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ARAŞTIRMA MAKALESİ / ORIGINAL ARTICLE

Impact of Baseline Patient Characteristics on Short- and Long-Term Overall Mortality in Elderly Patients with COVID-19: A Retrospective Cohort Study

COVID-19'lu Yaşlı Bireylerde Başlangıçtaki Hasta Özelliklerinin Kısa ve Uzun Dönem Genel Mortalite Üzerindeki Etkisi: Retrospektif Kohort Çalışması

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ABSTRACT

Aim: Elderly people encounter COVID-19 more frequently due to physiological changes associated with aging and underlying potential health conditions.The study aims to evaluate the impact of baseline patient characteristics on short- and long-term mortality in elderly patients aged 65 and over, classified as youngest-old, middle-aged, or oldest-old, who applied to the pandemic outpatient clinic and had not yet been vaccinated.

Materials and Methods: Symptomatic patients who attended the emergency department were enrolled in the study. Demographic data, symptoms, comorbidities, thoracic computed tomography (CT), and laboratory results were recorded at admission. The primary outcomes were all-cause short-term (within six months) and long-term (within four years) mortality.

Results: The study consists of 393 participants, with a mean age of 67.4 ± 9.8 years and 52.2% male. Considering the death rates in the last four years, it was determined that 72 (18.3%) cases died in the short term, and 104 (26.5%) cases died in the long term. It was found that chronic renal failure (CRF), coronary artery disease (CAD), middle-old and oldest-old-aged patients compared to the 50-64 age group were independent predictors of overall short-term mortality. It was determined that the following factors independently predicted overall long-term mortality: male gender, CAD, malignancy, CRF, fever, and dyspnea symptoms, and the patients of the youngest-old, middle-old, and oldest-old relative to the 50–64 age group.

Conclusion: Advanced age, male gender, symptoms of shortness of breath and fever, high D-dimer levels, the presence of CAD, malignancy, and CRF were related to a higher risk of death from COVID-19 infection in the elderly.

Keywords: Elderly Patients, COVID-19, Laboratory, Radiology, Symptoms, Mortality

ÖZ

Amaç: Yaşlı insanlar yaşlanma ve altta yatan potansiyel sağlık koşullarına bağlı olarak ortaya çıkan fizyolojik değişiklikler nedeniyle daha sık COVID-19 ile karşılaşmaktadır. Çalışmamızda pandemi polikliniğine başvuran, genç-yaşlı, orta-yaşlı ve ileri-yaşlı olarak sınıflandırılan 65 yaş ve üzeri yaşlı hastalarda hastaneye başvuru semptom ve bulgularının kısa ve uzun vadeli mortalite üzerindeki etkisinin değerlendirilmesi amaçlanmıştır.

Gereç ve Yöntemler: Acil servise başvuran semptomatik hastalar çalışmaya dahil edildi. Başvuru anında demografik veriler, semptomlar, komorbiditeler, toraks bilgisayarlı tomografi (BT) ve laboratuvar bulguları kaydedildi. Primer sonlanım noktası tüm nedenlere bağlı kısa dönem (altı ay içinde) ve uzun dönem (dört yıl içinde) ölümlerdi.

Bulgular: Araştırmaya yaş ortalaması 67,4±9,8 yıl olan ve %52,2'si erkek olan 393 hasta dahil edilmiştir. Son dört yıldaki ölüm oranlarına bakıldığında kısa dönemde 72 (%18,3) vakanın, uzun dönemde ise 104 (%26,5) vakanın öldüğü belirlendi. Kronik böbrek yetmezliği (KBY), koroner arter hastalığı (KAH), orta-yaşlı ve ileri-yaşlı hastaların 50-64 yaş grubuyla karşılaştırıldığında genel kısa dönem mortalitenin bağımsız belirleyicileri olduğu bulundu. Erkek cinsiyet, KAH, malignite, KBY, ateş ve nefes darlığı semptomları ile 50-64 yaş grubu ile karşılaştırıldığında genç-yaşlı, orta-yaşlı ve ileri-yaşlı olguların genel uzun dönem mortaliteyi bağımsız olarak öngördüğü belirlendi.

Sonuç: İleri yaş, erkek cinsiyet, nefes darlığı ve ateş semptomları, yüksek D-dimer düzeyleri, KAH, malignite ve KBY varlığı yaşlılarda daha yüksek COVID-19 enfeksiyonu kısa ve uzun dönem ölüm riski ile ilişkiliydi.

