Acıbadem Univ. Sağlık Bilim. Derg. 2024; 15 (3)
https://doi.org/ 10.31067/acusaglik.1362545

Evaluation of Pneumonia Severity and Lung Computed Tomography Findings in Covid-19 Patients

Melek Cihanbeylerden[1], Çağla Şafak[2], Cihat Tek[3], Muhammed Savran[4]

[1] Faculty of Medicine, Division of Allergy and Clinical Immunology, Hacettepe University Hospital, Ankara, Turkey

[2] Ankara University, Medical School, Department of Biostatistics, Ankara University Institute of Health Sciences, Ankara, Turkey

[3] Medikum Hospital, Department of Radiology, Antalya, Turkey

[4] Kahramanmaraş Necip Fazıl State Hospital, Department of Cardiovascular Surgery, Kahramanmaraş, Turkey

Melek CİHANBEYLERDEN
0000-0002-0810-087X

Çağla ŞAFAK
0000-0003-0451-2225

Cihat TEK
0000-0001-6673-1373

Muhammed SAVRAN
0000-0003-2688-6930

Correspondence: Melek Cihanbeylerden
Faculty of Medicine, Division of Allergy and Clinical Immunology, Hacettepe University Hospital, Ankara, Turkey
Phone: +90 553 703 17 10
E-mail: ytse_jammm@hotmail.com

Received: 19.09.2023
Accepted: 13.12.2023

ABSTRACT

Purpose: Examining clinical and imaging features can help deepen our understanding of the mechanisms of severe disease and improve clinical diagnosis and treatment We aimed to describe the relationship between the clinical, laboratory, and lung computed tomography (LCT) characteristics of patients with coronavirus 2019 (COVID-19) pneumonia and determine the severity of pneumonia in these patients.

Methods: The pneumonia severity index (PSI) score system, LCT images, and laboratory parameters at the time of first presentation to the emergency department were examined to assess the severity of COVID-19 pneumonia in adult patients.

Results: The sample consisted of 225 patients, 130 (57.8%) men and 95 (42.2%) women. The mean age of the sample was determined as 60.4 ± 16.04 years. 161 (71.6%) were have moderate disease, 62 (27.6) were severe disease and were followed up in the intensive care unit. Significant relationship was found between COVID-19-associated mortality and male gender ($p=0.045$), advanced age ($p<0.001$), a high neutrophil count in peripheral blood ($p<0.001$), a low eosinophil count ($p<0.001$), 5-49% lung involvement on LCT ($p<0.001$), and PSI groups IV and V ($p<0.001$). There is no statistically significant relationship increase in the CRP level with mortality ($p = 0.764$).

Conclusion: We determined the most significant factors for mortality as advanced age, low eosinophil and lymphocyte counts, increased lactate and ferritin levels, and PSI group V. In this review, we highlight the clinical evidence supporting for the risk factors for the severity and mortality of COVID-19.

Keywords: COVID-19; Pneumonia severity index; Computed tomography; Prognosis; Mortality

ÖZET

Amaç: Klinik ve görüntüleme özelliklerinin incelenmesi, ağır hastalık mekanizmalarına ilişkin anlayışımızı derinleştirmeye ve klinik tanı ve tedaviyi iyileştirmeye yardımcı olabilir. Koronavirus 2019 (COVID-19) pnömonisi olan hastaların klinik, laboratuvar ve akciğer bilgisayarlı tomografi (LCT) özellikleri arasındaki ilişkiyi tanımlamayı ve bu hastalarda pnömoninin şiddetini belirlemeyi amaçladık.

Yöntemler: COVID-19 pnömonisinin şiddetini değerlendirmek için acil servise ilk başvuru anındaki yetişkin hastaların, pnömoni şiddet indeksi (PSI) skor sistemi, LCT görüntüleri ve laboratuvar parametrelerini inceledik.

Bulgular: Örneklem 130'u (%57,8) erkek ve 95'i (%42,2) kadın olmak üzere 225 hastadan oluşuyordu. Örneklemin ortalama yaşı 60,4±16,04 yıl olarak belirlendi. Bu çalışmada 161 (%71,6) hasta orta derecede hastalık, 62 (%27,6) hasta ağır hastalıklı olup yoğun bakımda takip edildi. COVİD-19 ilişkili mortalite ile, erkek cinsiyet ($p=0,045$), ileri yaş ($p<0,001$), periferik kanda yüksek nötrofil sayısı ($p<0,001$), düşük eozinofil sayısı ($p<0,001$), LCT'de %5-49 akciğer tutulumu ($p<0,001$) ve PSI Grup IV ve V ($p<0,001$) arasında anlamlı ilişki bulundu.. CRP düzeyindeki artış ile mortalite arasında istatistiksel olarak anlamlı bir ilişkisi saptanmadı ($p=0,764$).

Sonuç: Mortalitenin en önemli faktörlerini ileri yaş, düşük eozinofil ve lenfosit sayısı, artmış laktat ve ferritin düzeyleri ve PSI Grup V olarak belirledik. Bu derlemede, COVID-19'un ciddiyeti ve mortalitesine ilişkin risk faktörlerini destekleyen klinik bulguları vurguluyoruz.

