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Original Article

Clinical Differences Between Elderly and Non-elderly Patients with COVID-19

Fatma Demirci Üçsular[1], Gülistan Karadeniz[1], Gülru Polat[1], Aysu Ayrancı[2], Enver Yalnız[1], Fatmanur Kazankaya[1], Filiz Güldaval[1], Melih Büyükşirin[1], Ceyda Anar[3]

[1]Department of Chest Disease University of Health Sciencies, Dr Suat Seren Chest Disease and Surgery Training and Research Hospital, İzmir, Turkey
[2]Department of Chest Diseases, İzmir Bakırçay University Çiğli Training and Research Hospital, İzmir, Turkey
[3]Department of Chest Diseases, İzmir Katip Çelebi University Faculty of Medicine, İzmir, Turkey

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Abstract

OBJECTIVE: Comorbidity frequency and mortality rates are higher in elderly patients with COVID-19. The disease is also more severe in elderly patients. This study aims to examine the characteristics of the COVID-19 disease, severity, comorbidities, and mortality rates in elderly patients by comparing them with nonelderly patients.

MATERIAL AND METHODS: This study was designed as a retrospective study. 469 patients who were followed up in outpatient, inpatient, and intensive care units with the diagnosis of COVID-19 between March 11, 2020, and June 01, 2020, were retrospectively included in the study. Patients were divided into two groups who were ≥65 years named as the "elderly group" and <65 years referred to as "nonelderly". Survival data was generated from the death notification system on August 02, 2020.

RESULTS: A total of 469 patients including elderly(n=101) and nonelderly(n=368) were included in the study retrospectively. The incidence of severe pneumonia(31%/12.6%) and critical illness(16%/5.8%), comorbidity (85%/37.2%) and hospitalization time(8/5 days) were significantly higher in the elderly group(p<0.05). 23 (22.8%) of elderly patients and 27(7.3%) of nonelderly patients died (p=0.000). Mortality was found to be 3.5 times higher than in the non-elderly group. The expected survival time was 145.85 days(CI 95%:133-158.66) in the elderly patients and 170.36 days(CI 95%:166-174.6) in the nonelderly patients (p<0.000). In ROC analysis, the sensitivity of age was 86%(73.3-94.2), specificity was 66.83%(62.1-71.3), and the cut-off>56 (AUC:0.775; p <0.001) in predicting mortality.

CONCLUSION: Mortality is high, comorbidities are more frequent, and the disease is more severe in elderly patients with COVID-19. Age above 56 can be used as a cut-off to predict mortality.

KEYWORDS: Comorbidity, COVID-19, elderly patient, mortality
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INTRODUCTION

Coronavirus disease 2019 (COVID-19) is an infectious disease caused by a new type of coronavirus called severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2). Coronavirus disease 2019 was first detected in a group of patients with pneumonia in Wuhan, China, in December 2019. The World Health Organization (WHO) declared COVID-19 disease as a pandemic because of the disease's rapid spread and severity all over the world.[1] As of November 15, 2020, the WHO had identified 53.7 million confirmed cases and 1.3 million deaths.[2] The number of patients and mortality rates still continue to increase.[3] Age and accompanying comorbidities are the most important determinants of mortality.[1] Since the beginning of the epidemic, more than 90% of deaths from COVID-19 seen in the world are at the age of 60 and over.[4] No consensus has yet been reached on what parameters the severity of the disease is related to the virus and the host.[5]

In the elderly population, COVID-19 disease is more severe and has the highest mortality.[6]

Studies have reported that COVID-19 infection progresses with a more severe clinical course, morbidity, and high mortality in elderly patients.[7-9] With increasing patient monitoring and literature during the pandemic, our experience with COVID-19 in elderly patients continues to increase. Therefore, in our study based on research questions like "Are the clinical features and disease course and mortality of COVID-19 patients with advanced age different?" and "What are the determinants of survival in COVID-19 patients with advanced age?," we aimed to evaluate the clinical characteristics of elderly patients in comparison with those who were non-elderly and to examine significant markers in survival.

