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RESEARCH

HOW DID COVID-19 PANDEMIC AFFECT THE OLDER PATIENTS? COMPARISON OF CLINICAL FEATURES IN OLDER VERSUS YOUNGER PATIENTS.

Abstract

İntroduction: COVID-19 infection may be atypically presented in the older adults with a poor prognosis. In this study, we aimed to investigate the clinical and laboratory differences of COVID-19 course in older patients.

Materials and Method: The demographic, clinical, laboratory and radiological data of the patients hospitalized with COVID-19 infection were compiled retrospectively. A randomized control group was created from younger patients. Chest tomography of the patients were examined and scored.

Results: Data of 100 older and 127 younger patients with COVID-19 infection, and 80 non-COVID older patients were evaluated retrospectively. While the mean CRP, fibrinogen, procalcitonin, urea, LDH, INR, PT, Troponin-I, CK-MB and total radiological lung score were significantly higher in older patients; the mean hemoglobin, hematocrit and d-dimer were significantly higher in younger patients. Lymphopenia was more common and the mortality rate was higher in the older adults. Lymphopenia, presence of comorbidity, being over the age of 75, and radiological lung involvement were identified as mortality risk factors in older patients. The cut-off values for mortality were as follows; age≥77 years, lymphocyte#≤ 700x103 cells/µL, CRP≥108.71 mg/L, d-dimer≥2.25 mg/L, fibrinogen≥383 mg/L, INR≥1.05, PT ≥12.5 seconds, aPTT≥31 seconds, Troponin-I≥19.1 pg/mL, total lung score≥6 points. COVID-19 did not increase mortality much more than other hospital-requiring clinical events in older adults (17% vs 26.25%).

Conclusion: The older adults require special attention in COVID-19 pandemic. Those with comorbidities, lymphopenia, high d-dimer levels, and extensive lung involvement in the initial tomography should be followed-up closely.

Keywords: Covıd-19; Aged; Geriatrics; Mortality; Radiology

INTRODUCTION

World Health Organization (WHO) indicated that the incidence of COVID-19 is higher in young and middle-aged adults, but mortality rates increase with age (1, 2). This fact is even more important in the European region, where the older population is highest (3). The population aged over 65 years constitutes about 8.7% of the entire population and has reached over 7 million in Turkey (4). Despite the similar proportion of older adults, the number of deaths observed in Turkey is lower than in many European countries (1, 2). From this point of view, sharing the clinical conditions determining mortality will be beneficial for developing global strategies to struggle with COVID-19.

The mortality - age relationship of COVID-19 has multifactorial mechanisms (3, 5). The infectious diseases may have atypical presentations and poorer progress in older people due to the decline in the immune, anatomical and physiological defense systems. Available data suggest that COVID-19 infection can begin with atypical presentations in a significant proportion of the older adults (2, 5, 6).

This fact may contribute to late diagnosis and even a fatal course in the older patients.

Laboratory and radiological findings may also evolve with advancing age. Conditions such as underlying chronic diseases, polypharmacy, and suppression in the aging bone marrow create a need for a different perspective in the examination of laboratory data in older patients (7, 8). Lung radiology may change late due to dehydration. In addition, the declined respiratory reserve, may be inadequate in the patient with lung involvement (2, 5, 7). Considering that the current COVID-19 screening strategies are based on the typical findings of the disease, a need for a specialized clinical perspective for older adults arises (3, 6). Limited data are available in the literature on the course of COVID-19 in older patients. In this study, we aimed to reveal what clinical and laboratory differences are observed in older people diagnosed with COVID-19 in comparison with younger people. To the best of our knowledge, this is the first study comparing the older patients with confirmed COVID-19 infection and the patients hospitalized with a pre-diagnosis of COVID-19 but excluded from COVID-19 by clinical findings and real-time reverse-transcriptase polymerase chain reaction (PCR) tests.

METHODS

We obtained approval from the local ethic committee. A retrospective review was carried out between the dates of May 15th and March 11th, the date of the first COVID-19 case in Turkey.

Study population:

All of the patients aged 65 and over who were hospitalized with a pre-diagnosis of COVID-19 were searched. Cases with missing clinical, laboratory or radiological data were excluded from the study. Patients with confirmed COVID-19 infection were assessed as PCR (+) older patients. Patients excluded from the diagnosis of COVID-19 due to clinical findings and at least twice PCR negativity were assessed as PCR (-) older patients. A randomized control group consisting of 127 younger patients (young and middle-aged adults) with positive PCR results was composed by sorting younger patients according to age and randomly selection by skipping at regular intervals.

Clinical and laboratory findings

Demographic and clinical features were scanned. Laboratory data were obtained from the blood tests on the first day of admission. The pre-hospitalization residencies were grouped as "home residents" and "health care center/nursing home residents".

Radiological assessment

Chest computed tomography (CT) images were examined by two radiologists. Disputes in the radiologists were resolved by consensus. If there is a lung involvement, the infiltration pattern was determined and grouped as "sub-pleural" (mainly containing peripheral third of the lung), "random"

(without dominance in the sub-pleural or central regions) or "diffuse" (continuous involvement). To measure the degree of lung involvement, a CT scoring system, a semi-quantitative evaluation method, was applied. Two lungs were evaluated in a total of 5 lobes. First, the extent of the lesion in each lobe was visually estimated, and a point between 1 and 5 was given due to the extent of the involvement (0 point: no involvement, 1 point: 1-25%, 2 points: 26-50%, 3 points: 51-75%, 4 points: 76-100%). Secondly, the total lung score ranged from 0 to 20 was obtained by summing the points of the five lobes.