Anahtar Kelimeler: Yaşlı Hasta, COVID-19, Laboratuvar, Radyoloji, Semptomlar, Mortalite

INTRODUCTION

The Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) infection outbreak, which emerged in Wuhan, China, at the end of 2019, was named Coronavirus Disease 2019 (COVID-19) by the World Health Organization (WHO) and was announced a pandemic on March 11, 2020 (1). Clinical signs of SARS-CoV-2 infection can vary widely in patients, ranging from no symptoms to severe disease (2). As of November 2022, a total of 17.052.695 cases and 101.511 deaths due to COVID-19 have been reported in Türkiye (3).

The number of older people is growing worldwide and in our country because of healthcare and technology improvements. In 2019, there were estimated to be about 7.5 billion people worldwide and 700 million older people (4). According to figures from Turkish Statistical Institute for our country, the number of elderly people have grown by 22.5% in the last five years and now make up 9.5% of the population. People who are 65 years of age or older are usually considered to be elderly (5).

Globally, elderly people are more likely to contract COVID-19. Pathophysiologic changes accompany aging, including weakened immune systems, chronic diseases, and declining cognitive function (6). To adequately examine geriatric conditions, it is vital to classify elderly people based on age, as diseases affecting this population also differ according to age. Nevertheless, most research conducted on the old has grouped all elderly individuals into one category. While there are various classification schemes for this demographic, research has identified three age groups for older adults: youngest-old at 65 to 74 years old, middle-old at 75 to 84 years old, and oldest-old at 85 years old (7). It is critical to summarize crucial variables linked with mortality to offer physicians, researchers, and the public credible evidence to effectively control the pandemic and minimize the mortality rate of older persons diagnosed with COVID-19. For this reason, we aimed to evaluate the impact of clinical, radiological, and laboratory findings on short- and long-term mortality in patients aged 65 and over who were classified as youngest-old, middle-aged, or oldest-old according to their age and who applied to the pandemic outpatient clinic.

MATERIALS AND METHODS

General Study Details

This retrospective cohort study includes patients who attended to the emergency department between November 1, 2020, and November 30, 2020. The socio-demographic data, symptoms, comorbidities, and radiological and biochemical findings of the cases at admission were recorded. Symptomatic individuals aged 50 and over who were not yet vaccinated and presented to the emergency department were enrolled in the study. Patients admitted to the intensive care unit without an examination from the emergency department and who did not have a thoracic computed tomography (CT) were excluded from the study. The study protocol is summarized in Figure 1. RT-PCR testing of nasopharyngeal and oropharyngeal swab samples was recognized as the definitive standard for the conclusive COVID-19 diagnosis. The Radiological Society of North America (RSNA) expert consensus statement classified chest CT patterns. This study was approved by the Uludağ University Faculty of Medicine Institutional Review Board (2023-26 / 24).

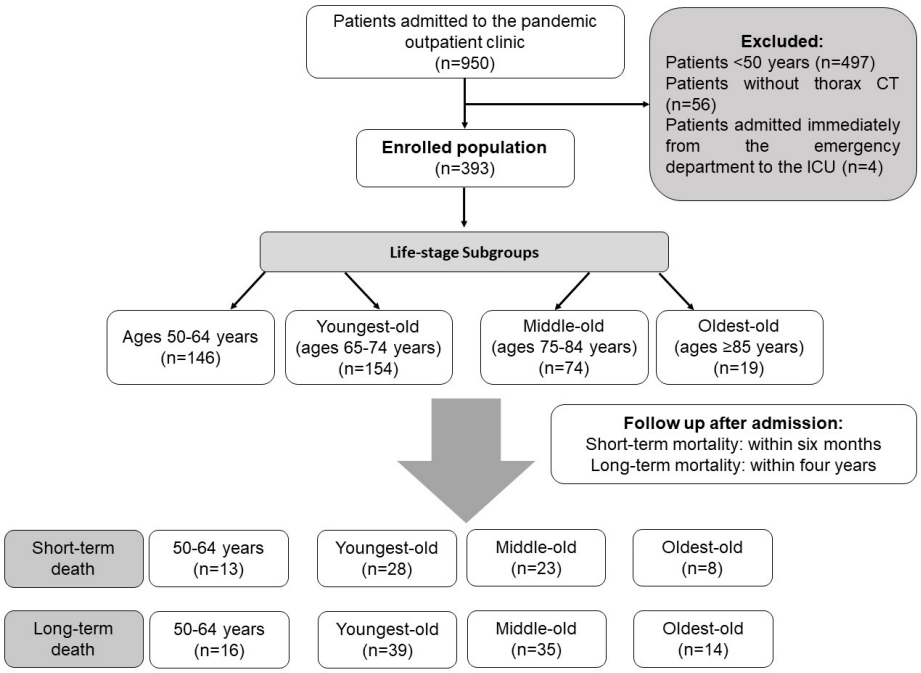

Figure 1. Study flow chart

Participants

Elderly persons between the ages of 65 and 74 were classed as "youngest-old", those between 75 and 84 as "middle-old", and those over 85 as "oldest-old".