Anahtar Kelimeler: COVID-19; Pnömoni şiddet indeksi; Bilgisayarlı tomografi; Prognoz; Mortalite

Coronavirus disease 2019 (COVID-19) is an illness caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) (1). The symptoms of this disease vary from patient to patient. The most common clinical symptoms are fatigue, cough, fever, anorexia, phlegm, shortness of breath (2). Additionally, confusion, shortness of breath, sore throat, headache, hemoptysis, chest tightness, nausea, vomiting, diarrhea and gastrointestinal complaints may also occur (3, 4). Although, most patients with COVID-19 have mild symptoms and a good prognosis, this infection can cause serious illnesses, including pulmonary edema, acute respiratory distress syndrome, multiple organ failure, and even death (5). Compared to patients with other diseases, severe COVID-19 cases have a poor prognosis and high mortality. The first step in managing COVID-19 is the accurate and rapid detection of SARS-CoV-2 enabled by the real-time reverse transcriptase-polymerase chain reaction (RT-PCR) (6). RT-PCR detects SARS-CoV-2 nucleic acids present in nasopharyngeal fluids (7). Imaging method such as lung computed tomography (LCT) has played an important role in the diagnosis and treatment of COVID-19 patients (8). Early and successful treatment of severe and critical cases is the key to reducing complications and mortality. To this end, it is very important to identify factors related to disease severity in clinical practice. We consider that examining clinical and imaging features can help deepen our understanding of the mechanisms of severe disease and improve clinical diagnosis and treatment. Therefore, in this study, we aimed to describe the relationship between the clinical, laboratory, and LCT characteristics of patients with COVID-19 pneumonia and determine the severity of pneumonia in these patients.

Materials and Methods

A total of 225 patients who were consecutively diagnosed with COVID-19 pneumonia, treated, and followed up at Ağrı State Hospital between January 18,2021 and March 24,2021 were included in this study. Ethical approval was obtained from the Planning and Coordination Board of the hospital with decision number 34.

The sample consisted of patients with a positive SARS-CoV-2 nucleic acid RT-PCR reaction in the nasopharyngeal and oropharyngeal upper respiratory tracts and radiological findings in LCT. Patients with normal LCT examinations were excluded from the study.

The patients' demographic characteristics, clinical findings, laboratory results, and the distribution and morphology of the lesions detected on LCT at the time of presentation were retrospectively analyzed. Clinical parameters included age, gender, symptoms at first admission (headache and sore throat, fever over 38 °C, shortness of breath, cough, diarrhea and vomiting, and myalgia), oxygen saturation measured by pulse oximetry, comorbidities [systemic hypertension (HT), diabetes mellitus (DM), coronary artery disease (CAD), chronic obstructive pulmonary disease (COPD), chronic liver disease, and malignancy], and laboratory findings were retrospectively examined and recorded. The severity of COVID-19 pneumonia was assessed using the pneumonia severity index (PSI), which is based on comorbidities, physical examination, laboratory and radiologic data. According to the risk of death at 30 days, patients were classified as low or moderate risk (PSI I–III) or high or severe risk (PSI IV–V) and divided into five groups according to PSI score.

Patients who did not have respiratory failure at the time of first admission to the hospital, those with pneumonia findings on LCT, and those admitted to the ward were evaluated to have moderate disease. Patients who had respiratory failure at admission and were followed up in the intensive care unit due to the invasive or non-invasive mechanical ventilator requirement were evaluated to have severe disease.

LCT Evaluation

The LCT findings were evaluated by an experienced radiologist. The LCT imaging findings of the patients were recorded according to the following characteristics:

1. Lesion localization: right lung [right upper lobe apical (RUA), right upper lobe anterior (RUAN), right upper lobe posterior (RUP), right middle lobe lateral (RML), right middle lobe medial (RMM), right middle lobe anterior (RMA), right lower lobe lateral (RLL), right lower lobe posterior (RLP), right lower lobe superior (RLS), and right lower lobe medial (RLM)] and left lung [left upper lobe lingula (LUL), left upper lobe anterior (LUA), left upper lobe apicoposterior (LUAP), left lower lobe anterior (LLA), left lower lobe lateral (LLL), left lower lobe posterior (LLP), and left lower lobe superior (LLS)]

2. Involvement areas of lesions: focal (single lesion), multiple (limited to two lobes in the lung), diffuse (multilobe; i.e., involvement of more than two lobes), unilateral, and bilateral

3. Distribution characteristics of lesions: subpleural, peribronchial, and random

4. Lesion density: ground glass opacity, consolidation, or mixed type

5. Evaluation of ground glass nodules, cobblestone appearance, halo sign, reversed halo sign, and air bronchogram according to the recommendations of the Nomenclature Committee of the Fleischner Society (9)

6. Scoring for the measurement of the total size of each lobe: score 0, uptake 0%; score 1, less than 5% involvement; score 2, 5-25% involvement; score 3, 26-49% involvement; score 4, 50-75% involvement; and score 5, more than 75% involvement.