Statistical analysis

The mean and standard deviation (± SD) were calculated for continuous variables and proportions were calculated for categorical variables. Chi-square and Fisher exact tests were used in univariate analysis of categorical variables; and Student-T and Wilcoxon rank-sum tests were used in univariate analysis of continuous variables. Tests were selected according to their usefulness to meet assumptions for binary comparisons. Survival analysis was made to investigate mortality as a time-to event outcome. Kaplan–Meier analysis for estimating the proportional surviving by time, bilateral log rank test for the comparison of the curves, and multivariate logistic regression analysis for determining the risk factors were used. In calculations, type I error rate alpha: 0.05 was accepted. P-value less than 0.05 was considered as statistically significant.

RESULTS

A total of 192 patients aged 65 and over were hospitalized in the COVID-19 clinic during the study period. The data of 180 were properly accessible.

Evaluation of all older patients hospitalized in the COVID-19 clinic

Demographic findings such as age, gender, body mass index (BMI) did not differ significantly between groups. While the mean hospital-stay length and the frequency of residence in a nursing home/health care center were higher in PCR (+) older patients; the mean body temperature, and the frequency of comorbidities and smoking history were significantly higher in PCR (-) older patients. Comorbidity was present in 74% of PCR (+) older patients, 37% of whom had multiple comorbidities. However, 95% of PCR (-) older patients had co-morbidities (multiple comorbidities in 71.25%). The major comorbidities and their frequencies observed in PCR (+) cases were hypertension (56%), diabetes mellitus (DM) (20%), coronary artery disease (15%), cerebrovascular events (10%), atrial fibrillation (AF) (9%), chronic obstructive pulmonary disease (COPD) (9%), Parkinson's disease (4%) and cancer (3%). Those of PCR (-) older adults were as follows; hypertension (66.25%), coronary artery disease (41.25%), DM (38.75%), COPD (16.25%), chronic kidney disease (12.5%), cancer (11.25%), AF (6.25%), congestive heart failure (5%), cerebrovascular accident (5%) and asthma (3.75%). It can be concluded that the high number of these comorbidities plays an important role in hospitalization indications and mortality frequencies of the PCR (-) older adults. The most notable laboratory data differences between the two groups are the significant elevation of the mean white blood cell count (Wbc), d-dimer, urea, creatinine and troponin-I in PCR (-) older patients. These differences were emerged due to bacterial infections and comorbid conditions, especially cardiac events. The mortality rate was higher in PCR (-) older patients (26.25% vs 17%). This was interpreted as COVID-19 does not increase mortality much more than other hospital-requiring clinical events in older adults (Table 1).

Evaluation of PCR (+) older adults and PCR (+) young and middle-aged control group

The demographic, clinical, laboratory and radiological data of the patients were compared between the groups (Table 2).

- Demographic and clinical findings: The younger patients had a mean body temperature of 0.7 degrees higher than the older adults. While the duration of hospitalization, residency in a nursing

Table 1. Comparison of clinical and laboratory data of PCR positive and negative older adults. Case numbers and % values of non-variable parameters, mean values and standard deviations (SD) of variable parameters are listed. PCR: polymerase chain reaction, BMI: body mass index, Wbc: white blood cell, Hgb: hemoglobin, Hct: hematocrit, Plt: platelet, Neut#: absolute neutrophil number, Lymph#: absolute lymphocyte number, Eos#: absolute eosinophil number, CRP: C-reactive protein, LDH: lactate dehydrogenase, INR: international normalized ratio, PT: prothrombin time, aPTT: activated partial thromboplastin time, Trop-I: Troponin-I CK-MB: creatine kinase-MB, ICU: intensive care unit, IMV: invasive mechanical ventilation, ARDS: acute respiratory distress syndrome.