Variables

The primary outcomes were all-cause short-term (within six months) and long-term (within four years) mortality. The patients' death or survival status was recorded from the national death notification system until November 19, 2023.

Statistical analysis

IBM SPSS Statistics for Windows Version 23.0 was used to analyze the data. The normal distribution of continuous variables was confirmed with the Shapiro-Wilk test. Categorical variables are shown as n (%), whereas continuous data were provided as mean ± standard deviation (SD) or median (interquartile range (IQR)) values. Pearson Chi-square test was used to compare categorical variables, and independent sample t-tests or Mann-Whitney U tests were used for comparisons between groups, depending on the normality test findings. Using univariate Cox regression, the variables reported in the univariate studies were first examined to determine risk factors considered significant in predicting mortality. Subsequently, the multivariate Cox regression model was constructed with the variables that met the $p<0.25$ threshold. The variables were selected using the backward stepwise LR approach, and the analysis's findings were presented. A summary was provided for the hazard ratios (HRs) and 95% confidence intervals (95% CIs). Kaplan-Meier survival analysis was performed using MedCalc Statistical Software (version 20.026, 2022; Ostend, Belgium; https: / / www.medcalc.org) and compared geriatric age groups using the log-rank test.

RESULTS

This study consisted of 393 COVID-19 participants in total. The mean age of cases was 67.4 ± 9.8 years, and 205 (52.2%) were male.

Of these patients, 248 (70.7%) had at least one comorbid condition. Hypertension (47.1%), diabetes mellitus (24.4%), and coronary artery disease (CAD) (18.8%) were the most prominent comorbid diseases. Based on the patients' age classification, 146 (37.2%) belonged to the 50-64 age group, 154 (392%) to the youngest-old (65–74 years), 74 (18.8%) to the middle-old (75–84 years), and 19 (4.8%) to the oldest-old (≥85 years). The sociodemographic characteristics, initial vital and laboratory findings, chest CT findings, and mortality status of the cases according to age groups are presented in Table I.

Considering the death rates in the last four years, it was determined that 72 (18.3%) cases died in the short-term, and 104 (26.5%) cases died in the long-term. Table II summarizes the factors contributing to the cases' short- and long-term mortality.

Table I. Characteristics of patients according to geriatric age classification

	Overall Patients (n=393)		50-64 years old patients (n=146)		Youngest-old patients (n=154)		Middle-old and oldest-old patients (n=93)		p-value
Age, years	67.4 ± 9.8		57.2 ± 4.2		69.1 ± 2.9		80.8 ± 4.5		**<0.001**[a]
Gender, male	205	(52.2)	77	(41)	68	(36.2)	43	(22.9)	0.311[b]
Comorbidity, n (%)	278	(70.7)	89	(32)	114	(41%)	75	(27)	**0.003**[b]
Hypertension	185	(47.1)	50	(27)	78	(42.2)	57	(30.8)	**<0.001**[b]
Diabetes Mellitus	96	(24.4)	37	(38.5)	38	(39.6)	21	(21.9)	0.886[b]
Coronary artery disease	74	(18.8)	17	(23)	31	(41.9)	26	(35.1)	**0.006**[b]
COPD	21	(5.3)	5	(23.8)	10	(47.6)	6	(28.6)	0.429[b]
Asthma	35	(8.9)	11	(31.4)	17	(48.6)	7	(20)	0.492[b]
Malignancy	22	(5.6)	9	(40.9)	8	(36.4)	5	(22.7)	0.930[b]
Chronic renal failure	15	(3.8)	2	(13.3)	9	(60)	4	(26.7)	0.125[b]
Congestive heart failure	13	(3.3)	0	0	6	(46.2)	7	(53.8)	**0.006**[b]
Initial vital signs, n (%)									
Fever	105	(26.7)	46	(43.8)	36	(34.3)	23	(21.9)	0.250[b]
Throat ache	24	(6.1)	12	(50%)	11	(45.8)	1	(4.2)	0.063[b]
Dyspnea	109	(27.7)	37	(33.9)	44	(40.4)	28	(25.7)	0.694[b]
Cough	176	(44.8)	70	(39.8)	66	(37.5)	40	(22.7)	0.625[b]
Fatigue	140	(35.6)	51	(36.9)	56	(40)	33	(23.6)	0.967[b]
Diarrhea	16	(4.1)	6	(37.5)	8	(50)	2	(12.5)	0.502[b]
Myalgia	55	(14)	26	(47.3)	24	(43.6)	5	(9.1)	**0.02**[b]
Smell and taste dysfunction	10	(2.5)	4	(40)	3	(30)	3	(30)	0.812[b]
Chest CT images, n (%)									
Typical	273	(69.5)	109	(39.9)	107	(39.2)	57	(20.9)	
Indeterminate	48	(12.2)	12	(25)	21	(43.8)	15	(31.3)	**0.038**[b]
Atypical	17	(4.3)	3	(17.6)	5	(29.4)	9	(52.9)	
Negative	55	(14)	22	(40)	21	(38.2)	12	(21.8)	
Initial laboratory findings									
c-reactive protein, mg / L	42.1 (10.5-107.2)		30.5 (5.6-85.8)		48.8 (13.6-102.3)		61.0 (12.8-161.0)		**0.007**[c]
d-dimer, mg / L	0.67 (0.41-1.25)		0.57 (0.36-0.95)		0.64 (0.40-1.21)		1.03 (0.57-1.90)		**<0.001**[c]
Ferritin, ng / mL	219 (102-611)		221 (94-562)		218 (89-603)		213 (115-629)		0.945[c]
Lymphocyte, per mm^3	1363 (860-1991)		1437 (977-1968)		1345 (819-2040)		1269 (806-2000)		0.588[c]
Mortality									
Short-term mortality	72	(18.3)	13	(18.1)	28	(38.9)	32	(43.1)	**<0.001**[b]
Long-term mortality	104	(26.5)	16	(15.4)	39	(37.5)	49	(47.1)	**<0.001**[b]

