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Can the Progression of COVID-19 Pneumonia be Predicted?

COVID-19 Pnömonisinin Progresyonu Öngörülebilir mi?

Fatma Demirci Üçsular[1], Gülistan Karadeniz[1], Gülru Polat[1], Damla Serçe Unat[1], Aysu Ayrancı[2], Enver Yalnız[1], Filiz Güldaval[1]

[1]*University of Health Sciences Türkiye, Dr. Suat Seren Chest Disease and Surgery Training and Research Hospital, Clinic of Chest Diseases, İzmir, Türkiye*

[2]*Bakırçay University Çiğli Training and Research Hospital, Department of Chest Diseases, İzmir, Türkiye*

ABSTRACT

Background: Coronavirus disease-2019 (COVID-19) remains a major cause of morbidity and mortality. There are many parameters affecting the progression of the disease. The purpose of the present study was to evaluate and compare the initial data of patients hospitalized with the diagnosis of COVID-19 pneumonia, who progressed during the hospitalization period, with other patients who recovered or remained stable, and to investigate the risk factors that can be used to predict the disease progression.

Materials and Methods: Patients, who received inpatient treatment with the diagnosis of COVID-19 pneumonia, were included in the study retrospectively. Two groups were created from all patients according to their progression in hospital follow-ups: Group 1: Progression group and group 2: Recovery/stabilization group. If patients had clinical, laboratory and/or radiological deterioration or died during follow-up, these patients were included in the progression group. If patients recovered or remained stable, these patients were also included in the recovery/stabilization group. The demographic data, initial hemogram, biochemical parameters and radiological data of the patients were recorded.

Results: It was determined in the univariate analysis that the age, smoking status, comorbidity, heart disease, chronic obstructive pulmonary disease, cancer, dyspnea, fever, leukocytosis, lymphopenia, elevated neutrophil-lymphocyte ratio (NLR), C-reactive protein, albumin, lactate dehydrogenase, ferritin, D-dimer, troponin-T, pro-B-type natriuretic peptide (pro-BNP) were risk factors predicting disease progression all p-values<0.05. In the multivariate logistic regression analysis, it was found that fever, NLR, and D-dimer could be used to predict the disease progression (p<0.05). In the ROC analysis, the sensitivity of NLR was 83.3%, specificity 57.5%, and cut-off >3.545 [area under curve (AUC)=0.752; p<0.001]; the sensitivity of pro-BNP was 71.8%, specificity 73.8%, and cut-off >332.8 (AUC=0.752; p<0.001), the sensitivity of troponin-T was 81.2%, specificity was 60.6%, and cut-off was >4.58 (AUC=0.730; p<0.001) in predicting progression.

Conclusion: The identification of risk factors predicting progression is important in reducing morbidity and mortality rates. Fever, NLR, D-dimer troponin-T and pro-BNP are important parameters that can be used to predict progression.

Keywords: COVID-19 pneumonia, progression, risk factors

ÖZ

Amaç: Koronavirüs hastalığı-2019 (COVID-19) önemli bir morbidite ve mortalite nedeni olmaya devam etmektedir. Hastalığın ilerlemesini etkileyen birçok parametre vardır. Çalışmanın amacı; COVID-19 pnömonisi tanısı ile hastaneye yatırılan ve yatış süresi boyunca progresyon gösteren hastaların ilk verilerini, iyileşen veya stabil kalan diğer hastalarla karşılaştırmak ve progresyonu öngörmede kullanılabilecek risk faktörlerini araştırmaktır.

Gereç ve Yöntemler: COVID-19 pnömonisi tanısıyla yatarak tedavi alan hastalar retrospektif olarak çalışmaya dahil edildi. Tüm hastalardan hastane takiplerindeki seyirlerine göre 2 grup oluşturuldu: 1. grup: Progresyon grubu ve 2. grup: İyileşme/stabilizasyon grubu. Hastalarda klinik, laboratuvar ve/veya radyolojik kötüleşme görüldüyse veya takipler sırasında hastalar eks olduysa, bu hastalar progresyon grubuna alındı. İyileşme veya stabil seyrettiyse, bu hastalar da iyileşme/stabilizasyon grubuna dahil edildi. Hastaların demografik verileri, başlangıç hemogram ve biyokimyasal parametreleri ve radyolojik verileri kaydedildi.