		PCR (+) older adults (n: 100)	PCR (-) older adults (n: 80)	p
Age (years) (SD)		73.68 (8.06)	75.34 (7.29)	0. 061
Gender	Female (n, %)	57 (57%)	35 (43.75%)	0.099
	Male (n, %)	43 (43%)	45 (56.25%)	
BMI (SD)		26.08 (2.88)	25.96 (2.69)	0.764
Fever (°C)		36.70 (0.5)	37.40 (0.6)	0.065
Hospital stay, days (SD)		11.85 (4.87)	6.69 (3.78)	<0.001
Nursing home/health care center (n, %)		12 (12%)	1 (1.25%)	0.007
Comorbidity (n, %)		74 (74%)	76 (95%)	0.001
Dementia / Alzheimer's disease (n, %)		8 (8%)	6 (7.5%)	>0.999
Smoking history (n, %)		13 (13%)	23 (28.75%)	0.033
Wbc, $x10^3$ cells/µL (SD)		5551.00 (2079.36)	9117.50 (4217.53)	<0.001
Hgb, g/dL (SD)		13.07 (1.61)	12.47 (1.91)	0.028
Hct, % (SD)		38.87 (4.69)	37.79 (5.68)	0.210
Plt, $x10^3$ cells/µL (SD)		207950.00 (78560.45)	235150.00 (92022.30)	0.029
Neut#, $x10^3$ cells/µL (SD)		3659.00 (1815.82)	6945.00 (4009.23)	<0.001
Lymph#, $x10^3$ cells/µL (SD)		1333.70 (616.76)	1448.75 (1101.21)	0.992
Eos#, $x10^3$ cells/µL (SD)		50.10 (75.82)	125.00 (138.25)	<0.001
CRP, mg/L (SD)		42.71 (60.08)	76.87 (86.63)	0.003
D-dimer, mg/L (SD)		2.19 (8.14)	4.02 (10.12)	<0.001
Fibrinogen, mg/dL (SD)		388.32 (126.56)	461.82 (173.46)	0.036
Ferritin, ng/mL (SD)		253.86 (295.61)	342.47 (406.52)	0.699
Procalcitonin, ng/mL (SD)		0.37 (1.44)	1.01 (3.33)	0.003
Urea, mg/dl (SD)		44.34 (26.83)	62.60 (34.63)	<0.001
Creatinine, mg/dL (SD)		0.98 (0.38)	1.42 (1.07)	<0.001
LDH, U/L (SD)		293.23 (245.26)	324.48 (147.35)	0.006
INR (SD)		1.12 (0.46)	1.26 (0.89)	0.223
PT, seconds (SD)		12.83 (4.03)	14.82 (10.02)	0.127
aPTT, seconds (SD)		29.65 (7.22)	35.58 (40.55)	0.782
Trop-I, pg/mL (SD)		47.88 (180.69)	227.65 (1358.40)	<0.001
CK-MB, ng/mL (SD)		3.17 (4.61)	7.80 (27.31)	0.003
Transfer to ICU (n, %)		23 (23.00%)	28 (35.00%)	0.096
IMV (n, %)		16 (16.00%)	15 (18.75%)	0.693
Acute cardiac events (n, %)		10 (10.00%)	15 (18.75%)	0.128
ARDS (n, %)		11 (11.00%)	4 (5.00%)	0. 181
Acute renal failure (n, %)		22 (22.00%)	25 (31.25%)	0.175
Sepsis (n, %)		13 (13.00%)	14 (17.50%)	0.410
Mortality (n, %)		17 (17.00%)	21 (26.25%)	0.145

home/health care center, presence of comorbidity, and dementia/Alzheimer's disease were observed more frequently in older patients, the frequency of smoking was significantly higher in younger patients (Table 2). Comorbidities were rarer in younger patients with a frequency of 29% (multiple comorbidities in 10%). The major comorbidities observed in younger cases were hypertension (13.38%), diabetes mellitus (DM) (6.29%), COPD (3.93%), coronary artery disease (3.15%), asthma (2.36%).

- Laboratory findings: While the mean C-reactive protein (CRP), fibrinogen, procalcitonin, urea, lactate dehydrogenase (LDH), international normalized ratio (INR), prothrombin time (PT), Troponin-I and creatine kinase-MB (CK-MB) values were significantly higher in older patients; the mean hemoglobin, hematocrit and d-dimer values were significantly higher in younger patients (Table 2). Lymphopenia (lymphocyte#<1000x103 cells/μL) was present in 40% of older adults, and 26.7% of younger patients.

- Radiological findings: Lung involvement was observed significantly more frequently in the older adults. The most common radiological pattern was peripheral infiltration and the greatest amount of involvement was in the lower lobes, especially right lower lobe, in the both age groups. The total lung score was significantly higher in the older adults (Table 2).

- Survival analysis: Considering older patients and the control group together, a total of 227 cases were divided to "survival" and "mortality" groups. The mean age, body temperature, length of hospital-stay, Wbc, platelet, neutrophil#, lymphocyte#, CRP, d-dimer, fibrinogen, procalcitonin, urea, creatinine, LDH, INR, PT, activated partial thromboplastin time (aPTT), troponin-I, CK-MB; the presence of comorbidity and dementia/Alzheimer's disease; the frequency of radiological involvement and the mean total lung scores had significant differences between groups (Table 3). A separate mortality assessment was performed only in older patients (Table 4). The mean body temperatures did not have significant difference between survival groups among older patients. While gender was not statistically significant in the overall mortality assessment, male gender mortality was significant in older adults.