Data are presented as mean±SD, median (25-75), and n(%). a. independent samples t-test, b. Mann-Whitney U test c. Pearson's Chi-square test COPD: Chronic obstructive pulmonary disease

Table II. Factors associated with short- and long-term mortality

	Overall Patients (n=393)		Short term mortality					Long term mortality				
			Dead (n=72)		Alive (n=321)		p-value	Dead (n=104)		Alive (n=289)		p-value
Age, years	67.4 ± 9.8		73.2 ± 9.7		66.2 ± 9.4		**<0.001**[a]	73.8 ± 9.6		65.2 ± 8.9		**<0.001**[a]
Age category, n (%)												
50-64 years old patients	146	(37.2)	13	(8.9)	133	(91.1)	**<0.001**[b]	16	(11)	130	(89)	**<0.001**[b]
Youngest-old	154	(39.2)	28	(18.2)	126	(81.8)		39	(25.3)	115	(74.7)	
Middle-old	74	(18.8)	23	(31.1)	51	(68.8)		35	(47.3)	39	(52.7)	
Oldest-old	19	(4.8)	8	(42.8)	11	(57.9)		14	(73.7)	5	(26.3)	
Gender, male	205	(52.2)	50	(24.4)	155	(75.6)	**0.001**[b]	69	(33.7)	136	(66.3)	**<0.001**[b]
Comorbidity, n (%)												
Hypertension	185	(47.1)	32	(17.3)	153	(82.7)	0.621[b]	54	(29.2)	131	(70.8)	0.248[b]
Diabetes Mellitus	96	(24.4)	18	(18.8)	78	(81.3)	0.900[b]	25	(26)	71	(74)	0.914[b]
Coronary artery disease	74	(18.8)	21	(28.4)	53	(71.6)	**0.013**[b]	29	(39.2)	45	(60.8)	**0.006**[b]
COPD	21	(5.3)	5	(23.8)	16	(76.2)	0.504[b]	8	(38.1)	13	(61.9)	0.214[b]
Asthma	35	(8.9)	3	(8.6)	32	(91.4)	0.118[b]	5	(14.3)	30	(85.7)	0.087[b]
Malignancy	22	(5.6)	7	(9.7)	15	(68.2)	0.092[b]	13	(59.1)	9	(40.9)	**<0.001**[b]
Chronic renal failure	15	(3.8)	7	(46.7)	8	(53.3)	**0.004**[b]	9	(60)	6	(10)	**0.003**[b]
Congestive heart failure	13	(3.3)	4	(30.8)	9	(69.2)	0.238[b]	7	(53.8)	6	(46.2)	**0.023**[b]
Initial vital signs, n (%)												
Fever	105	(26.7)	23	(31.9)	82	(71.8)	0.267[b]	35	(33.3)	70	(66.7)	0.062[b]
Throat ache	24	(6.1)	4	(5.6)	20	(83.3)	0.829[b]	4	(16.7)	20	(83.3)	0.262[b]
Dyspnea	109	(27.7)	31	(28.4)	78	(71.6)	**0.001**[b]	43	(39.4)	66	(60.8)	**<0.001**[b]
Cough	176	(27.7)	27	(15.3)	149	(84.7)	0.169[b]	41	(23.3)	135	(76.7)	0.200[b]
Fatigue	140	(35.6)	29	(20.7)	111	(79.3)	0.361[b]	42	(30)	98	(70)	0.237[b]
Diarrhea	16	(4.1)	6	(37.5)	10	(62.5)	**0.043**[b]	7	(43.8)	9	(56.3)	0.110[b]
Myalgia	55	(14)	5	(9.1)	50	(90.9)	0.056[b]	9	(16.4)	46	(83.4)	0.067[b]
Smell and taste dysfunction	10	(2.5)	1	(10)	9	(90)	0.491[b]	3	(30)	7	(70)	0.797[b]
Chest CT images, n (%)												
Typical	273	(69.5)	57	(20.9)	216	(79.7)	**0.008**[b]	72	(26.4)	201	(73.6)	0.113[b]
Indeterminate	48	(12.2)	11	(22.9)	37	(77.1)		18	(37.5)	30	(62.5)	
Atypical	17	(4.3)	3	(17.6)	14	(82.4)		5	(29.4)	12	(70.6)	
Negative	55	(14)	1	(1.8)	54	(98.2)		9	(16.4)	46	(83.6)	
Initial laboratory findings												
c-reactive protein, mg / L	42.1 (10.5-107.2)		137.4 (57.1-201.2)		34.6 (6.6-77.2)		**<0.001**[b]	92.4 (34.8-182.5)		31.2 (5.7-76.0)		**<0.001**[b]
d-dimer, mg / L	0.67 (0.41-1.25)		1.17 (0.64-2.34)		0.62 (0.38-1.09)		**<0.001**[b]	1.12 (0.64-2.22)		0.59 (0.38-1.00)		**<0.001**[b]
Ferritin, ng / mL	219 (102-611)		656 (237-1125)		189 (88-447)		**<0.001**[b]	370 (166-875)		189 (87-457)		**<0.001**[b]
Lymphocyte, per mm^3	1363 (860-1991)		865 (692-1238)		1500 (980-2130)		**<0.001**[b]	960 (710-1438)		1510 (1000-2120)		**<0.001**[b]