Bulgular: Univariate analizde; yaş, sigara, komorbidite, kalp hastalığı, KOAH, kanser, nefes darlığı, ateş, lökositoz, lenfopeni, nötrofil-lenfosit oranı (NLR) yüksekliği, C-reaktif protein, albümin, laktat dehidrogenaz, ferritin, D-dimer, troponin T, pro-B tipi natriüretik

Address for Correspondence: Fatma Demirci Üçsular, University of Health Sciences Türkiye, Dr. Suat Seren Chest Disease and Surgery Training and Research Hospital, Clinic of Chest Diseases, İzmir, Türkiye

Phone: +90 544 645 27 67 E-mail: fatmaucsular@gmail.com **ORCID ID:** orcid.org/0000-0003-3746-3095

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ÖZ

peptitin (pro-BNP) hastalığın progresyonunu öngören risk faktörleri olduğunu saptadık (tüm p-değerleri<0,05). Multivariate logistic regression analizinde; sıcaklık, NLR ve D-dimerin progresyonu predikte etmede kullanılabileceğini saptadık (p<0,05). ROC analizinde; progresyonu öngörmede; NLR'nin sensivitesi %83,3, spesifitesi %57,5, cut-off >3,545 [eğri altındaki alan (EAA)=0,752; p<0,001], pro-BNP'nin sensivitesi %71,8, spesifitesi %73,8, cut-off >332,8 (EAA=0,752; p<0,001), troponin-T'nin sensivitesi %81,2, spesifitesi %60,6, cut-off >4.58 (EAA=0,730; p<0,001) olarak belirledik.

Sonuç: Progresyonu öngören risk faktörlerinin belirlenmesi morbidite ve mortalite oranlarını azaltmada önemlidir. Ateş, NLR, D-dimer troponin-T ve pro-BNP progresyonu öngörmede kullanılabilecek önemli parametrelerdir.

Anahtar Kelimeler: COVID-19 pnömonisi, progresyon, risk faktörleri

Introduction

Severe acute respiratory syndrome-coronavirus-2 (SARS-CoV-2) has a highly contagiouse and pathogenicity and has caused "Coronavirus disease-2019 (COVID-19)" since the last months of 2019 and the pandemic process continues.

The clinical manifestations of COVID-19 appear in a wide range from asymptomatic to critical disease and mortality (1). Because of the overcrowding of hospitals due to COVID-19 pandemic, studies were needed on which parameters could be used to predict the worsening of the disease and mortality in terms of demographic, clinical, hematological, biochemical, and radiological data. In the present study, the purpose was to compare the initial data of the patients who were hospitalized with the diagnosis of COVID-19 and who had progression during the hospitalization period with other patients who recovered or remained stable and to investigate the risk factors that can be used to predict the disease progression.

Material and Methods

This study was conducted following the Declaration of Helsinki and approved by the Ethics Committee of University of Health Sciences Türkiye, Dr. Suat Seren Chest Disease and Surgery Training and Research Hospital and by the Turkish Ministry of Health, COVID-19 Scientific Research Evaluation Committee (approval date/no: 22.07.2020/49109414-604.02).

The patients who were aged 18 years and over receiving inpatient treatment with the diagnosis of COVID-19 pneumonia between 11.03.2020 and 15.05.2020 were retrospectively included in the study. Patients receiving outpatient treatment were excluded from the study. According to the Guidelines by the Scientific Committee of Ministry, the SARS-CoV-2 real-time reverse-transcriptase-polymerase chain reaction (RT-PCR) test and/or SARS-CoV-2 rapid antibody test was performed for the patients who had a history of contact in the last 14 days and/or symptoms such as cough, fever, and dyspnea (2). RT-PCR test was performed on the date of admission to the hospital from the nasal and pharyngeal area at least once with swab samples. RT-PCR test was repeated for 3 consecutive days for the patients who came back negative. Patients who had positive results were included in the study. Patients given outpatient treatment, patients with negative RT-PCR test and/or SARS-CoV-2 rapid antibody test were excluded from the study.