- Analysis of mortality risk factors: When regression analysis is performed for data with Akaike's information criterion (AIC) review, the age (HR:1.11, CI:1.04-1.20) (p=0.006), length of hospital-stay (HR:0.83, CI:0.69-0.98) (p=0.038), and uremia (HR:1.05, CI:1.02-1.08) (p=0.004) were determined as statistically significant risk factors for all PCR (+) patients. When we apply the AIC modeling to the data of PCR (+) older adults separately, only uremia was found to be statistically significant risk factor (HR:1.04, CI:1.01-1.08) (p=0.024). In terms of mortality analysis, Kaplan-Meier analysis was also performed. When older and younger PCR (+) cases were examined together, older age, male gender, and presence of comorbidities were determined as mortality risk factors. When only older patients were examined, lymphopenia, presence of comorbidities, age of 75, and radiological lung involvement were identified as mortality risk factors. Although mortality was observed more frequently in smokers, smoking was not found as a significant risk factor for mortality (Figure 1). As known, "older adults" has been defined as a chronological age of 65 years old or older. On the other hand, according to what is generally accepted, those whose age are between 65-74 are considered to be "early elderly", while those over 75 years old as "late elderly". In this regard, we considered it appropriate to look at the effect of being early and late elderly on mortality. Indeed, being late elderly was found as a mortality risk factor. Lymphopenia was also a mortality risk factor in older ages (Figure 1). The cut-off values for mortality were as follows; age≥77 years, lymphocyte#≤700x103 cells/μL, CRP≥108.71 mg/L, d dimer≥2.25 mg/L, fibrinogen≥383 mg/L, INR≥1.05, PT≥12.5 seconds, aPTT≥31 seconds, Troponin I≥ 19.1 pg/mL, total lung score≥6 points. It was observed that mortality increased significantly above these values in PCR (+) older patients.

Table 2. Comparison of demographic, clinical, laboratory and radiological data of PCR positive older and younger adults. Case numbers and % values of non-variable parameters, mean values and standard deviations (SD) of variable parameters are listed. PCR: polymerase chain reaction, BMI: body mass index, ICU: intensive care unit, IMV: invasive mechanical ventilation, ARDS: acute respiratory distress syndrome, Wbc: white blood cell, Hgb: hemoglobin, Hct: hematocrit, Plt: platelet, Neut#: absolute neutrophil number, Lymph#: absolute lymphocyte number, Eos#: absolute eosinophil number, CRP: C-reactive protein, LDH: lactate dehydrogenase, INR: international normalized ratio, PT: prothrombin time, aPTT: activated partial thromboplastin time, Trop-I: Troponin-I CK-MB: creatine kinase-MB.

		PCR (+) older adults (n: 100)	PCR (+) young and middle-aged adults (n: 127)	p
	Age (years) (SD)	73.68 (8.06)	42.74 (12.83)	<0.001
Gender	Female (n, %)	57 (57.00%)	67 (52.76%)	0.592
	Male (n, %)	43 (43.00%)	60 (47.24%)	
	BMI (SD)	26.08 (2.88)	25.89 (3.16)	0.420
	Fever (°C)	36.70 (0.5)	37.50	0.045
	Hospital stay, days (SD)	11.85 (4.87)	10.77 (3.91)	0.049
	Nursing home/health care center (n, %)	12 (12.24%)	0 (0.00%)	<0.001
	Comorbidity (n, %)	74 (74.00%)	29 (22.83%)	<0.001
	Dementia / Alzheimer's disease (n, %)	8 (8.00%)	0 (0.00%)	0.001
	Smoking history (n, %)	11 (13.25%)	38 (39.18%)	<0.001
	Wbc, x10^3 cells/µL (SD)	5551.00 (2079.36)	5360.47 (2266.31)	0.405
	Hgb, g/dL (SD)	13.07 (1.61)	13.75 (1.72)	<0.001
	Hct,% (SD)	38.87 (4.69)	40.38 (5.58)	0.001
	Plt, x10^3 cells/µL (SD)	207950.00 (78560.45)	205748.03 (61159.69)	0.594
	Neut#, x10^3 cells/µL (SD)	3659.00 (1815.82)	3392.91 (1981.83)	0.227
	Lymph#, x10^3 cells/µL (SD)	1333.70 (616.76)	1405.51 (544.86)	0.182
	Eos#, x10^3 cells/µL (SD)	50.10 (75.82)	59.06 (86.70)	0.490
	CRP, mg/L (SD)	42.71 (60.08)	21.64 (44.85)	<0.001
	D-dimer, mg/L (SD)	2.19 (8.14)	2.99 (25.94)	<0.001
	Fibrinogen, mg/dL (SD)	388.32 (126.56)	318.71 (110.93)	0.006
	Ferritin, ng/mL (SD)	253.86 (295.61)	245.55 (288.93)	0.875
	Procalcitonin, ng/mL (SD)	0.37 (1.44)	0.16 (0.56)	0.022
	Urea, mg/dl (SD)	44.34 (26.83)	28.23 (16.79)	<0.001
	Creatinine, mg/dL (SD)	0.98 (0.38)	0.89 (0.20)	0.251
	LDH, U/L (SD)	293.23 (245.26)	248.43 (165.67)	0.020
	INR (SD)	1.12 (0.46)	0.99 (0.07)	0.026
	PT, seconds (SD)	12.83 (4.03)	11.74 (0.80)	0.045
	aPTT, seconds (SD)	29.65 (7.22)	28.13 (5.08)	0.716
	Trop-I, pg/mL (SD)	47.88 (180.69)	5.41 (11.43)	<0.001
	CK-MB, ng/mL (SD)	3.17 (4.61)	1.24 (1.26)	<0.001
	Transfer to ICU (n, %)	23 (23.00%)	4 (3.15%)	<0.001
	IMV (n, %)	16 (16.00%)	3 (2.36%)	<0.001
	Acute cardiac events (n, %)	10 (10.00%)	2 (1.57%)	0.006
	ARDS (n, %)	11 (11.00%)	3 (2.36%)	0.010
	Acute renal failure (n, %)	22 (22.00%)	9 (7.09%)	0.002
	Sepsis (n, %)	13 (13.00%)	3 (2.36%)	0.003
	Mortality (n, %)	17 (17.00%)	2 (1.57%)	<0.001
Radiological lung infiltration	No infiltration (n, %)	19 (20.88%)	36 (32.43%)	0.027
	Peripheral infiltration (n, %)	40 (43.96%)	46 (41.44%)	
	Randomized infiltration (n, %)	28 (30.77%)	18 (16.22%)	
	Diffuse infiltration (n, %)	4 (4.40%)	11 (9.91%)	
Radiological infiltration score	Right upper lobe (SD)	0.67 (0.75)	0.52 (0.77)	0.075
	Right middle lobe (SD)	0.65 (0.94)	0.50 (0.88)	0.109
	Right lower lobe (SD)	1.00 (0.93)	0.81 (0.95)	0.067
	Left upper lobe (SD)	0.60 (0.73)	0.53 (0.78)	0.244
	Left lower lobe (SD)	0.87 (0.93)	0.80 (0.97)	0.423
	Total lung score (SD)	3.78 (3.70)	3.13 (3.88)	0.050