Statistical Analysis

Statistical analyses for the study were undertaken using SPSS v. 11.5 (IBM Inc., Chicago, IL, USA) software. The relationship between the variables evaluated in the study and the patients' survival status was investigated using the chi-square test. In order to determine factors affecting the risk of mortality, the logistic regression analysis was performed with the stepwise model selection algorithm, and the variables that were significant in the multivariate model were reported using the odds ratio and 95% confidence interval. A p value of <0.05 was considered statistically significant.

Results

Clinical Symptoms and Characteristics

The sample consisted of 225, patients: 130 (57.8%) men and 95 (42.2%) women. None of the patients were children or pregnant. The mean age of the sample was determined to be 60.4 ± 16.0 years.

There was a history of DM in 47 (20.9%) patients, HT in 83 (36.9%), CAD in 53 (23.6%), COPD in 36 (16.0%), CLD in four (1.8%), and malignancy in three (1.3%). The clinical symptoms of the patients at the time of first admission were as follows: fever over 38 °C in 62 (27.6%) patients, myalgia in 107 (47.6%), headache or sore throat in 73 (32.4%), cough in 144 (64.0%), shortness of breath in 163 (72.4%), and diarrhea or vomiting in 18 (8.0%).

Of these patients, 161 (71.6%) were assessed to have moderate disease while 62 (27.6%) patients were evaluated to have severe disease and were followed up in the intensive care unit. Mortality occurred in 53 (23%) patients, of whom three patients (1%) had been initially evaluated to have moderate disease. Fifty (22%) patients that were assessed to have severe disease at first admission died during intensive care follow-up. While no mortality was observed among the patients aged 18-35 years ($p < 0.001$), 48 (90.5%) of those who died were aged 60-90 years ($p < 0.001$). Thirty-seven (69%) of the patients in the mortality group were male. All the patients in this group had dyspnea symptoms at the time of first admission to the hospital ($p < 0.001$).

Oxygen saturation ranged from 40% to 98%, with a mean value of 83.88% ± 12.59%.

Laboratory Examinations

We detected an increase in C-reactive protein (CRP) levels in a total of 224 (99.6%) patients. Due to the increase in the diffuse CRP level, no statistically significant relationship could be established with mortality ($p = 0.764$). Although thrombocytopenia is common among severe viral infections, we found a decrease in platelet count in 42 (18.7%) of our patients and 10 (18.8%) of those who died ($p = 0.966$). We observed a normal international normalized ratio (INR) level in 210 (93.3%) patients and a high fibrinogen level in 152 (67.6%). Mortality had a statistically significant correlation with a low basophil count in peripheral blood ($p = 0.002$), low lymphocyte count ($p < 0.001$), low eosinophil count ($p < 0.001$), increased lactate dehydrogenase (LDH) ($p < 0.001$), and increased d-dimer ($p = 0.003$). Table 1 shows the laboratory examinations of the patients included in the study.

Table 1: Laboratory examinations of the patients			
Variable	**Survivor n (%)**	**Non-survivor n (%)**	**p**
WBC (x10^3/µL)			
<4	30 (17.4)	1 (1.9)	<0.001*
4-10	120 (69.8)	27 (50.9)	
10<	22 (12.8)	25 (47.2)	
NEU (x10^3/µL)			
<2	18 (10.5)	2 (3.8)	<0.001*
2-7	116 (67.4)	13 (24.5)	
7<	38 (22.1)	38 (71.7)	
BASO (x10^3/µL)			
0-0.01	57 (33.1)	6 (11.3)	0.002*
0.01<	115 (66.9)	47 (88.7)	
EOS (x10^3/µL)			
<0.02	86 (50.0)	43 (81.1)	<0.001*
0.02-0.5	44 (25.6)	8 (15.1)	
0.5<	42 (24.4)	2 (3.8)	
LYM (ml)			
<800	31 (18.0)	37 (69.8)	<0.001*
800<	141 (82.0)	16 (30.2)	
CRE (mg/dL)			
<0.67	37 (21.5)	4 (7.5)	<0.001*
0.67-1.17	109 (63.4)	25 (47.2)	
1.17<	26 (15.1)	24 (45.3)	
Urea (mg/dL)			
<17	9 (5.2)	0 (0.0)	<0.001*
17-43	117 (68.1)	12 (22.6)	
43<	46 (26.7)	41 (77.4)	
ALT (U/L)			
0-50	150 (87.2)	45 (84.9)	0.666
50<	22 (12.8)	8 (15.1)	
AST (U/L)			
0-50	154 (89.5)	33 (62.3)	<0.001*
50<	18 (10.5)	20 (37.7)	
POTAS (mEq/L)			
<5.1	164 (95.3)	40 (75.5)	<0.001*
5.1<	8 (4.7)	13 (24.5)	
Lactate (mmol/L)			
0.5-1.6	120 (69.8)	16 (30.2)	<0.001*
1.6<	52 (30.2)	37 (69.8)	
LDH (U/L)			
0-248	76 (44.2)	2 (3.8)	<0.001*
248<	96 (55.8)	51 (96.2)	
TROP (ng/ml)			
0-19.8	150 (87.2)	23 (43.4)	<0.001*
19.8<	22 (12.8)	30 (56.6)	
D-dimer (ng/ml)			
0-0.5	26 (15.1)	0 (0.0)	0.003*
0.5<	146 (84.9)	53 (100.0)	
Ferritin (ng/ml)			
<306	103 (59.9)	8 (15.1)	<0.001*
306<	69 (40.1)	45 (84.9)	