The patients were grouped according to severity as mild-to-moderate pneumonia, severe pneumonia, and critical disease [i.e. acute respiratory distress syndrome (ARDS), other organ failures, or sepsis]. Mild-to-moderate pneumonia: Respiratory rate <30/minute, SpO_2 >93%, pneumonic infiltration less than 50%. Severe pneumonia: Respiratory rate ⩾30/minute, SpO_2 <90%, patients who had bilateral diffuse pneumonia findings on chest X-ray or tomography. Critical disease: PaO_2/FiO_2<300, SpO_2<90%, hypotension and heart rate >100/minute, acute organ dysfunction development, elevated troponin and arrhythmia, and those with lactate >2 mmol (3).

Patients with COVID-19 pneumonia were divided into 2 groups according to the change in their clinical course during hospital follow-up. Specific criteria were as follows: Progression group: Mild-moderate pneumonia changed to severe pneumonia or critical disease or death; severe pneumonia changed to critical disease or death; critical disease progressed to death. Recovery/stabilization group: Mild-moderate pneumonia, severe pneumonia, and critical disease remained unchanged; mild-moderate pneumonia recovered; severe pneumonia changed to mild-moderate pneumonia; critical-type changed to severe or mild-modreate pneumonia.

In inpatients with COVID-19 pneumonia, the epidemiological and demographic data, contact histories, complaints, habits, comorbidities, initial vital signs, and room air oxygen saturation of the patients were also recorded. Initial hemogram, serum biochemical parameters [i.e. renal and liver functions, lactate dehydrogenase (LDH) and ferritin levels], coagulation profile [i.e. D-dimer, activated partial thromboplastin time, prothrombin time (PT)], myocardial enzymes, C-reactive protein (CRP) values, and treatments

given at the hospitalization were documented from the electronic medical records. Chest radiographs and/or thorax computed tomography (CT) findings were evaluated by a radiologist. The distribution of the lung lesions and the pattern of the lesions were also recorded. The patients were included in one of two groups according to the change in their clinical, laboratory and radiological data during the hospitalization period. The patients who died during the hospitalization period were recorded.

Statistical Analysis

Data were analyzed using the International Business Machines Corporation Statistical Package for the Statistical Package for Social Sciences 22.0 (IBM SPSS Corp.; Armonk, NY, USA) package program. The mean values, standard deviation values, and categorical variables were presented as numbers and percentages. The conformity of continuous variables to the normal distribution was examined by considering graphical research, normality tests, and sampling size. It was found that these variables did not meet the "normal distribution" conditions in all subgroups, and the non-parametric "Mann-Whitney U test" was used for the comparison of the independent groups. The ROC analysis was conducted for the variables that had significant differences and the most appropriate cut-off value was determined according to the Youden index. Dichotomous variables were formed according to these cut-off values. The categorical independent variables are presented in the cross tables as frequencies and percentages, their distributions were compared with the chi-square test, and the univariate odds ratio was calculated. The variables with $p<0.200$ were included in the multivariate logistic regression analysis as independent variables and multivariate odds ratios were calculated with the backward stepwise method (Wald). The margin of error for the first type was determined as α:0.05 and tested as double-tailed in all statistical comparison tests. In the case of $p<0.05$, the difference between the groups was considered statistically significant.