Corresponding author: Fatma Demirci Üçsular, e-mail: fatmaucsular@gmail.com

MATERIAL AND METHODS

Study Design

A total of 469 patients with a possible/confirmed diagnosis of COVID-19 between March 11, 2020, and June 1, 2020, were included in the study retrospectively.

Study Population

Patients who were followed up in outpatient, inpatient, and intensive care units with a possible/confirmed diagnosis of COVID-19 were divided into 2 groups: elderly (≥65 years) (n = 101) and non-elderly (<65 years) (n = 368). Among the patients who applied to our hospital within the same date range, those other than COVID-19 diagnosis were excluded from the study. All patients were diagnosed according to the guidelines by the Scientific Committee of the Health Ministry[10]. While patients with symptoms such as fever, cough, shortness of breath, myalgia, those with a history of contact in the last 14 days and those with bilateral ground glass appearance in computed tomography (CT) were defined as "possible cases," among the possible cases, SARS-CoV-2 real-time reverse transcriptase polymerase chain reaction (RT-PCR)-positive patients and/or SARS-CoV-2 rapid antibody test were named as "confirmed cases."

Patients were divided into 2 groups as >65 years old named the "elderly group" and <65 years being the "non-elderly group." An RT-PCR test was performed with nasopharyngeal swabs in all patients. The test was repeated at least twice in patients whose test was negative at the baseline. The clinical features, comorbidities, baseline radiological views (x-ray and/or thoracic CT), routine laboratory parameters including inflammatory biomarkers, treatment protocols, and days of hospitalization in hospitalized patients were obtained from the hospital information system.

The classification of severity in patients was also made according to the COVID-19 guide of our country's Ministry of Health. These were asymptomatic, acute respiratory disease, mild-moderate pneumonia, severe pneumonia, and critical illness. Critical illness includes acute respiratory distress syndrome (ARDS), septic shock and/or multiorgan failure. If it is severe pneumonia, it consists of patients with respiratory rate >30/min, oxygen saturation ≤93%, and more than 50% infiltration on CT (9). The treatment was arranged in line with the COVID-19 treatment guide of the Ministry of Health, which was determined according to the severity of the disease. Hydroxychloroquine was given primarily to asymptomatic patients, patients with acute respiratory disease, and patients with mild to moderate pneumonia. Favipravir or lopinavir/ritonavir was administered to patients with severe pneumonia or clinical and radiological progression despite hydroxychloroquine use. Survival data were generated from the death notification system on August 2, 2020.

Statistical Analysis

Data were analyzed using the International Business Machines Corporation Statistical Package for the Statistical Package for Social Sciences 22.0 (IBM SPSS Corp.; Armonk, NY, USA) package program. Continuous variables were tested by testing their suitability for normal distribution, and it was decided that not all variables were compatible with normal distribution conditions. Quantitative variables, median, min., and max. values were presented and non-parametric methods were used for comparisons of these variables. Comparisons of independent groups were made with the Mann–Whitney *U* test. Qualitative variables were presented as frequencies and percentages with cross tables and their distributions were compared with chi-Square test methods. The Kaplan–Meier method was used in survival analysis, and survival comparisons between groups were made by the log-rank test. The effect of age on survival was evaluated by receiver operating characteristic (ROC) analysis, and the most appropriate cut-off value predicting survival was calculated according to the Youden index. All factors affecting mortality were analyzed by Cox regression analysis using the backward step method according to the Wald value. In all tests, the first type of error margin *P* was determined as .05 and was tested bilaterally. If the *P*-value was less than .05, the difference between the groups was considered statistically significant. This study was approved by the Ethics committee of University of Health Sciencies, Dr Suat Seren Chest Disease and Surgery Training and Research Hospital and by the Turkish Ministry of Health, COVID-19 Scientific Research Committee (Approval No: 49109414-604.02).

RESULTS

A total of 469 patients, including elderly (≥65 years) (n = 101) and non-elderly (<65 years) (n = 368) patients, were retrospectively analyzed. The mean age of all patients was 51.3 (18-95) years. The presence of at least 1 comorbidity was approximately 2 times higher in the elderly group (85%/37.2% and $P < .000$). In patients over 65 years of age, hypertension (HT) (47%) followed by chronic obstructive pulmonary disease (COPD) (25.7%), diabetes mellitus (24%), cardiovascular disease (CVD) (24%), and malignancy (17%) were seen. The incidence of these comorbidities was significantly higher compared to the non-elderly group (*P*-values of .000, .003, .000, .000, and .003, respectively).

