping? Int J Mol Sci 2020;21:3916.
22. Emilsson V, Gudmundsson EF, Aspelund T, Jonsson BG, Gudjonsson A, Launer LJ, *et al.* ACE2 levels are altered in comorbidities linked to severe outcome in COVID 19. medRxiv [Preprint]. 2020 Jun 5:2020.06.04.20122044. doi: 10.1101/2020.06.04.20122044. PMID: 32511628; PMCID: PMC7276056.
23. Hess DC, Eldahshan W, Rutkowski E. COVID-19-related stroke. Transl Stroke Res 2020;11:322-5.
24. Choi JY, Lee HK, Park JH, Cho SJ, Kwon M, Jo C, *et al.* Altered COVID-19 receptor ACE2 expression in a higher risk group for cerebrovascular disease and ischemic stroke. Biochem Biophys Res Commun 2020;528:413-9.
25. Patel U, Malik P, Shah D, Patel A, Dhamoon M, Jani V. Pre-existing cerebrovascular disease and poor outcomes of COVID-19 hospitalized patients: A meta-analysis. J Neurol 2021;268:240-7.
26. Atkins JL, Masoli JA, Delgado J, Pilling LC, Kuo CL, Kuchel GA, *et al.* Preexisting comorbidities predicting COVID-19 and mortality in the UK Biobank Community Cohort. J Gerontol A Biol Sci Med Sci 2020;75:2224-30.
27. Phelps M, Christensen DM, Gerds T, Fosbøl E, Torp-Pedersen C, Schou M, *et al.* Cardiovascular comorbidities as predictors for severe COVID-19 infection or death. Eur Heart J Qual Care Clin Outcomes 2021;7:172-80.