Results

General Characteristics and Clinical Presentations

In this study 233 patients with COVID-19 associated pneumonia included 134 males and 99 females. Median age (minimum-maximum) was 63 (28-91) years in the progression group (n=54) and 52 (20-85) years in the recovery/stabilization group (n=179) (p=0.00). In the progression group, the number of aged ≥65 years, a number of intensive care treatment were significantly higher than the recovery/stabilization group (all p-values <0.05). The progression group had a significantly higher proportion of patients with a history of smoking than the recovery/stabilization group. Frequency of any comorbidity (p=0.007), heart disease, chronic obstructive pulmonary disease (COPD) and malignancy ($p<0.05$) was higher in the progression group than the recovery/stabilization group. Dyspnea and fatigue were more common symptom in the progression group when compared to the recovery/stabilization group (66.7% vs. 32.4%, 57.4% vs. 40.2%, $p<0.05$). In the progression group, the number of patients with body fever >37.5 °C (p=0.042) and blood oxygen saturation ≤93% ($p<0.001$) were higher than the recovery/stabilization group. 57.4% of patients in the progression group (n=31) died (Table 1).

Laboratory Indices and Imaging Characteristics

Laboratory data of patients diagnosed with COVID-19 pneumonia were evaluated at the time of admission. When compared with the recovery/stabilization group, these results showed that leukocyte, neutrophil, neutrophil-lymphocyte ratio (NLR), CRP, LDH, ferritin, D-dimer, PT, international normalized ratio (INR), glucose, creatinine, troponin-T, pro-B-type natriuretic peptide (pro-BNP), and FiO_2 were significantly higher in the progression group than the recovery/stabilization group ($p<0.05$). In addition in the progression group, lymphocyte, monocyte, albumin, and blood oxygen saturation were significantly lower than recovery/stabilization group ($p<0.05$). On the X-ray chest radiography, the bilateral distribution of lesions was significantly more in the progression group than the improvement/stabilization group (84%/63.4%, p=0.012). When the lesion distribution on thorax CT is evaluated; while the lesions mostly showed a central or peripheral distribution in the recovery/stabilization group, the lesions involved all zones (diffuse distribution) in the progression group (p=0.002) (Table 2).

Risk Factors for Disease Progression in Patients with COVID-19 Pneumonia

The risk factors that were found to be significantly associated with the progression of the disease in univariate and multivariate logistic regression analysis are given in Table 3 below.

The Predictors of Progression of COVID-19 Pneumonia Were Determined by ROC Analysis

The sensitivity of NLR was 83.3%, specificity 57.5%, and cut-off >3.545 [area under curve (AUC)=0.752; $p<0.001$], the sensitivity of pro-BNP was 71.8%, specificity 73.8%, and cut-off >332.8 (AUC=0.752; $p<0.001$), the sensitivity of troponin-T was 81.2%, specificity 60.6%, and cut-off >4.58 (AUC=0.730; $p<0.001$) (Figure 1).

Table 1. Demographic data and clinical findings of COVID-19 patients in the progression group and recovery/stabilization group