In elderly patients, dyspnea, sputum, and hemoptysis were more common symptoms compared to the other group (*P*-values of .000, .000, .042, respectively). When compared with the non-elderly group, the majority of elderly patients were treated and followed up in the hospital (service or intensive care unit) ($P < .000$). While there were no asymptomatic patients in the elderly group, the number of patients with severe pneumonia and critical illness was higher than the non-elderly group (both $P = .000$). In addition, the mean hospitalization time was longer in the elderly group (8/5 days) ($P = .000$) (Table 1).

When the laboratory findings were evaluated comparatively, while lymphocyte, hemoglobin, albumin, oxygen saturation values were lower in the elderly group, international normalized ratio, D-dimer, C-reactive protein, creatinine, ferritin, and troponin values were found to be significantly higher (all *P*-values < .05). The number of patients with radiological lung involvement and diffuse distribution of lesions on high-resolution computed tomography (HRCT) was higher in the elderly group (all of $P < .05$) (Table 2).

Table 1. Demographic and Clinical Characteristics of the Patients with COVID-19

	Elderly Patients (n = 101)	Non-elderly Patients (n = 368)	*P*
Male gender, n (%)	60 (59.4%)	216 (58.7%)	.898
Smoking status:	33 (2-120)	18 (1-150)	.000
Smoking (pack/year), median (min-max)	6 (6.1%)	72 (20.2%)	.000
Smoker, n (%)	49 (50%)	70 (19.7%)	
Ex-smoker, n (%)	43 (43.9%)	214 (60.1%)	
Non-smoker, n (%)			
Outpatient treatment, n (%)	3 (3%)	58 (16%)	.000
Inpatient treatment, n (%)	75 (74%)	276 (75%)	
Intensive care treatment, n (%)	23 (23%)	34 (9%)	
Any comorbidity, n (%)	85 (85%)	137 (37.2%)	.000
Hypertension, n (%)	47 (47%)	60 (16.3%)	.000
Diabetes mellitus, n (%)	24 (24%)	43 (11.7%)	.003
Cardiac disease, n (%)	24 (24.0%)	22 (6.0%)	.000
COPD, n (%)	26 (25.7%)	20 (5.4%)	.000
Asthma, n (%)	2 (2) %	17 (4.6%)	.390
Malignancy, n (%)	17 (17%)	25 (6.8%)	.003
Cerebrovascular disease, n (%)	4 (4%)	4 (1.1%)	.068
Contact history, n (%)	11 (11.1%)	125 (34.1%)	.000
Cough, n (%)	63 (62.4%)	219 (59.5%)	.602
Dyspnea, n (%)	61 (60.4%)	116 (31.5)	.000
Sputum, n (%)	22 (21.8%)	27 (7.3%)	.000
Headache, n (%)	6 (5.9%)	4 (11.1%)	.171
Weakness, n (%)	39 (38.6%)	132 (35.9%)	.612
Anorexia, n (%)	15 (14.9%)	43 (11.7%)	.493
Nausea, n (%)	12 (11.9%)	28 (7.6%)	.246
Myalgia, n (%)	19 (19%)	73 (19.8%)	.964
Diarrhea, n (%)	3 (3%)	31 (8.4%)	.081
Hemoptysis, n (%)	4 (4%)	3 (0.8%)	.042
Anosmia, n (%)	5 (5%)	17 (4.6%)	.796
Fever >37.5°C, n (%)	31 (30.7%)	133 (36.1%)	.309
Possible/definite case, %	44 / 56	33.3 / 6	.048
RT-PCR positivity, n (%)	51 (51%)	235 (64.2%)	.016
Spectrum of disease (severity), n (%)	0 (0.0%)	36 (9.9%)	.000
Asymptomatic	6 (6%)	42 (11.5%)	
Acute respiratory disease	47 (47%)	220 (60.3%)	
Mild-moderate pneumonia	31 (31%)	46 (12.6%)	
Severe pneumonia	16 (16%)	21 (5.8%)	
Critical illness			
Hospitalization duration (day)	8 (5-53)	5 (2-95)	.000
IMV use, n (%)	16 (15.8%)	21 (5.7%)	.002
Mortality, n (%)	23 (22.8%)	27 (7.3%)	.000

COPD, chronic obstructive pulmonary disease; RT-PCR, real-time reverse-transcriptase polymerase chain reaction; IMV, invasive mechanical ventilation.