Data are presented as mean±SD, median (25-75), and n(%).
a. independent samples t-test, b. Mann-Whitney U test c. Pearson's Chi-square test
COPD: Chronic obstructive pulmonary disease

The univariate Cox regression analysis assessing the factors influencing overall short-term mortality revealed that dyspnea ($p < 0.001$), CAD, ($p = 0.003$), malignancy ($p < 0.001$), chronic renal failure (CRF) ($p < 0.001$), congestive heart failure ($p=0.026$), and male gender ($p = 0.001$)

were significant predictors. The youngest old age (p = 0.021), middle-old age (p < 0.001), and oldest-old age (p < 0.001) were revealed to be significant predictors of short-term mortality in the univariate analysis when cases between the ages of 50 and 64 were selected as a reference. Middle-old age (HR: 3.43; 95%CI: 1.59-6.99, p = 0.001), oldest-old age (HR: 3.48; 95%CI: 1.25-9.64, p = 0.016), CAD (HR: 2.02; 95%CI: 1.12-3.54, p = 0.013), and CRF (HR: 2.99; 95%CI: 1.31-6.82, p = 0.009) were the domains that maintained significance as predictors of short-term mortality in the multivariate analysis (Table III).

Table III. Univariate and multivariate Cox regression analyses evaluating the factors affecting overall short- and long-term mortality