	Progression group (n=54)	Recovery/stabilization group (n=179)	p
Age (years)	63 (28-91)	52 (20-85)	0.00
Age group ≥65 <65	 19 (35.2) 35 (64.8)	 31 (17.3) 148 (82.7)	0.009
Male gender	37 (68.5%)	97 (54.2%)	0.087
Smoking (pack/year)	33 (5-100)	20 (1-150)	0.019
Smoking status Smoker Ex-smoker Non-smoker	 4 (8) 26 (52) 20 (40)	 34 (19.2) 34 (19.2) 109 (61.6)	0.000
Contact history	9 (16.7)	61 (34.3)	0.021
Inpatient treatment **Inpatient + intensive care treatment** **Intensive care treatment**	21 (38.9) 13 (24.1) 20 (37)	171 (95.5) 6 (3.4) 2 (1.1)	0.000
Any comorbidity	37 (68.5)	83 (46.4)	0.007
Hypertension	18 (33.3)	48 (26.8)	0.448
Diabetes mellitus	11 (20.4)	22 (12.3)	0.180
Cardiac disease	9 (16.7)	12 (6.7)	0.032
COPD	11 (20.4)	10 (5.6)	0.002
Asthma	0 (0)	7 (3.9)	0.358
Malignancy	11 (20.4)	10 (5.6)	0.002
Cough	32 (59.3)	116 (64.8)	0.561
Dyspnea	36 (66.7)	58 (32.4)	0.000
Sputum	9 (16.7)	15 (8.4)	0.133
Headache	6 (11.1)	18 (10.1)	1.00
Weakness	31 (57.4)	72 (40.2)	0.038
Nausea	8 (14.8)	12 (6.7)	0.092
Myalgia	8 (14.8)	41 (22.9)	0.277
Diarrhea	3 (5.6)	12 (6.7)	1.000
Anosmia	1 (1.9)	8 (4.5)	0.689
Heart rate (beats/min)	90 (53-156)	88 (62-140)	0.035
Respiratory rate (breaths/min)	23 (11-36)	18 (10-32)	0.00
Body temperature >37.5 °C	26 (48.1)	57 (31.8)	0.042
Blood oxygen saturation, %	89 (64-99)	95(80-98)	0.00
Blood oxygen saturation ≤93%	39 (72.2)	44 (24.6)	0.00
RT-PCR positivity	51 (94.4)	14 7(82.1)	0.045
Spectrum of disease (severity) Mild-moderate pneumonia Severe pneumonia Critical illness	 35 (64.8) 13 (24.1) 6 (11.1)	 133 (74.3) 28 (15.6) 18 (10.1)	0.326
Time of stay in service (day)	13 (3-27)	7 (3-21)	0.00
Time of stay in the ICU (day)	8 (1-37)	13 (4-30)	0.569
Mortality, n (%)	31 (57.4)	0 (0.00)	0.000

Data are presented as median (interquartile range) or number (%), COPD: Chronic obstructive pulmonary disease, RT-PCR: Reverse transcription-polymerase chain reaction, ICU: Intensive care unit, COVID-19: Coronavirus disease-2019

Table 2. Laboratory findings and imaging characteristics of COVID-19 patients in the progression group and recovery/stabilization group

	Progression group (n=54)	Recovery/stabilization group (n=179)	p
Leukocyte x10³ µL	7850 (13000-31900)	5800 (2600-30900)	0.001
Leukcytosis (>10.000)	17 (31.2)	22 (12.3)	0.002
Neutrophil x10³ µL	6100 (1000-28100)	3800 (1100-30300)	0.00
Lymphocyte x10³ µL	800 (100-3000)	1100 (100-5500)	0.00
Lymphopenia (<800)	23 (42.6)	33 (18.4)	0.001
Monocyte x10³ µL	400 (100-8613)	500 (0-6000)	0.011
NLR	7.42 (1.08-93.67)	3.33 (0.63-75.75)	0.00
Hemoglobin gr/dL	12.9 (8.30-16.7)	13.20 (7.8-17.30)	0.129
Platelet x10³ µL	249500 (65000-649000)	215000 (62000-840000)	0.070
PT (sec)	13.2 (7.48-53.5)	12.5 (10.6-16.9)	0.002
APTT (sec)	26.5 (19.9-95.2)	25.5 (19.8-48.4)	0.342
INR	1.11 (0.89-4.80)	1.04 (0.8-1.44)	0.001
D-dimer, ng/mL	1426 (304-10000)	717 (121-10000)	0.00
D-dimer >1000 ng/mL	35 (71.4)	48 (30.4)	0.00
Albumine, gr/dL	3.19 (1.48-4.10)	3.96 (2.05-5.02)	0.00
Albumine <4 gr/dL	44 (95.7)	74 (52.9)	0.00
Aspartate aminotransferase, U/L	25 (11-97)	23 (10-134)	0.147
Alanine aminotransferase, U/L	21 (4-140)	22 (5-93)	0.764
Total bilurubin, mg/dL	0.41 (0.10-1.47)	0.35 (0.08-2.0)	0.185
Lactate dehydrogenase, U/L	351 (125-969)	228 (97-785)	0.00
Lactate dehydrogenase >243 U/L	32 (71.1)	60 (44.4)	0.003
Glucose mg/dL	125 (57-297)	109 (61-500)	0.008
Glucose ≥120 mg/dL	31 (57.4)	64 (35.8)	0.007
Creatinine, mg/dL	0.96 (0.49-4.10)	0.79 (0.45-2.55)	0.001
C-reactive protein, mg/dL	10.40 (0.07-39)	4.53 (0.08-79.2)	0.00
C-reactive protein >10 mg/dL	29 (53.7)	41 (22.9)	0.00
Ferritin, ng/mL	625 (91-2227)	214 (9-1585)	0.00
Ferritin >500 ng/mL	26 (57.8)	29 (21)	0.00
Troponin-T, ng/L	8.10 (0.0-1664)	3.76 (0.0-105.1)	0.00
Pro-BNP pg/mL	666 (7-36000)	78 (7-8327)	0.00
Blood oxygen saturation, %	89 (64-99)	95 (80-98)	0.00
Blood oxygen saturation ≤93%	39 (72.2)	44 (24.6)	0.00
FiO_2, %	31 (21-200)	21 (21-93)	0.00
pO_2/FiO_2	191 (67-382)	234 (137-331)	0.110
Lesion in X-ray graphic Bilateral Unilateral	 42 (84) 8 (16)	 85 (63.4) 49 (36.6)	0.012
Distribution of lesions on HRCT Central Peripheric Diffuse	 1 (1.9) 18 (34) 34 (64.2)	 8 (4.6) 103 (58.9) 64 (36.6)	0.002