When compared with the non-elderly group, the elderly group had more patients receiving low-molecular-weight heparin ($P < .000$), corticosteroid ($P = .011$), and oxygen therapy ($P = .000$) (Table 3). Twenty-three (22.8%) of the elderly patients and 27 (7.3%) of non-elderly patients died ($P = .000$). It was observed that mortality increased 3.5 times in elderly patients compared with the non-elderly group.

Expected survival time during 200 days of follow-up was found to be 145.85 days (95% CI, 133-158.66) in the elderly age group and 170.36 days (95% CI, 166-174.6) in the non-elderly age group ($P < .000$). When compared with the non-elderly age group, the mortality risk in the elderly age group was found to be 3.35 times higher (95% CI; 1.92-5.84; $P < .000$) (Figure 1). In addition, in the Cox regression

Table 2. Laboratory and Radiology Findings of the Patients with COVID-19

	Elderly Patients (n = 101)	Non-elderly Patients (n = 368)	*P*
White blood cell count, $\times10^3$µL	7800 (533-29 300)	6600 (2600-31 900)	.019
Neutrophil count, $\times10^3$ µL	5300 (1000-28 000)	4400 (400-30 300)	.000
Lymphocyte count, $\times10^3$ µL	1000 (100-9600)	1300 (100-5500)	.000
Hemoglobin, g/dL	12.4 (8-17.1)	13.4 (7.8-17.7)	.000
Platelet count, $\times10^3$ µL	246 (65-694)	231(28-400)	.067
PT (seconds)	13 (11.1-53.5)	12.4 (7.48-54.5)	.01
APTT (seconds)	26.9 (21.5-95.2)	25.8 (11.4-95.2)	.014
INR	1.1 (0.9-9,8)	1.03 (0.80-4.97)	.000
D-dimer, ng/mL	1250 (233-10 000)	624 (114-10.000)	.000
Albumin, g/dL	3.36 (1.48-43.4)	4 (1.81-45.8)	.000
Alanine aminotransferase, U/L	19 (4-92)	22 (4-168)	.025
Aspartate aminotransferase, U/L	22 (6-97)	20 (7-134)	.310
T bilurubin, mmol/dL	0.44 (0.06-1.47)	0.34 (0.08-2)	.03
Lactate dehydrogenase, U/L	249.5 (119-949)	218 (97-2246)	.218
Creatinine, mg/dL	0.94 (0.46-3.16)	0.79 (0.35-21)	.000
C-reactive protein, mg/dL	8.24 (0.18-54.6)	3.11 (0.02-79.2)	.000
Ferritin, ng/mL	278 (11.3-2552)	192 (8.4-2665)	.02
Troponin T, ng/L	14.6 (2.9-217 000)	3.53 (0.00-815)	.00
Creatine kinase, U/L	76 (17-477)	79 (23-5888)	.406
O_2Sat, % mean (min-max)	93 (73.9-99.9)	95.5 (64-100)	.000
FiO_2,% mean (min-max)	28 (21-100)	21 (21-200)	.000
Lactate, mmol/L	2.10 (0.7-5.4)	1.7 (0.6-14.10)	.418
pO_2/FiO_2, mean (min-max)	261 (73.6-900)	245 (0.25-475)	.627
Presence of lesion in x-ray graphics, n (%)	84 (84.8%)	213 (59.5%)	.000
Lesion in HRCT, n (%)	93 (96.6%)	306 (87.7%)	.015
Distribution of lesions on HRCT: Diffuse, n (%) Central, n (%) Peripheric, n (%)	52 (64.2%) 3 (3.7%) 26 (32.1%)	120 (40.5%) 19 (6.4%) 157 (53%)	.001