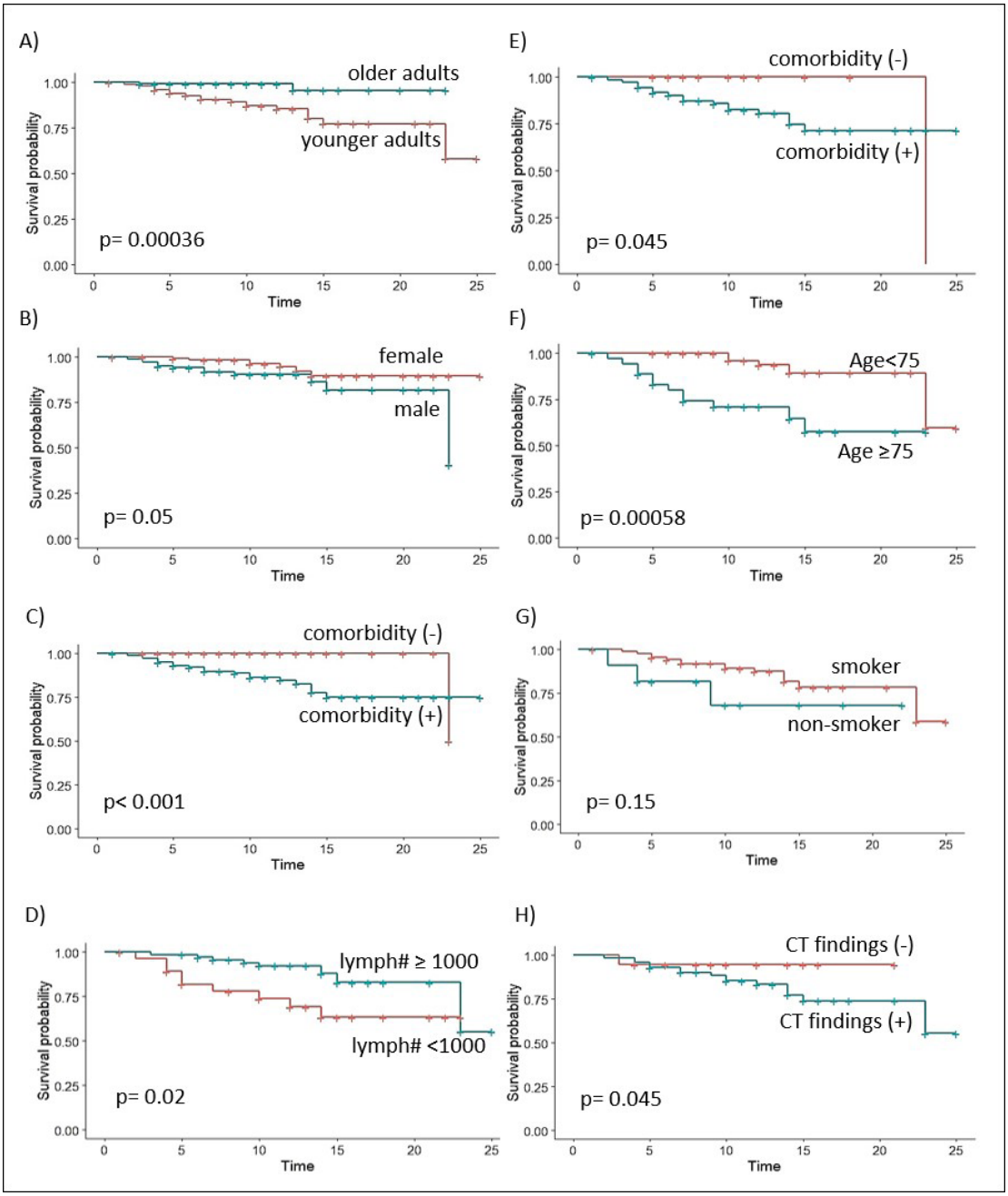
Table 3. Comparison of PCR positive cases according to their survival and mortality status regardless of age (older and younger adults together). Case numbers and % values of non-variable parameters, mean values and standard deviations (SD) of variable parameters are listed. PCR: polymerase chain reaction, BMI: body mass index, Wbc: white blood cell, Hgb: hemoglobin, Hct: hematocrit, Plt: platelet, Neut#: absolute neutrophil number, Lymph#: absolute lymphocyte number, Eos#: absolute eosinophil number, CRP: C-reactive protein, LDH: lactate dehydrogenase, INR: international normalized ratio, PT: prothrombin time, aPTT: activated partial thromboplastin time, Trop-I: Troponin-I CK-MB: creatine kinase-MB, ICU: intensive care unit, IMV: invasive mechanical ventilation, ARDS: acute respiratory distress syndrome.