Data are presented as median (interquartile range) or number (%), NLR: Neutrophil-to-lymphocyte ratio, PT: Prothrombin time, aPTT: Activated partial thromboplastin time, INR: International normalized ratio, Pro-BNP: Pro-brain natriuretic peptide, HRCT: High resolution computed tomography, COVID-19: Coronavirus disease-2019

Table 3. Univariate and multivariate analysis results of risk factors for disease progression in COVID-19 patients (n=233)

Univariate analysis				Multivariate analysis		
Variables	**OR**	**95% CI**	**p**	**OR**	**95% CI**	**p**
Age (≥65 years)	2.592	1.314-5.113	0.009			
History of smoking	2.404	1.216-4.56	0.01			
Comorbidity	2.517	1.321-4.798	0.004			
COPD	4.323	1.727-10.843	0.002			
Cardiac disease	2.783	1.104-7.018	0.032			
Cancer	4.323	1.724-10.843	0.002			
Body temperature >37.5 °C	1.987	1.070-3.693	0.042	2.91	1.35-6.30	0.007
Dyspnea	4.172	2.186-7.965	0.00			
Blood oxygen saturation ≤93%	7.977	4.018-15.838	0.00			
Leukcytosis (>10.000)	3.279	1.584-6.785	0.002			
Lymphopenia (<800)	3.283	1.699-6.342	0.001			
NLR >3.55	6.776	3.123-14.703	0.00	4.03	1.71-9.49	0.001
C-reactive protein >10 mg/dL	3.904	2.062-3.793	0.00			
Albumine <4 gr/dL	19.622	4.578-84.101	0.00			
Lactate dehydrogenase >243 U/L	3.077	1.485-6.376	0.003			
Ferritin >500 ng/mL	5.143	2.505-10.561	0.00			
D-dimer >1.000 ng/mL	5.729	2.827-11.612	0.00	3.89	1.75-8.61	0.001
Troponin-T >4.58 ng/L	6.660	2.988-14.849	0.00			
Pro-BNP >333 pg/mL	7.159	2.908-17.627	0.00			

COPD: Chronic obstructive pulmonary disease, NLR: Neutrophil-to-lymphocyte ratio, Pro-BNP: Pro-brain natriuretic peptide, COVID-19: Coronavirus disease-2019