*WBC: White blood cell, NEU: Neutrophil, BASO: Basophil, EOS: Eosinophil, LYM: Lymphocyte, CRE: Creatinine, ALT: Alanine aminotransferase, AST: Aspartate aminotransferase, POTAS: Potassium, LDH: Lactate dehydrogenase, TROP: Troponin, *p < 0.05*

LCT Findings

Lesion localization

There were 188 (83.5%) patients with the involvement of both lungs, 36 (16%) with the involvement of one lung, 195 (87.1%) with left lung involvement, and 216 (96.4%) with right lung involvement. In the mortality group, significant uptake was observed in the RML (p = 0.004), RLP (p = 0.001), and LLP (p < 0.001) segments (Table 2).

Table 2: Lesion involvement areas of the patients on lung computed tomography

Variable	Survivor n (%)	Non-survivor n (%)	p
RUA	45 (26.2)	28 (52.8)	<0.001*
RUAN	88 (51.2)	37 (69.8)	0.017*
RUP	88 (51.2)	39 (73.6)	0.004*
RML	90 (52.3)	40 (75.5)	0.003*
RMM	59 (34.3)	31 (58.5)	0.002*
RLA	80 (46.5)	36 (67.9)	0.006*
RLL	83 (48.3)	39 (73.6)	0.001*
RLP	114 (66.3)	48 (90.6)	0.001*
RLS	99 (57.6)	41 (77.4)	0.009*
RLM	63 (36.6)	32 (60.4)	0.002*
LUL	86 (50.0)	43 (81.1)	<0.001*
LUA	69 (40.1)	36 (67.9)	<0.001*
LUAP	85 (49.4)	36 (67.9)	0.018*
LLA	70 (40.7)	31 (58.5)	0.023*
LLL	81 (47.1)	40 (75.5)	<0.001*
LLP	102 (59.3)	48 (90.6)	<0.001*
LLS	84 (48.8)	40 (75.5)	0.001*
Focal	26 (15.1)	1 (1.9)	0.010*
Diffuse, multi-lobe	127 (73.8)	49 (92.5)	0.004*
Bilateral	138 (80.2)	50 (94.3)	0.015*
Subpleural	142 (82,6)	33 (62,3)	0.002*
Peribronchial	4 (2.3)	0 (0.0)	0.339
Random	27 (15.7)	20 (37.7)	0.001*

***RUA:** Right upper lobe apical, **RUAN:** Right upper lobe anterior, **RUP:** right upper lobe posterior, **RML:** right middle lobe lateral, **RMM:** right middle lobe medial, **RIA:** right lower lobe anterior, **RLL:** right lower lobe lateral, **RLP:** right lower lobe posterior, **RLS:** right lower lobe superior, **RLM:** right lower lobe medial, **LUL:** left upper lobe lingula, **LUA:** left upper lobe anterior, **LUAP:** left upper lobe apicoposterior, **LLA:** left lower lobe anterior, **LLL:** left lower lobe lateral, **LLP:** left lower lobe posterior, **LLS:** left lower lobe superior, *p < 0.05*

Lesion Involvement Score

We found a significant correlation between the percentage of involvement on LCT and high ferritin, increased CRP, increased d-dimer, and low lymphocyte levels. In the survivor group, 88 (51.1%) patients had a score of 2.5 and five (2.9%) had a score of 5 in terms of lung involvement areas at the time of first admission. In the mortality group, LCT involvement was observed in 15 (28.3%) patients with a score of 2, 15 (28.3%) with a score of 3, and nine (16.9%) with a score of 5 (Figure 1). The risk of mortality increased as the percentage of involvement on LCT rose above 5% (p < 0.001).

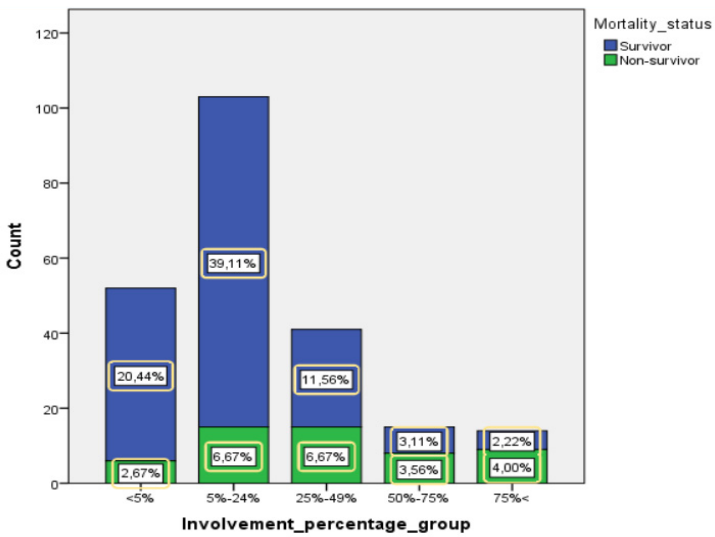

Figure 1: Percentages of lesion involvement areas on lung computed tomography for the survivor and non-survivor groups