	Short-term Mortality						**Long-term Mortality**					
	Univariate Analysis			**Multivariate Analysis**			**Univariate Analysis**			**Multivariate Analysis**		
	HR	95% CI	p-value	HR	95% CI	p-value	HR	95% CI	p-value	HR	95% CI	p-value
Gender *Reference cat. female*	2.25	1.36-3.72	**0.001**	-	-	-	2.02	1.34-3.03	<0.001	1.71	1.10-2.64	**0.017**
Age category *Reference cat. 50-64 years old patients*												
Youngest old	2.16	1.12-4.18	**0.021**	1.56	0.76-3.19	0.221	2.48	1.38-4.45	0.02	2.19	1.19-4.04	**0.011**
Middle-old	4.08	2.06-8.06	**<0.001**	3.43	1.59-6.99	**0.001**	5.28	2.92-9.55	<0.001	4.64	2.47-8.71	**<0.001**
Oldest-old	6.23	2.58-15.04	**<0.001**	3.48	1.25-9.64	**0.016**	10.23	4.98-21.01	<0.001	8.71	4.05-18.72	**<0.001**
Comorbidity, n (%)												
Hypertension	0.90	0.56-1.43	0.663	-	-	-	1.21	0.82-1.77	0.330	-	-	-
Diabetes Mellitus	0.98	0.63-1.54	0.950	-	-	-	0.96	0.61-1.51	0.880	-	-	-
Coronary artery disease	1.90	1.25-2.92	**0.003**	2.02	1.12-3.54	**0.013**	1.92	1.25-2.95	0.003	1.63	1.04-2.61	**0.048**
COPD	1.58	0.76-3.25	0.213	-	-	-	1.57	0.76-3.24	0.210	-	-	-
Asthma	0.48	0.19-1.17	0.107	-	-	-	0.46	0.18-1.13	0.093	-	-	-
Malignancy	2.70	1.51-4.83	**<0.001**	-	-	-	2.89	1.61-5.18	<0.001	2.46	1.27-4.87	**0.008**
Chronic renal failure	3.25	1.64-6.44	**<0.001**	2.99	1.31-6.82	**0.009**	3.39	1.71-6.73	<0.001	2.43	1.13-5.21	**0.002**
Congestive heart failure	2.39	1.10-5.14	**0.026**	-	-	-	2.53	1.17-5.46	0.017	-	-	-
Initial vital signs, n (%)												
Fever	1.44	0.96-2.16	0.077	-	-	-	1.47	0.98-2.22	0.060	1.91	1.21-3.04	**0.005**
Throat ache	0.61	0.22-1.63	0.319	-	-	-	0.58	0.21-1.61	0.290	-	-	-
Dyspnea	2.07	1.40-3.06	**<0.001**	-	-	-	2.09	1.41-3.09	**<0.001**	1.92	1.26-2.91	**0.002**
Cough	0.77	0.53-1.14	0.203	-	-	-	0.75	0.51-1.12	0.116	-	-	-
Fatigue	1.24	0.84-1.84	0.075	-	-	-	1.25	0.85-1.85	0.261	-	-	-
Diarrhea	2.01	0.93-4.33	0.075	-	-	-	2.03	0.94-4.39	0.069	-	-	-
Myalgia	0.53	0.26-1.04	0.075	-	-	-	0.52	0.22-1.02	0.590	-	-	-
Smell and taste dysfunction	1.07	0.34-3.38	0.905	-	-	-	1.05	0.33-3.31	0.059	-	-	-
Chest CT images, n (%) *Reference cat. negative*												
Typical	12.63	1.75-91.27	**0.012**	6.49	0.87-48.10	0.067	1.83	0.92-3.67	0.086	-	-	-
Indeterminate	14.70	1.89-113.87	**0.010**	11.01	1.36-88.63	**0.027**	2.69	1.21-6.01	**0.015**	-	-	-
Atypical	10.05	1.09-101.41	**0.041**	5.96	0.56-59.31	0.128	1.95	0.65-5.83	0.229	-	-	-
Initial laboratory findings												
c-reactive protein, mg / L	1.01	1.0-1.1	**<0.001**	-	-	-	1.01	1.0-1.1	**<0.001**	-	-	-
D-dimer, mg / L	1.05	1.02-1.08	**<0.001**	1.05	1.02-1.09	**0.004**	1.05	1.02-1.09	**<0.001**	1.06	1.03-1.09	**<0.001**
Ferritin, ng / mL	1.01	1.0-1.1	**<0.001**	-	-	-	1.01	1.0-1.1	**<0.001**	-	-	-
Lymphocyte, per mm^3	0.99	0.98-0.99	**<0.001**	-	-	-	0.99	0.98-0.99	**<0.001**	-	-	-

COPD: Chronic obstructive pulmonary disease

When cases between the ages of 50 and 64 were used as a reference, it was discovered that the youngest old age (p = 0.02), middle old age (p < 0.001), and oldest-old age (p < 0.001) were significant predictors of long-term mortality in the univariate Cox regression model. Male gender (p < 0.001), CAD (p = 0.003), malignancy (p < 0.001), CRF (p < 0.001), congestive heart failure (p = 0.017), and dyspnea (p<0.001) were also found to be significant predictors of overall long-term mortality.