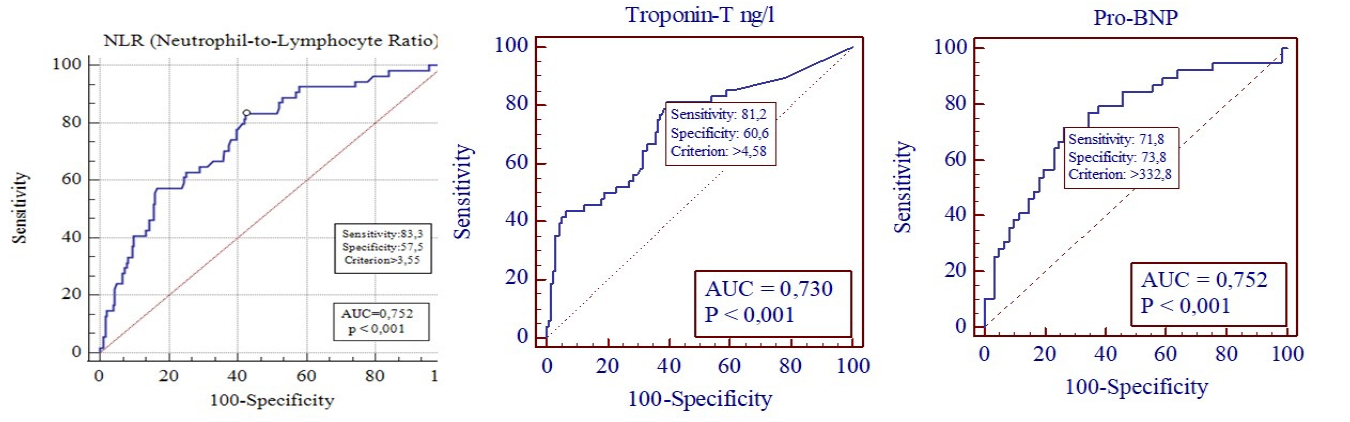

Figure 1. ROC analysis of COVID-19 patients
COVID-19: Coronavirus disease-2019, Pro-BNP: Pro-brain natriuretic peptide, AUC: Area under the curue

Discussion

The clinical course of the disease in COVID-19 infection differs according to age and comorbidities. Severe pneumonia resulting in critical illness and sometimes death may be seen in those with advanced age (>65) and comorbidities. In young people, COVID-19 pneumonia is usually mild to moderate and has been reported to result in recovery (1,4,5). The disease sometimes deteriorates rapidly and can even result in death. Therefore, we planned to investigate the factors predicting disease progression.

In the present study, it was found that the median age, advanced age (≥65 years), smoking and the presence of any comorbidy in the progression group were significantly higher than the recovery/stabilization group (p<0.05). In univariate analysis; it was found that age, smoking, comorbidity, heart disease, COPD, cancer, dyspnea, and fever were risk factors that predicted the disease progression.

In a study in which Lee et al. (6) compared hospitalized mortal and non-mortal advanced-age (≥65 years old) COVID-19 patients, it was reported that male gender, age, and comorbidity were higher in the group that had a mortal group, and advanced age was the most important risk factor for mortality.

Toker et al. (7) retrospectively analyzed 561 COVID-19 patients as intensive care unit (ICU)/non-ICU group and death/survived group. They reported that advanced age, coronary artery disease and malignancy, leukocyte count over ten thousand, lymphopenia, elevation of urea and creatinine, CRP, procalcitonin, LDH, D-dimer and cTnI parameters were significant risk factors for ICU and mortality (7).