Lesion Morphology

In our sample, 205 (91.3%) patients presented with ground glass opacities and dominant bilateral lower zone involvement, which is considered typical COVID 19 involvement. These patients were diagnosed with COVID-19 in a short time due to LCT findings at first admission. Five (2.2%) patients had pulmonary edema due to heart failure and 20 (8.8%) had atypical LCT findings. Sixteen (30%) patients had air bronchograms, 35 (66%) had a ground glass appearance, and 15 (23.3%) had a cobblestone appearance (Table 3). According to the statistical analysis, there was a significant correlation between mortality and the presence of an air bronchogram (p = 0.01) and cobblestone appearance (p < 0.001) on LCT (Table 3).

Table 3: Comparation of lung computed tomography lesion morphology of the patients			
Variable	**Survivor n (%)**	**Non-survivor n (%)**	**p**
Ground glass opacity			0.170
	130 (75.6)	35 (66.0)	
Consolidation			0.087
	2 (1.2)	3 (5.7)	
Mixed type			0.262
	36 (20.9)	15 (28.3)	
Air bronchogram			0.010*
	25 (14.5)	16 (30.2)	
Cobblestone appearance			<0.001*
	9 (5.2)	15 (28.3)	
Halo sign			0.479
	6 (3.5)	1 (1.9)	
Reversed halo sign			0.400
	7 (4.1)	1 (1.9)	
Ground glass nodule			0.059
	11 (6.4)	0 (0.0)	
**p < 0.05*			

COVID-19 PSI

We found that 64 (37.2%) of the surviving patients were in PSI group II at the time of first admission. In the mortality group, no patient was in PSI group I at admission ($p < 0.001$) (Figure 2). Of the patients who died, three (5.7%) were in PSI group II ($p < 0.001$), four (7.5%) were in PSI group III ($p = 0.046$), 21 (39.6%) were in PSI group IV ($p < 0.001$), and 25 (47.1%) were in PSI group V ($p < 0.001$).

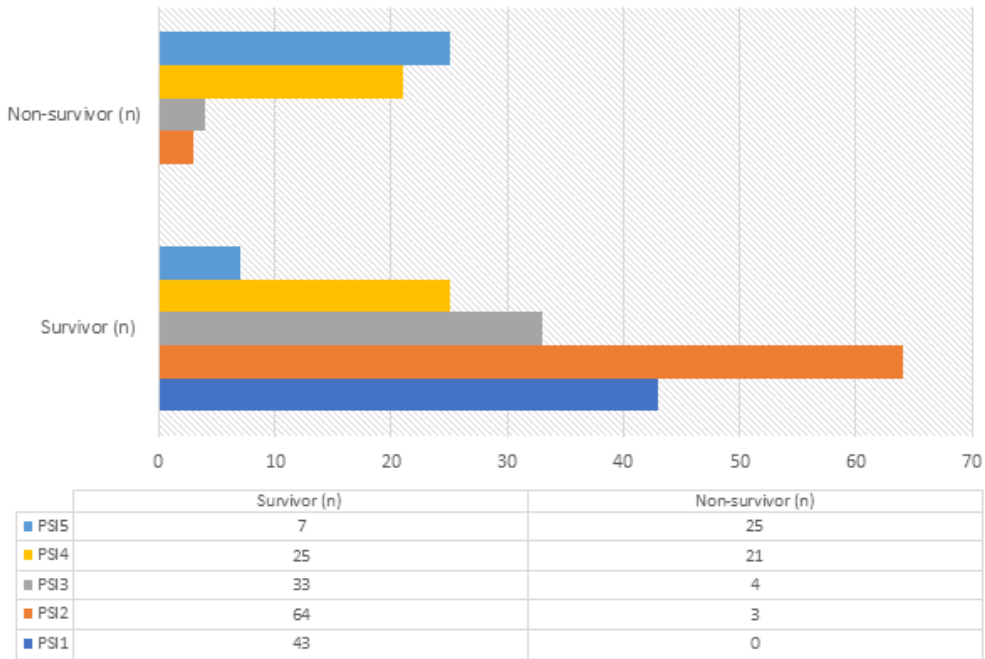

Figure 2: PSI (Pneumonia severity index) of the surviving and non-surviving patients

In this study, the relationships between parameters that were statistically significantly correlated with mortality were also examined in the logistic regression analysis by creating a multivariate model. The data are presented in Table IV (Hosmer Lemeshow Test p=0.287; Nagelkere R2=0.570).