		Survival group (n: 208)	Mortality group (n: 19)	p
	Age (years) (SD)	54.62 (18.53)	75.53 (10.67)	<0.001
Gender	Female (n, %)	117 (56.25%)	7 (36.84%)	0.148
	Male (n, %)	91 (43.75%)	12 (63.16%)	
	BMI (SD)	25.97 (2.89)	26.10 (4.31)	0.580
	Fever (°C)	37.10 (0.5)	37.66 (0.8)	0.043
	Hospital stay, days (SD)	11.48 (4.22)	8.74 (5.41)	0.011
	Nursing home/health care center (n, %)	11 (5.37%)	1 (5.26%)	>0.999
	Comorbidity (n, %)	85 (40.87%)	18 (94.74%)	<0.001
	Dementia / Alzheimer's disease (n, %)	5 (2.40%)	3 (15.79%)	0.021
	Smoking history (n, %)	45 (27.27%)	4 (26.67%)	>0.999
	Wbc, x10^3 cells/µL (SD)	5265.29 (1775.60)	7405.26 (4377.27)	0.019
	Hgb, g/dL (SD)	13.49 (1.71)	13.01 (1.62)	0.077
	Hct,% (SD)	39.80 (5.28)	38.81 (4.88)	0.093
	Plt, x10^3 cells/µL (SD)	209451.92 (69177.48)	176789.47 (63857.98)	0.012
	Neut#, x10^3 cells/µL (SD)	3310.58 (1458.83)	5694.74 (3984.48)	<0.001
	Lymph#, x10^3 cells/µL (SD)	1397.93 (567.21)	1110.53 (637.61)	0.018
	Eos#, x10^3 cells/µL (SD)	56.30 (81.38)	42.11 (90.16)	0.169
	CRP, mg/L (SD)	23.43 (38.84)	111.94 (101.18)	<0.001
	D-dimer, mg/L (SD)	2.31 (19.90)	5.94 (17.31)	0.003
	Fibrinogen, mg/dL (SD)	340.64 (110.28)	453.23 (171.94)	0.011
	Ferritin, ng/mL (SD)	221.23 (232.39)	420.28 (498.88)	0.136
	Procalcitonin, ng/mL (SD)	0.13 (0.45)	1.43 (2.96)	<0.001
	Urea, mg/dl (SD)	32.04 (16.78)	71.32 (44.81)	<0.001
	Creatinine, mg/dL (SD)	0.89 (0.21)	1.35 (0.59)	<0.001
	LDH, U/L (SD)	248.32 (158.54)	483.05 (429.27)	<0.001
	INR (SD)	1.05 (0.36)	1.15 (0.19)	<0.001
	PT, seconds (SD)	12.13 (3.11)	13.63 (2.17)	<0.001
	aPTT, seconds (SD)	27.97 (5.44)	33.85 (7.99)	0.003
	Trop-I, pg/mL (SD)	11.40 (47.98)	148.19 (353.28)	<0.001
	CK-MB, ng/mL (SD)	1.85 (2.97)	4.41 (5.39)	<0.001
	Transfer to ICU (n, %)	9 (4.33%)	18 (94.74%)	<0.001
	IMV (n, %)	3 (1.44%)	16 (84.21%)	<0.001
	Acute cardiac events (n, %)	4 (1.92%)	8 (42.11%)	<0.001
	ARDS (n, %)	1 (0.48%)	13 (68.42%)	<0.001
	Acute renal failure (n, %)	15 (7.21%)	16 (84.21%)	<0.001
	Sepsis (n, %)	2 (0.96%)	14 (73.68%)	<0.001
Radiological lung infiltration	No infiltration (n, %)	54 (29.19%)	17 (8.42%)	0.026
	Peripheral infiltration (n, %)	80 (43.24%)	1 (5.88%)	
	Randomized infiltration (n, %)	38 (20.54%)	6 (35.29%)	
	Diffuse infiltration (n, %)	13 (7.03%)	2 (11.76%)	
Radiological infiltration score	Right upper lobe (SD)	0.54 (0.71)	1.12 (1.11)	0.015
	Right middle lobe (SD)	0.48 (0.83)	1.47 (1.23)	<0.001
	Right lower lobe (SD)	0.81 (0.88)	1.82 (1.13)	<0.001
	Left upper lobe (SD)	0.51 (0.73)	1.12 (0.86)	<0.001
	Left lower lobe (SD)	0.77 (0.91)	1.53 (1.12)	0.001
	Total lung score (SD)	3.09 (3.50)	7.06 (5.07)	<0.001

Table 4. Comparison of death and survival groups of PCR (+) older adults. Case numbers and % values of non-variable parameters, mean values and standard deviations (SD) of variable parameters are listed. PCR: polymerase chain reaction, BMI: body mass index, Wbc: white blood cell, Hgb: hemoglobin, Hct: hematocrit, Plt: platelet, Neut#: absolute neutrophil number, Lymph#: absolute lymphocyte number, Eos#: absolute eosinophil number, CRP: C-reactive protein, LDH: lactate dehydrogenase, INR: international normalized ratio, PT: prothrombin *time*, aPTT: activated partial thromboplastin time, Trop-I: Troponin-I CK-MB: *creatine kinase-MB*, ICU: intensive care unit, IMV: *invasive mechanical ventilation*, ARDS: acute respiratory distress syndrome.