Pneumonia and ARDS are the most important and most common COVID-19 complications. During the worsening of the disease, an uncontrolled excessive inflammatory response and subsequent tissue damage are observed. Leukocytes form an important cell group in the systemic inflammatory response in severe disease. Lymphopenia and eosinopenia are also seen (8). The subgroup of leukocytes are used as an index to determine the severity of the immune response. NLR is a biomarker of the systemic inflammatory response (9). Wu et al. (10) found that severe disease was associated with neutrophilia and lymphopenia in COVID-19 patients in the ICU. In another study, neutrophilia and high NLR were found to be correlated with the severity of the disease and poor outcomes (11). In the present study, leukocyte, neutrophil, and NLR were significantly elevated in the progression group when compared to the recovery/stabilization group, and lymphopenia was also significantly more higher. It was determined that laboratory parameters such as leukocytosis, lymphopenia, high NLR, CRP, albumin, LDH, ferritin, D-dimer were the risk factors for disease progression (in univariate analysis). In ROC analysis, the cut-off value of (NLR >3.545) that predicted progression was found in this study. Jimeno et al. (12) found that age, cardiovascular disease, and high CRP and NLR were associated with mortality. The results showed that higher temperature, elevated NLR, and D-dimer were are risk factors for disease progression in multivariate logistic models.

When compared to other viral infections, the risk of venous thromboembolism and pulmonary thromboembolism is higher in severe infections of SARS-CoV-2 (13). Abnormally elevated hypercoagulability markers, increased levels of D-dimer, and thrombocytopenia were also associated with poor prognosis and mortality in COVID-19 (13,14,15). In this study, PT, INR, and D-dimer values were found significantly higher in the progression group, compared to recovery/stabilization group.

In both univariate and multivariate logistic regression analysis, it was determined that elevated D-dimer (>1.000 ng/mL) increased the progression of COVID-19 pneumonia 5.72 and 3.89 times, respectively.

Myocardial damage is associated with the severity and prognosis of the disease in COVID-19 patients (16). In a study, it was conducted on hospitalized patients with COVID-19 diagnosis, troponin-T and NT-pro-BNP levels were found to be significantly higher in patients who died when compared to survivors (17). Selçuk et al. (18) retrospectively analyzed 137 hospitalized patients diagnosed with COVID-19 without heart failure in two groups; mortal and surviving. In multivarite analysis, age, NT-pro BNP, troponin-I, leukocyte, and creatinine levels were associated with in-hospital mortality.

In the ROC analysis, they found the value of NT-pro-BNP predicted in-hospital mortality as 260 ng/L reflecting a sensitivity of 82%, a specificity of 93% (AUC: 0.86; 95% confidence interval: 0.76-0.97) (18).

In the present study, when compared to recovery/stabilization group, it was found that the cardiovascular disease, troponin-T, and pro-BNP levels was significantly higher in patients who progressed and had a mortal. It was determined that troponin-T, pro-BNP and NLR are independently associated with progression in ROC analysis, and that these biomarkers can be used as prognostic factors.

Study Limitations

The study had a narrow design. Larger multicenter studies are needed in this respect. The study was conducted on the data that were obtained in the period when there was no COVID-19 vaccine anywhere in the world. For this reason, no comment could be made on the positive effects of vaccination on the course of the disease and mortality.

Conclusion

Identifying potential risk factors that predict the course of the disease has great importance in reducing morbidity and mortality. We believe that identifying the risk factors that predict the progression of the disease will make a significant contribution to patient-based follow-up and treatment decisions, and, to reducing morbidity and mortality.

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Ethics

Ethics Committee Approval: All procedures performed in studies involving human participants were in accordance with the national ethical standards and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards. The study was approved by the Ethics committee of University of Health Sciences Türkiye, Dr. Suat Seren Chest Disease and Surgery Training and Research Hospital, and by the Turkish Ministry of Health, COVID-19 Scientific Research Evaluation Committee (approval date/no: 22.07.2020/49109414-604.02).

Informed Consent: The study was designed retrospectively.

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Authorship Contributions

Surgical and Medical Practices: F.D.Ü., G.P., D.S.U., Concept: F.D.Ü., G.K., A.A., Design: F.D.Ü., G.P., A.A., E.Y., F.G., Data Collection or Processing: F.D.Ü, G.K., G.P., D.S.U., A.A., E.Y., F.G., Analysis or Interpretation: F.D.Ü., G.K., G.P., Literature Search: F.D.Ü., G.K., D.S.U., E.Y., F.G., Writing: F.D.Ü., G.K.

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