Table 4: Results of univariate and multivariate analyses with the logistic regression

		Univariate		Multivariate	
Variable	**Non-survivor n (%)**	**Odds**	**p**	**Odds**	**p**
Gender					
Female	16 (16.8)	1			
Male	37 (28.5)	1.964 (1.017-3.796)	0.045*		
Age					
<60 years	5 (6.6)	1		1	
≥60 years	48 (37.8)	8.628 (3.254-22.879)	<0.001*	3.532 (1.130-11.037)	0.030*
PSI group V	25 (78.1)	21.046 (8.313-53.284)	<0.001*	8.393 (2.869-24.551)	<0.001*
EOS (x10^3/µL)					
<0.02	43 (33.3)	4300(2.031-9.105)		3.162 (1.141-8.759)	
≥0.02	10 (10.4)	1	<0.001*	1	0.027*
LYM (ml)					
<800	37 (54.4)	10.518(5.204-21.258)		4.049 (1.706-9.611)	
≥800	16 (10.2)	1	<0.001*	1	0.002*
Lactate (mmol/L)					
0,5-1.6	16 (11.8)	1		1	
>1.6	37 (41.6)	5.337 (2.729-10.436)	<0.001*	3.196 (1.315-7.765)	0.010*
Ferritin (ng/ml)					
<306	8 (7.2)	1		1	
≥306	45 (39.5)	8.397 (3.730-18.903)	<0.001*	4.327 (1.461-12.816)	0.008*
COPD	14 (38.9)	2.448 (1.148-5.218)	0.020*		
CAD	19 (35.8)	2.268 (1.155-4.456)	0.017*		
Bilateral involvement on LCT	50 (26.6)	4.106 (1.207-13.964)	0.024*		
Subpleural involvement on LCT	33 (18.9)	0.349 (0.176-0.689)	0.002*		
Involvement percentage					
<5% (Score 1)	6 (11.5)	1			
5-25% (Score 2)	15 (14.6)	1.307 (0.475-3.594)	0.604		
26-49% (Score 3)	15 (36.6)	4.423 (1.53-12.791)	0.006*		
50-75% (Score 4)	8 (53.3)	8.762 (2.331-32.928)	0.001*		
>75% (Score 5)	9 (64.3)	13.800 (1.233-5. 243)	<0.001*		
WBC (x10^3/µL)					
<10,000	28 (15.7)	1	<0.001*		
≥10,000	25 (53.2)	6.088 (3.021-12.268)			
NEU (x10^3/µL)					
<7000	15 (10.1)	1			
≥7000	38 (50.0)	8.933 (4.446-17.950)	<0.001*		
BASO (x10^3/µL)					
0-0.01	6 (9.5)	1			
>0.01	47 (29.0)	3.883 (1.567-9.617)	0.003*		
CRE (mg/dL)					
<1.17	29 (16.6)	1			
≥1.17	24 (48.0)	4.647 (2.347-9.201)	<0.001*		
Urea (mg/dL)					
<43	12 (8.7)	1			
≥43	41 (47.1)	9.359 (4.526-19.352)	<0.001*		
AST (U/L)					
0-50	33 (17.6)	1			
>50	20 (52.6)	5.185 (2.475-10.862)	<0.001*		
POTAS (mEq/L)					
<5.1	40 (19.6)	1			
≥5.1	13 (61.9)	6.662 (2.587-17.161)	<0.001*		
TROP (ng/ml)					
0-19.8	23 (13.3)	1			
>19.8	30 (57.7)	8.893 (4.400-17.976)	<0.001*		
PT (sec)					
<16	44 (21.2)	1			
≥16	9 (52.9)	4.193 (1.529-11.499)	0.005*		
INR					
<1.24	46 (21.7)	1			
≥1.24	7 (53.8)	4.210 (1.349-13.141)	0.013*		

COPD: *Chronic obstructive pulmonary disease,* ***CAD:*** *Coronary artery disease,* ***PSI:*** *Pneumonia severity index ,* ***WBC:*** *White blood cell,* ***NEU:*** *Neutrophil,* ***BASO:*** *Basophil,* ***EOS:*** *Eosinophil,* ***LYM:*** *Lymphocyte,* ***CRE:*** *Creatinine,* ***AST:*** *Aspartate aminotransferase,* ***POTAS:*** *Potassium,* ***TROP:*** *Troponin, PT: Prothrombin time,* ***INR:*** *International normalized ratio,* ***LCT:*** *Lung computed tomography, *p < 0.05, Hosmer Lemeshow Test p=0.287; Nagelkere R2=0.570*

Discussion

In our study, we found that severe COVID-19 was more common in patients aged 60-90 years and those with comorbidities, such as COPD, DM, HT, and CAD. When the moderate-risk patient group was compared with the severe cases, the symptoms of headache, sore throat, and dyspnea were more common in the latter. In both the survivor and mortality groups, we found a higher rate of severe disease among the male patients. In contrast, some studies reported that gender was not a risk factor for COVID-19 (5, 10).