		Survival group (n: 83)	Mortality group (n: 17)	p
	Age (years) (SD)	72.73 (7.97)	78.29 (7.05)	0.004
Gender	Female (n, %)	51 (61.45%)	6 (35.29%)	0.050
	Male (n, %)	32 (38.55%)	11 (64.71%)	
	BMI (SD)	26.15 (2.83)	25.72 (3.22)	0.424
	Fever (°C)	36.62 (0.4)	37.09 (0.7)	0.065
	Hospital stay, days (SD)	12.47 (4.53)	8.82 (5.46)	0.004
	Nursing home/health care center (n, %)	11 (13.58%)	1 (5.88%)	0.686
	Comorbidity (n, %)	58 (69.88%)	16 (94.12%)	0.046
	Dementia / Alzheimer's disease (n, %)	5 (6.02%)	3 (17.65%)	0.043
	Smoking history (n, %)	8 (9.64%)	3 (17.65%)	0.392
	Wbc, x10^3 cells/µL (SD)	5403.61 (2035.92)	6270.59 (2201.64)	0.167
	Hgb, g/dL (SD)	13.04 (1.62)	13.18 (1.62)	0.894
	Hct,% (SD)	38.79 (4.66)	39.27 (4.94)	0.901
	Plt, x10^3 cells/µL (SD)	216987.95 (81023.86)	163823.53 (45278.63)	0.002
	Neut#, x10^3 cells/µL (SD)	3442.17 (1667.71)	4717.65 (2170.90)	0.017
	Lymph#, x10^3 cells/µL (SD)	1404.46 (609.25)	988.24 (546.45)	0.004
	Eos#, x10^3 cells/µL (SD)	50.72 (72.12)	47.06 (94.32)	0.368
	CRP, mg/L (SD)	30.31 (40.00)	102.50 (97.08)	<0.001
	D-dimer, mg/L (SD)	1.40 (3.84)	6.09 (17.87)	0.050
	Fibrinogen, mg/dL (SD)	368.05 (102.95)	462.67 (176.03)	0.050
	Ferritin, ng/mL (SD)	228.38 (255.80)	330.30 (395.84)	0.289
	Procalcitonin, ng/mL (SD)	0.11 (0.27)	1.48 (3.12)	<0.001
	Urea, mg/dl (SD)	39.82 (21.84)	66.41 (37.24)	<0.001
	Creatinine, mg/dL (SD)	0.91 (0.26)	1.33 (0.61)	<0.001
	LDH, U/L (SD)	272.06 (225.07)	395.35 (314.02)	0.005
	INR (SD)	1.12 (0.51)	1.15 (0.20)	0.005
	PT, seconds (SD)	12.60 (4.38)	13.68 (2.28)	0.002
	aPTT, seconds (SD)	27.86 (6.04)	34.37 (8.13)	0.002
	Trop-I, pg/mL (SD)	21.65 (74.10)	158.96 (372.82)	<0.001
	CK-MB, ng/mL (SD)	2.81 (4.28)	4.63 (5.67)	0.111
	Transfer to ICU (n, %)	7 (8.43%)	16 (94.12%)	<0.001
	IMV (n, %)	2 (2.41%)	14 (82.35%)	<0.001
	Acute cardiac events (n, %)	3 (3.61%)	7 (41.18%)	<0.001
	ARDS (n, %)	0 (0.00%)	11 (64.71%)	<0.001
	Acute renal failure (n, %)	8 (9.64%)	14 (82.35%)	<0.001
	Sepsis (n, %)	1 (1.20%)	12 (70.59%)	<0.001
Radiological lung infiltration	No infiltration (n, %)	18 (24.00%)	1 (6.25%)	0.160
	Peripheral infiltration (n, %)	34 (45.33%)	6 (37.50%)	
	Randomized infiltration (n, %)	20 (26.67%)	8 (50.00%)	
	Diffuse infiltration (n, %)	3 (4.00%)	1 (6.25%)	
Radiological infiltration score	Right upper lobe (SD)	0.61 (0.71)	0.94 (0.85)	0.136
	Right middle lobe (SD)	0.51 (0.84)	1.31 (1.08)	<0.001
	Right lower lobe (SD)	0.85 (0.85)	1.69 (1.01)	0.002
	Left upper lobe (SD)	0.52 (0.70)	1.00 (0.73)	0.007
	Left lower lobe (SD)	0.76 (0.90)	1.38 (0.96)	0.007
	Total lung score (SD)	3.24 (3.38)	6.31 (4.16)	0.001