Male gender (HR: 1.71; 95%CI: 1.10-2.64, p = 0.017), youngest old age (HR: 2.19; 95%CI: 1.19-4.04, p = 0.011), middle-old age (HR: 4.64; 95%CI: 2.47-8.71, p < 0.001), oldest-old age (HR: 8.71; 95%CI: 4.05-18.72, p < 0.001), CAD (HR: 1.63; 95%CI: 1.04-2.61, p = 0.048), malignancy (HR: 2.46; 95%CI: 1.27-4.87, p = 0.008), CRF (HR: 2.43; 95%CI: 1.13-5.21, p = 0.002), fever (HR: 1.91; 95%CI: 1.21-3.04, p = 0.005) and dyspnea (HR: 1.92; 95%CI: 1.26-2.91, p = 0.002) were the domains that maintained significance as predictors of long-term mortality in the multivariate analysis (Table III). The median (IQR) follow-up duration for cases excluding dead patients was 1104 (1093-1211) days. Figures 2a and 2b show Kaplan-Meier curves for time to death.

Kaplan-Meier survival curves for overall short- and long-term mortality separated by age group are shown in Figures 2a and 2b.

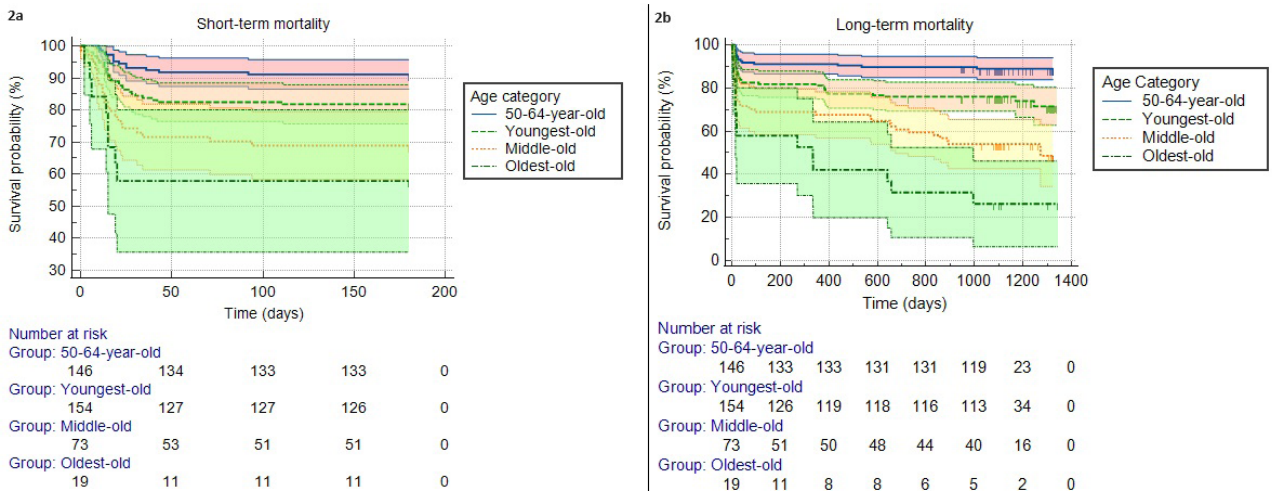

Figure 2a and 2b. Kaplan-Meier survival curves for overall short- and long-term mortality separated by age group

The mean survival times between the 50–64-year-old patients (mean ± SE: 166.3 ± 3.6 days), the youngest-old patients (mean ± SE: 151.1 ± 4.9 days), the middle-old patients (mean ± SE: 130.2 ± 8.7 days), and the oldest-old patients (mean ± SE: 109.2 ± 19.1 days) showed a significant difference based on short-term mortality (p<0.001). The mean survival times for patients aged 50-64 (mean ± SE: 1194.6 ± 31.3 days), youngest-old (mean ± SE: 1039.8 ± 42.6 days), middle-old (mean ± SE: 821.7 ± 67.7 days), and oldest-old (mean ± SE: 528.5 ± 127.5 days) showed a significant difference based on long-term mortality (p<0.001).

DISCUSSION

This study investigated factors predicting short and long-term mortality in elderly cases with COVID-19. It was found that CAD, CRF, middle-old, and oldest-old-aged patients compared to the 50-64 age group were independent predictors of overall short-term mortality. It was determined

that the following factors independently predicted overall long-term mortality: male gender, CAD, malignancy, CRF, fever, and dyspnea symptoms, and the patients of the youngest-old, middle-old, and oldest-old relatives aged 50–64 age group.

Age groups classified as middle-old and oldest-old are linked to higher risks of both short and long-term death. The youngest-old age group also had a 2.19-fold higher risk of long-term death when compared to the 50–64 age group. Yanez et al. observed that those over 65 had significantly higher COVID-19 death rates than younger ones (8). Because aging causes reduced functioning of multiple systems, including the immune system, advanced age has been determined as an important risk factor for mortality in COVID-19 (9). Two critical aspects of the aging immune system are immunosenescence and inflamm-aging (10). The condition known as "inflamm-aging," which is the accumulation of systemic inflammatory mediators in the aging body, exacerbates many chronic illnesses and increases immune system disturbance (11). This condition also contributes to immunosenescence, which is the term for the weakening immune system that happens in elderly people. Immunosenescence refers to how aging affects both innate and adaptive immunity (11,12) . Regardless of whether COVID-19 is the cause of this increased immunosenescence, it does indicate that these patients will be more susceptible to infections in the future, have impaired immunological responses to vaccinations, and have an increased risk of developing autoimmune diseases (13).