Concerning the laboratory findings, we found that increased leukocyte-neutrophil count, lactate, LDH, troponin, and ferritin levels, decreased lymphocyte-basophil-eosinophil count were associated with mortality of COVID-19. Unlike the results of previous studies, our study showed that severe illness or an intensive care requirement due to SARS-CoV-2 pneumonia was associated with leukocytosis rather than leukopenia (11, 12). In a study by Li et al., (13) a correlation was found between severe COVID-19 and high alanine aminotransferase, aspartate aminotransferase, and creatinine levels. However, we did not observed such a relationship in our study. Qin et al. (14) suggested that lymphocyte count should be monitored in terms of a possible decrease in the early screening of severe COVID-19 and diagnosis and treatment of the disease. A decrease in basophil count was present in almost all of our patients that died. A decrease in basophil count can also assist in the early diagnosis of the disease. The significant decrease in the eosinophil level in the early period is also remarkable. Our multivariate logistic regression analysis revealed that low eosinophil and lymphocyte counts and increased lactate and ferritin levels were the most significant parameters affecting mortality. Fibrinogen is frequently elevated in patients with sepsis but may also be low in severe cases of disseminated intravascular coagulation (DIC). Decreased fibrinogen is also an important criterion for the diagnosis of overt DIC (15). Although the degree of elevation has not been shown to be consistently associated with mortality, it has been found to be strongly associated with the interleukin (IL)-6 level (16). In some studies, the progressive decrease in the fibrinogen level has been strongly associated with mortality, but this tends to occur very late in the disease course (17). In our study, increased fibrinogen was observed in 40 (75%) of the patients that died and 112 (65.1%) of the survivors. Since, the increase in fibrinogen was increased in both survivor and mortality groups, we did not find a significant relationship between this protein and mortality.

LCT findings constitute another groups of prognostic factors that directly reflect the extent of pneumonia. Diffuse pneumonia is also a previously known prognostic factor in Middle East respiratory syndrome and SARS pneumonia (17). According to a recent study, less than <73% inflated lungs was an indicator of intensive care requirement and death (18). Therefore, measuring the pneumonia burden using the LCT score and the number of lobes or segments will help classify patients according to severity (18). Previous studies reported that 56% of LCT scans were normal in the early phase (0-2 days after symptom onset) while abnormal LCT findings became more frequent six to 11 days after symptom onset (19, 20). In the current study, we examined the LCT images taken at admission in the early stage of the disease and found a significant positive correlation between the percentage of involvement on LCT and mortality. We found that LCT involvement of 5-49% at the time of admission was a significant indicator of mortality, and the number of deaths increased as the percentage of involvement increased. Although, an LCT score of 2 and above does not necessarily indicate diffuse pneumonia, it should not be overlooked, and these patients should be carefully followed up to monitor the progression of severe pneumonia.

In our study, we detected ground glass opacity appearance, bilateral, subpleural, and involvement of more than two lobes on LCT very common. In severe cases, air bronchogram and cobblestone appearance were more common than in non-severe cases. The LCT scores of the whole lung and each lobe were significantly higher in the severe group than in the non-severe group. Among the non-survivors, the involvement of the RML, RLP, RLS, LUL, LLL, LLP, and LLS segments was more frequently seen compared to the remaining patients. In a study by Chon Y et al., (21) although consolidation opacity was frequently observed in patients in the severe group, it was not found to be an indicator of poor prognosis. In our study, although consolidation was detected in a small number of patients in the whole study group, air bronchograms were significantly more common in the mortality group. Five (2.2%) patients had pulmonary edema due to heart failure and 20 (8.8%) had atypical LCT findings. These patients could not be diagnosed with COVID-19 for a long time, which caused delayed treatment and prolonged their length of hospital stay. Although the appearance of pulmonary edema is rare, it should be kept in mind in patients with COVID-19.

PSI is a well-known scoring system to assess the severity of community-acquired pneumonia and has also been validated in the practice of viral pneumonia (22). To determine whether PSI can be used to assess COVID-19 disease severity, we calculated this score for each patient. In our mortality group, 21 of the patients were in PSI group IV and 25 were in PSI group V, and we found a significant relationship between an increase in the PSI score and the number of deaths. In addition, there was a significant correlation between the PSI score and increased ferritin, increased d-dimer, decreased lymphocytes, and increased CRP levels, which are known as mortality indicators. The multivariate logistic regression analysis showed that being in PSI group V was one of the most significant factors affecting mortality.

This was a multifaceted study involving the combination of clinical, laboratory, and radiological evaluations. As a limitation, the relatively small sample size of the severe group can be considered.

Conclusion

This review summarizes the potential risk factors for COVID-19 infection, severity, and mortality in adults. In this single-center retrospective study, we determined the most significant factors for mortality as advanced age, low eosinophil and lymphocyte counts, increased lactate and ferritin levels, and PSI group V. In this review, we highlight the clinical evidence supporting for the risk factors for the severity and mortality of COVID-19. Identifying potential risk factors for COVID-19 severity and mortality may improve the management of COVID-19 patients.

Declarations

Funding
The authors declare that the study received no funding.

Conflict of Interest
The authors declare no competing interests.

Ethics Approval
All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. This study was conducted at the Ağrı State Hospital. Ethical approval was obtained from the Planning and Coordination Board of the hospital with the decision number 34.

Availability of Data and Material
All data is available

Authors' Contribution:
MC: Design the work and the acquisition, analysis, and interpretation of data for the work. Drafting the work and revising it critically for important intellectual content.

CS: Design the work and the acquisition, analysis, and interpretation of data for the work.
CT: Conception and design of the work. Final approval of the version to be published. Agreement to be accountable for all aspects of the work in ensuring that questions related to the accuracy and integrity of any part of the work are appropriately investigated and resolved.
MS: Conception and design of the work. Final approval of the version to be published. Revising it critically for important intellectual content.
All authors approved the final version of the manuscript to be published.