Figure 1. Kaplan-Meier survival curves for demographic variables. A) effect of age on mortality in all patients, B) effect of gender on mortality regardless of age, C) effect of presence of comorbidity on mortality regardless of age, D) effect of lymphopenia on mortality in elderly, E) effect of presence of comorbidity on mortality in elderly, F) effect of being over 75 years old on mortality in elderly, G) effect of smoking on mortality in elderly, H) effect of presence of radiological lung infiltration on mortality in elderly. lymph#: absolute lymphocyte number



DISCUSSION

This study was carried out to reveal the course and the mortality risk factors of COVID-19 in older patients. Although our results support the previous knowledge that COVID-19 is worse in the elderly, it can be concluded that COVID-19 does not have a higher mortality rate than other diseases among older patients. To our knowledge, this is the first study to compare the prognosis of COVID-19 with other clinical conditions requiring hospitalization in older patients.

While COVID-19 is more common in young and middle-aged adults, mortality is higher in the older patients (9, 10). Among all deaths the percentage of older patients was found as 96.5% in Italy, 80.8% in China, 80% in USA (11-13). Age-related immune system changes, comorbidities and atypical clinical presentations may lead to increased mortality by complicating the diagnosis and the treatment of COVID-19 in older adults. The body temperature tends to be lower in elderly up to -1°C, even in patients with infection, than younger ones (2, 14, 15). Non-specific symptoms such as general condition disorders, confusion, urinary/stool incontinence may be the primary symptoms of pneumonia in older people (5, 16, 17). In accordance with previous reports, we observed that younger patients had a mean body temperature of 0.7 degrees higher than the older ones at the time of hospital admission. In other words, low fever should not exclude COVID-19 in the older adults.

Comorbidities are also one of the worsening factors of COVID-19 prognosis (10, 18, 19). Cardiovascular diseases have been reported as the most common comorbidities associated with mortality (17, 19, 20). Diabetes Mellitus and coronary artery diseases follow them (21). In the present study, the incidence of comorbidities increased significantly with age, and the mortality was correlated with the frequency of comorbidities. It can be clearly stated that the older adults with cardiovascular diseases and DM constitute the riskiest population for COVID-19 infection.

Increase in LDH, ferritin and CRP are common laboratory changes in patients with COVID-19 (18, 19). Lymphopenia was detected in 90% of the patients in New York and has been associated with mortality (21). High d-dimer and procalcitonin levels, and coagulopathy were also found to be related to severe disease (13, 18, 21). Despite the fact that the basal values and laboratory responses of older people to infection may differ from younger people, we still have limited data on laboratory changes in the older patients with COVID-19 infection. In the study of Liu et al., the mean Wbc, neutrophil# and CRP were significantly higher and the lymphopenia was more common in the older patients (22). They interpreted this situation as the older patients with COVID-19 infection are also prone to bacterial infections. In this study, the mean CRP, fibrinogen, procalcitonin, urea, LDH, INR, PT, Troponin-I and CK-MB levels were higher in older patients; and there were significant differences between survival groups in terms of Wbc, platelet, neutrophil#, lymphocyte#, CRP, d-dimer, fibrinogen, procalcitonin, urea, creatinine, LDH levels, cardiac enzymes and coagulation markers. Lymphopenia was a mortality risk factor especially for older adults. We took the results of previous studies a step further and examined the cut-off values for mortality. The mortality rate was increasing with cut-off values of lymphocyte# above 700×10^3 cells/μL, CRP over 108.71 mg/L, d-dimer over 2.25 mg/L, fibrinogen over 383 mg/L. Older patients who exceed these cut-off values should be followed much more closely.

Thorax CT has a big role in the diagnosis of COVID-19 infection and predicting its prognosis (10, 23-25). However, data about the radiological findings of older patients is still limited. Right lower lobe of the lung was identified as the most frequently involved area (23). Using a scoring system similar to ours, Chung et al. associated the mean total lung score with mortality (23). Similarly, we observed the right lower lobe as the most common area involved, and the radiological involvement in "initial CT" was a mortality risk factor among all age

groups. The total lung score was lower than that of Chung et al. with a mean of 3.78 points in the older and 3.13 points in the younger patients. Li et al.'s study focused on the association of "initial CT" findings with mortality in patients aged 60 years and older (24). They reported that high CT score was a mortality risk factor in older patients. Liu et al. stated that the incidence of multiple lobe infiltration is significantly common in older patients (22). Similar to the previous results, we observed multiple lobe lung involvement more frequently in the older adults, with a peripheral pattern in lower lobes. The mean total lung scores had significant differences between older adults and younger patients, and also between survival groups. The radiological lung involvement was identified as a mortality risk factor for patients with total lung score above 6 points.

In conclusion, we emphasize that older adults, especially aged over 75 years, are worse affected by COVID-19 pandemic. While COVID-19 infection may show atypical presentations in older adults, a favorable course on prognosis can be achieved with a specialized clinical perspective. Older patients with lymphopenia, high d-dimer and fibrinogen levels, multiple comorbidities and significant pulmonary involvement in the initial CT should be considered as at high risk for mortality and be followed-up closely. Being single-centered and retrospective are the limitations of our study. Because we are a 3rd level health institution and critical patients are more frequently referred to our hospital, the mortality rates determined in this study should not be reflected in the general population in Turkey.

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