PT, prothrombin time; APTT, activated partial thromboplastin time; INR, international normalized ratio; O_2Sat, oxygen saturation; FiO_2, fractionated oxygen; HRCT, high-resolution computed tomography.

analysis, compared with patients under 50 years of age, mortality risk increased 7.21 times (95% CI; 2.73-19.05; *P* = .00) in patients 50-64 years old, 9.20 times in patients aged 65-80 years old (95% CI; 3.37-25.11; *P* = .00), and 22.96 times (95% CI; 7.28-72.42; *P* = .00) in the >80 years old group (Figure 2). In ROC analysis, the sensitivity of age in predicting mortality risk was 86% (73.3-94.2), specificity was 66.83% (62.1-71.3), and the cut-off was >56 (area under the curve = 0.775; *P* < .001) (Figure 3).

In addition, in the log-rank test Kaplan–Meier analysis of elderly patients, the male gender hazards ratios (HR): 2.6 (95% CI; 1.14-6.0; *P* = .046), D-dimer >1000 ng/mL HR: 5.3 (95% CI; 2.26-12.57; *P* = .0025), creatinine ≥1.1 mg/dL HR: 3.1 (95% CI; 1.2-7.6; *P* = .0041), lymphocyte count <800 HR: 2.9 (95% CI; 1.07-8.0; *P* = .007), shortness of breath HR: 5.2 (95% CI; 2.29-11.9; *P* = .0027), and troponin T ≥14 ng/L HR: 11 (95% CI; 4.6-25.9; *P* < .001) were found to increase mortality significantly (Figure 4).

DISCUSSION

When compared with the non-elderly group, the study showed that the disease progresses more mortally and severely in elderly patients, the risk of death increases gradually in proportion to age, and survival significantly decreases in elderly patients. Symptoms of dyspnea, sputum, and hemoptysis were more common in elderly patients, comorbidities and inflammatory markers were higher, radiological involvement of the lung was more frequent, and hospitalization was longer. We found with survival analysis that the male gender, dyspnea, high D-dimer, lymphopenia, cardiac injuries (high troponin), and renal dysfunction (high creatinine) were associated with mortality in elderly patients.

Table 3. Treatment Features of Patients with COVID-19

	Elderly Patients (n = 101)	Non-elderly Patients (n = 368)	*P*
Hydroxichloroquine, n (%)	92 (91.1%)	341 (92.7%)	.752
Azithromycine, n (%)	65 (66.3%)	237 (65.5%)	.874
Moxifloxacine, n (%)	34 (34.3%)	93 (25.7%)	.088
Other antibiotics, n (%)	37 (37%)	57 (15.9%)	.000
Oseltamivir, n (%)	60 (60.6%)	235(65.1%)	.409
Favipiravir, n (%)	24 (24.2%)	55 (15.2%)	.048
Lopinavir/ritonavir, n (%)	4 (4.6%)	6 (1.7%)	.233
Tocilizumab, n (%)	1 (1.1%)	2 (0.2%)	.711
LMWH, n (%)	68 (68.7%)	147 (40.5%)	.000
Corticosteroid, n (%)	19 (19.2%)	34 (9.4%)	.011
Oxygen treatment, n (%)	54 (54.5%)	76 (20.9%)	.000
CP, n (%)	1 (4.5%)	2 (5.9%)	1.000

LMWH, low-molecular-weight heparin; CP, convalescent plasma.

In a study by Li et al[1], in 204 elderly patients (>60 years old) diagnosed with COVID 19, the most common symptoms were fever, cough, and dyspnea, and the most common underlying disease was HT. It was stated that age and concomitant diseases are the most important risk factors for death. Each 5-year increase in age increased the risk of death 1.55 times. In univariate Cox regression analysis, HR of risk factors for mortality were 5.3 for >70 years (95% CI; 3.1-9.0) and 3.1 for any comorbidity (95% CI; 1.6-5.8). In multivariate analysis, dyspnea, advanced age, neutrophilia, and higher cardiac troponin I were found to be independently associated with death. In our study, we found that the presence of any comorbidity, frequency of comorbidity, dyspnea, sputum, and hemoptysis were higher in the elderly group.