References

1. Loeffelholz MJ, Tang Y-W. Laboratory diagnosis of emerging human coronavirus infections–the state of the art. EMi, 2020;9(1):747-56. DOI: 10.1080/22221751.2020.1745095
2. Xu X-W, Wu X-X, Jiang X-G, et al. Clinical findings in a group of patients infected with the 2019 novel coronavirus (SARS-Cov-2) outside of Wuhan, China: retrospective case series. BMJ. 2020;368. DOI: 10.1136/bmj.m606
3. Wu Z, McGoogan JM. Characteristics of and important lessons from the coronavirus disease 2019 (COVID-19) outbreak in China: summary of a report of 72 314 cases from the Chinese Center for Disease Control and Prevention. JAMA. 2020;323(13):1239-42. DOI: 10.1001/jama.2020.2648
4. Pan L, Mu M, Yang P, et al. Clinical characteristics of COVID-19 patients with digestive symptoms in Hubei, China: a descriptive, cross-sectional, multicenter study. The AJG. 2020;115. DOI: 10.14309/ajg.0000000000000620
5. Li K, Wu J, Wu F, et al. The clinical and chest CT features associated with severe and critical COVID-19 pneumonia. Invest Radiol. 2020. DOI: 10.1097/RLI.0000000000000672
6. Liu R, Han H, Liu F, et al. Positive rate of RT-PCR detection of SARS-CoV-2 infection in 4880 cases from one hospital in Wuhan, China, from Jan to Feb 2020. CCA. 2020;505:172-5. DOI: 10.1016/j.cca.2020.03.009
7. Control CfD, Prevention. Research use only real-time RT-PCR protocol for identification of 2019-nCoV. 2020.
8. Wang S, Kang B, Ma J, et al. A deep learning algorithm using CT images to screen for Corona Virus Disease (COVID-19). ESR. 2021;31:6096-104. DOI: 10.1007/s00330-021-07715-1

9. Hansell DM, Bankier AA, MacMahon H, et al. Fleischner Society: glossary of terms for thoracic imaging. Radiol. 2008;246(3):697-722. DOI: 10.1148/radiol.2462070712
10. Wang D, Hu B, Hu C, et al. Clinical characteristics of 138 hospitalized patients with 2019 novel coronavirus–infected pneumonia in Wuhan, China. JAMA. 2020;323(11):1061-9. DOI: 10.1001/jama.2020.1585
11. Guan W-j, Ni Z-y, Hu Y, et al. Clinical characteristics of coronavirus disease 2019 in China. NEJM. 2020;382(18):1708-20. DOI: 10.1056/NEJMoa2002032
12. Huang C, Wang Y, Li X, et al. Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. Lancet. 2020;395(10223):497-506. DOI: 10.1016/ S0140-6736(20)30183-5
13. Li J, He X, Yuan Y, et al. Meta-analysis investigating the relationship between clinical features, outcomes, and severity of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) pneumonia. AJIC. 2021;49(1):82-9. DOI: 10.1016/j.ajic.2020.06.008
14. Qin C, Zhou L, Hu Z, et al. Dysregulation of immune response in patients with coronavirus 2019 (COVID-19) in Wuhan, China. CID. 2020;71(15):762-8. DOI: 10.1093/cid/ciaa248
15. Taylor Jr FB, Toh C-H, Hoots KW, et al. Towards definition, clinical and laboratory criteria, and a scoring system for disseminated intravascular coagulation. JTH. 2001;86(11):1327-30. DOI: 10.1055/s-0037-1616068
16. Tang N, Li D, Wang X, et al. Abnormal coagulation parameters are associated with poor prognosis in patients with novel coronavirus pneumonia. JTH. 2020;18(4):844-7. DOI: 10.1111/jth.14768
17. Zou Z, Yang Y, Chen J, et al. Prognostic factors for severe acute respiratory syndrome: a clinical analysis of 165 cases. CID .2004;38(4):483-9. DOI: 10.1086/380973
18. Colombi D, Bodini FC, Petrini M, et al. Well-aerated lung on admitting chest CT to predict adverse outcome in COVID-19 pneumonia. Radiol. 2020;296(2):E86-E96. DOI: 10.1148/radiol.2020201433
19. Wang Y, Dong C, Hu Y, et al. Temporal changes of CT findings in 90 patients with COVID-19 pneumonia: a longitudinal study. Radiol. 2020;296(2):E55-E64. DOI: 10.1148/radiol.2020200843
20. Bernheim A, Mei X, Huang M, et al. Chest CT findings in coronavirus disease-19 (COVID-19): relationship to duration of infection. Radiol. 2020;295(3):685-91. DOI: 10.1148/radiol.2020200463
21. Chon Y, Kim JY, Suh YJ, et al. Adverse initial CT findings associated with poor prognosis of coronavirus disease. J Korean Med Sci . 2020;35(34). DOI: 10.3346/jkms.2020.35.e316
22. Kim M-A, Park JS, Lee CW, et al. Pneumonia severity index in viral community acquired pneumonia in adults. PONE. 2019;14(3):e0210102. DOI: 10.1371/journal.pone.0210102