Male gender is an established risk factor for severe COVID-19. Although the entire global number of confirmed COVID-19 cases across all age categories is roughly balanced by gender, hospitalizations and ICU admissions are significantly more common in men, as is case mortality (14, 15). In univariate analysis, male gender was associated with a 2.2-fold increased short-term risk and a 2.02-fold increased long-term risk of death; this rate remained significant in multivariate analysis, with male gender conferring a 1.71-fold increased risk of long-term death. Moradi et al. stated that among older individuals with COVID-19, the male gender is a risk factor for mortality. This could be related to angiotensin-converting enzyme 2 (ACE-2), a COVID-19 receptor (16). Males are thought to be more susceptible to COVID-19 infection and death due to the possible increased expression of ACE-2 (17).

Multivariate analysis revealed that congestive heart failure was linked to a 2.02-fold increased risk and CRF to a 2.9-fold increased risk of short-term death. A 1.63-fold greater risk for CAD, a 2.46-fold increased risk for malignancy, and a 2.43-fold increased risk for CRF were shown to be associated with long-term mortality. The increased COVID-19 mortality seen in older comorbid patients may be explained by a synergistic negative effect of advanced age and the number of concomitant comorbidities on the health status of the elderly (18). A systematic review showed that cardiovascular diseases, respiratory disorders, nervous system diseases, kidney diseases, and malignancy were related to a greater mortality risk among older COVID-19 patients (19). COVID-19-related cardiovascular diseases can be increased in patients with comorbidities that impact the microvasculature or the myocardium. Additionally, both aging and various comorbidities were found to enhance the expression of SARS-CoV-2 cellular entering receptors, directly impacting the severity of COVID-19 (20, 21).

In a univariate analysis, the presence of dyspnea symptoms at the time of admission was linked to a 2.07-fold higher risk of short-term death. While there was no influence on short-term mortality

in multivariate analysis, dyspnea was linked with a 1.92-fold increase in long-term mortality, and the presence of fever symptoms at the time of admission was associated with a 1.91-fold increase in long-term mortality. Li et al. showed that dyspnea was an independent predictor of death (22).

Typical (6.49-fold) and indeterminate (11.01-fold) radiological results increased the probability of short-term mortality but did not influence long-term mortality. Sönmez et al. reported that increasing lung involvement in thorax CT was related to a higher risk of death (23). Elevated D-dimer levels were linked to both short- and long-term mortality risk in multivariate analysis. It has been reported that D-dimer elevation is an independent predictor of death and complications (24).

Limitations

This study has some limitations that should be addressed. First, the study's retrospective approach raises the possibility of data errors and incomplete records.

Second, the study population consisted of symptomatic patients aged 50 and up who had not yet been immunized and presented to the emergency room. The exclusion of asymptomatic and vaccinated patients may restrict the findings' generalizability to the larger community of older COVID-19 patients.

Third, the study fails to record the initial vital signs, specific medications used, length of hospital stays, in-hospital mortalities, co-infection conditions, or specified causes of death. These characteristics may have offered new information on the clinical development and prognosis of COVID-19 in older people.

Fourth, the follow-up duration for long-term mortality was only four years. While this time period gives useful information about the long-term effects of COVID-19, it may not fully represent the disease's long-term impact on elderly people, especially those with chronic health issues.

CONCLUSION

Advanced age, male gender, symptoms of shortness of breath and fever, high D-dimer levels, and the presence of CAD, malignancy, and CRF were related to a higher risk of death from COVID-19 infection in the elderly. The findings of this analysis could assist healthcare physicians in identifying high-risk individuals, facilitating appropriate corrective steps, and reducing death among this vulnerable population.

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Conflict of Interest

There is no conflict of interest

Financial Support

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Ethical Declaration

This study was approved by the Bursa Uludağ University Faculty of Medicine Institutional Review Board (2023-26 / 24**).**

Author contributions

Idea: ÖAG, AU, Design: ÖAG, AU, Supervision: HA, MK, EU, Instrumentation: DÖT, OET, Data collection and processing: DÖT, OET, Analysis and interpretation: ÖAG, Literature review: NAAÖ, UÖ, ED , AGD, Writing: ÖAG, Critical review: DE, FC

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