In the study by Niu et al[11], they found dyspnea more frequently seen in older age and incidence of COPD increased with age. Similarly, in the elderly group, we found that dyspnea and comorbidities were more frequent.

In the study by Wang et al.[12] they compared the mortal and non-mortal patients >60 years old. They found age, dyspnea, and frequency of comorbidities to be significantly higher in the mortal group. They reported that dyspnea, CVD, COPD, lymphopenia, and ARDS can predict the risk of death. Tanaka et al[13] found that male gender, the presence of comorbidity, and moderate and severe disease were associated with mortality in elderly patients with a diagnosis of COVID-19.

In the study by Lee et al[14], they compared 20 mortal and 78 non-mortal elderly patients hospitalized with a diagnosis of COVID-19 (≥65 years old) and found age to be the most important risk factor for mortality and mechanical ventilation/high-flow nasal cannula use. The mortality rate

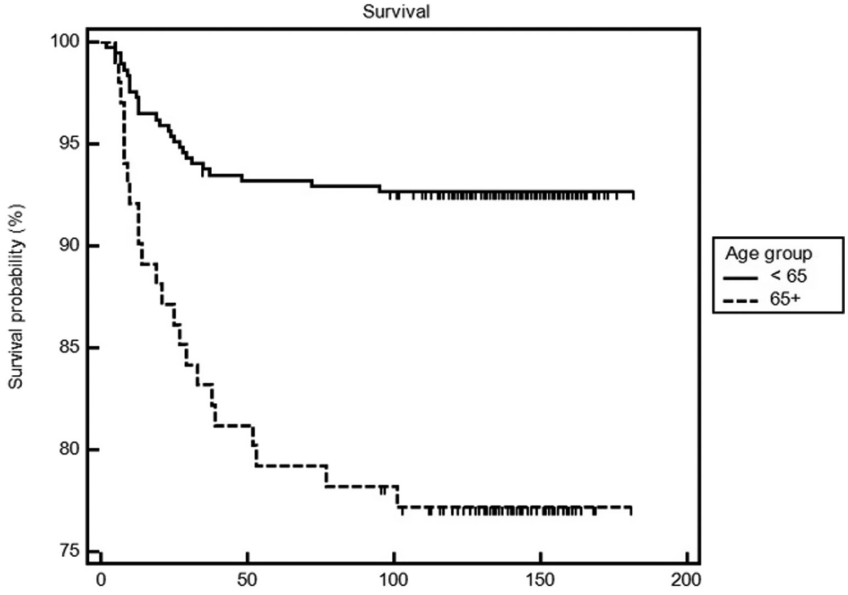

Figure 1. Survival analysis of patients ≥65 and <65 years old (Kaplan–Meier graph).

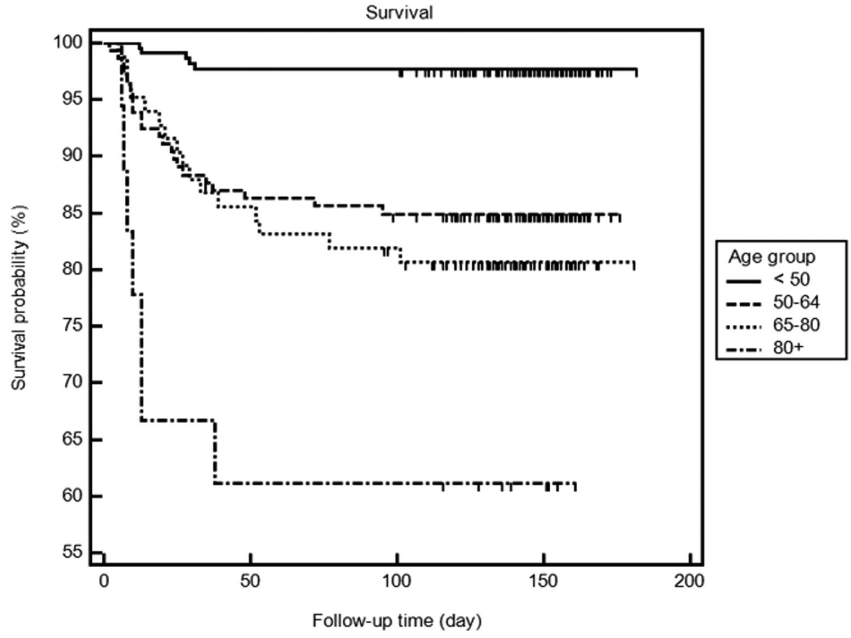

Figure 2. Survival analysis among age groups (Kaplan–Meier graph).

was found to be 20.4% in all patients. Male gender, age, and the presence of any comorbidity were higher in the mortal group.

It has been shown in many studies that advanced age is associated with mortality.[7,15] In previous studies, COVID-19 mortality rates were reported as 2%-5% in all patients, 8.0%[8,12,16-18] in the age of 70-79 years, and 14.8%[18] over 80 years. On the other hand, Lee et al[14] found mortality rate to be 20.4% in patients ≥65 years old. In our study, we found mortality to be 7.3% in the non-elderly group and 22.8% in the elderly group. We thought that the high mortality rates might be due to the longer follow-up times compared to the current studies. In addition, in our study, most of the mild cases were treated at home. The majority of the patients included in the study were in the moderate, severe and critical disease group. Therefore, mortality rates were found to be higher than in the literature.

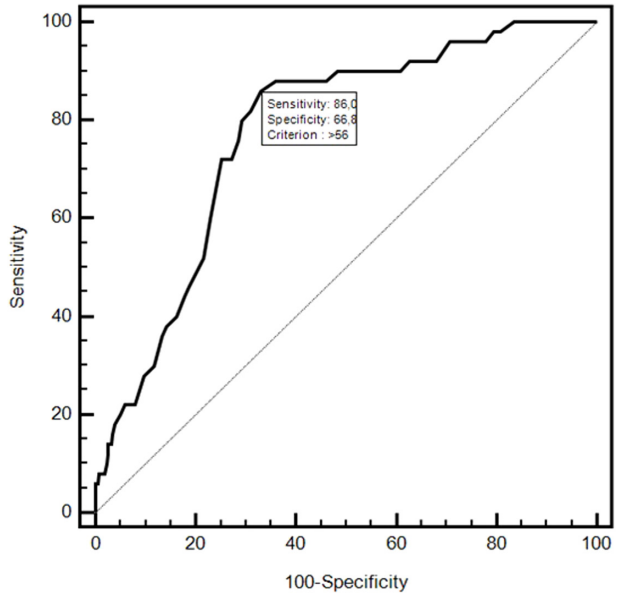

Figure 3. ROC analysis of COVID-19 patients. ROC, receiver operating characteristic; COVID-19, coronavirus disease 2019.

In a study evaluating mortality rates and risk factors in Turkey, it was determined that over 65 years of age, male gender, dyspnea, severe pneumonia, and comorbidities were positively associated with mortality.[19]

There are few studies that have analyzed survival in COVID-19 patients. We also analyzed the survival of the patients. During the 200-day follow-up, we found that the expected survival time was significantly less in the elderly patients than in the non-elderly group. We found the risk of death in the elderly patients 3.35 times higher than the non-elderly patients. Compared to <50 years of age, we found that the risk of death increased significantly with increasing age in other age groups.

Similar to previous studies,[11,18] we also saw more severe pneumonia and critical illness in the elderly patients. Invasive mechanical ventilation and oxygen use were also higher in the elderly. In 1 study, it was stated that patients with hypoxemia had higher mortality.[20] Diffuse involvement was seen significantly more in the elderly patients in HRCT. This was proportional to the fact that there were more elderly patients in severe pneumonia and critically ill group. In the study by Li et al[21], it was reported that the use of systemic corticosteroid and oxygen therapy was higher in the patients with severe disease than the non-severe group. In our study, also, most of the elderly patients had severe disease (severe pneumonia and critical illness) and our rate of corticosteroid and oxygen use was higher in this group than the other group.

We found that the male gender, dyspnea, high D-dimer, creatinine, troponin, and lymphopenia increased the risk of mortality in elderly patients.

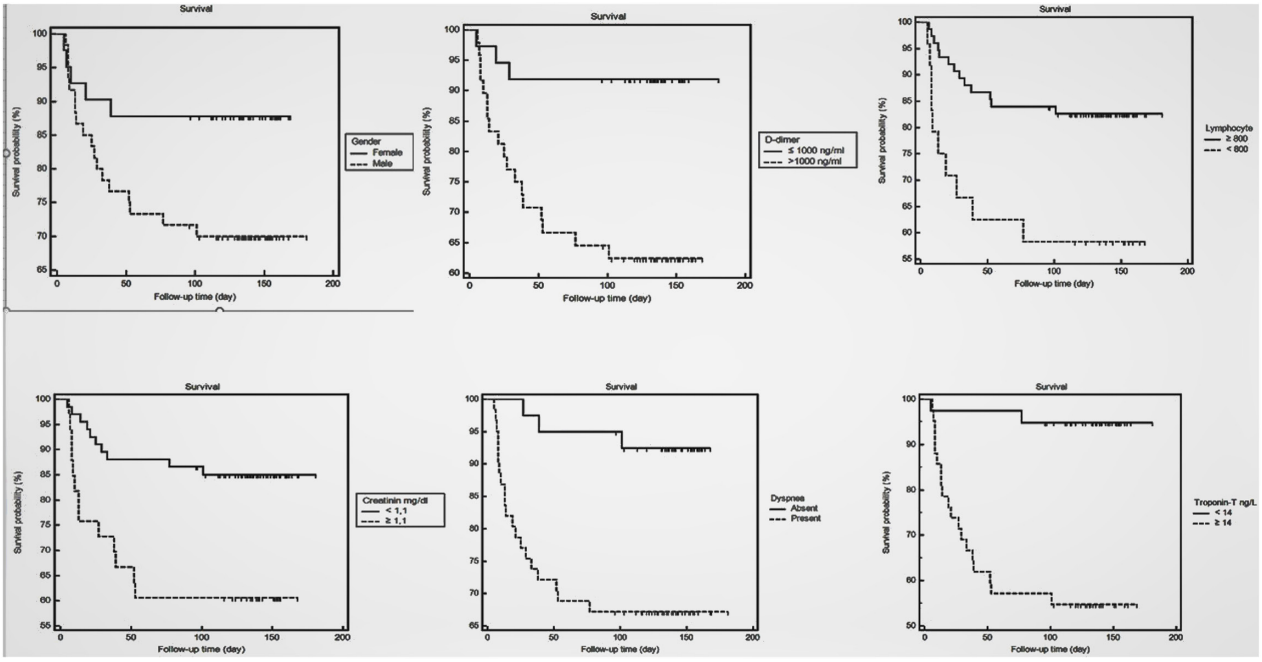

Figure 4. Kaplan–Meier analysis of log-rank test in elderly patients

In many recent phase III studies, vaccination against SARS CoV-2 has been shown to reduce disease spread, incidence, severe disease and death rates.[22-24] Our study was carried out in the period when vaccine applications had not yet started.

The limitations of this study are it being a retrospective study, the lack of anamnesis information due to the data being taken from medical records, and the failure to examine standard laboratory parameters in each patient. In addition, while data are collected by scanning patients from the death notification system in terms of survival, we can also add that patients do not usually have control laboratory and radiological data during this period.

CONCLUSION

Compared to the non-elderly patients with COVID-19, mortality is higher, comorbidities are more frequent, and the disease is more severe in elderly patients. In addition to inflammatory biomarkers, the male gender, dyspnea, and comorbidities are important parameters in predicting mortality. Compared to the patients under 50 years of age, the risk of mortality gradually increases with increasing age. The age of 56 can be used as a cut-off to determine mortality risk. More comprehensive studies are needed to evaluate the mortality and prognostic factors of elderly patients with COVID-19 after the spread of vaccination.

Ethics Committee Approval: This study was approved by the Ethics committee of University of Health Sciencies, Dr Suat Seren Chest Disease and Surgery Training and Research Hospital and by the Turkish Ministry of Health, COVID-19 Scientific Research Committee (Approval No: 49109414-604.02).

Informed Consent: This study was carried out retrospectively using the recorded data of the patients in the health information systems, and does not include images that may identify the person.

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