Turk Thorac J 2021; 22(3): 190-198 DOI: 10.5152/TurkThoracJ.2021.21025

Original Article

Can the Usage of the Chest X-Ray Scoring During Hospitalization in Patients with COVID-19 Predict the Severity of the Disease?

Selma Aydoğan Eroğlu[1], Zeynep Çagavi[2], Tekin Yıldız[1], Zuhal Karakurt[1], On behalf of COVID Interest Group

[1]Department of Chest Diseases, Istanbul Sureyyapasa Chest Diseases and Thoracic Surgery Training and Research Hospital, University of Health Sciences, İstanbul, Turkey
[2]Department of Radiology, Sancaktepe Prof. Dr. IlhanVarank Training and Research Hospital, İstanbul, Turkey

Cite this article as: Aydoğan Eroğlu S, Çagavi Z, Yıldız T, Karakurt Z. COVID Interest Group. Can the usage of the chest X-ray scoring during hospitalization in patients with COVID-19 predict the severity of the dısease? *Turk Thorac J.* 2021; 22(3): 190-198.

Abstract

OBJECTIVE: The prevalence of radiological involvement is considered a poor prognostic factor for coronavirus disease 2019 (COVID-19). In our study, we aimed to investigate the threshold value of the chest X-ray (CXR) score, which would require the patient to be transferred to the intensive care unit (ICU) through scoring the CXR of COVID-19 patients receiving in-patient treatment.

MATERIAL AND METHODS: The patients that tested positive for COVID-19 on the basis of the polymerase chain reaction (PCR) test, who was hospitalized in our hospital between the dates of March 15 and May 30, 2020, were included in the study. The CXRs of these patients taken during hospitalization were scored. The threshold value of the CXR score of the patients transferred to the ICU was calculated. Patients were grouped according to the threshold value of the CXR score, and demographic data and other recorded parameters were compared.

RESULTS: A total of 301 patients were included in this retrospective cross-sectional study. It was determined that finding of a CXR score threshold value of 5 or above during hospitalization predicted a transfer to the ICU with 90% sensitivity and 80% specificity. The use of broad-spectrum antibiotics, the laboratory parameters (leukocyte, neutrophil, C-reactive protein (CRP), procalcitonin, troponin, D-dimer, ferritin), and rate of transfer to ICU were found to be significantly higher in the group with a CXR score of 5 and above, compared to the group with CXR score below 5 ($P < .001$ in each).

CONCLUSION: Finding high CXR scores during hospitalization due to COVID-19 may act as a warning in terms of the severity of the disease. It may be beneficial to examine the chest X-ray images during hospitalization with utmost care and take these images into account.

KEYWORDS: Score, intensive care, chest X-ray
Received: *February 8, 2021* ***Accepted:*** *March 19, 2021*

INTRODUCTION

COVID-19 (coronavirus disease 2019), which first appeared in the city of Wuhan in China in December 2019 and was later named as severe acute respiratory syndrome coronavirus 2 (SARS-COV-2) by the International Virus Committee, spread all over the world in a short period of time and was declared as a pandemic by the World Health Organization (WHO) on March 11, 2020.[1,2] COVID-19 has become one of the most important causes of morbidity and mortality all across the world within the period elapsed since the first confirmed case. As of January 5, 2021, 1.8 million people died in the world for reasons associated with COVID-19.[3]

Studies conducted on COVID-19 so far have shown that advanced age, comorbidities, male gender, and certain laboratory parameters are associated with worse prognosis along with widespread radiological involvement.[4,5] In most of these studies, the relationship between the severity of radiological involvement and disease severity and prognosis was determined using thorax computed tomography (CT).[6-9] Thorax CT may not be immediately available in every hospital, and it may pose a risk in terms of cross-contamination. For this reason, a chest X-ray (CXR) may be preferable at certain times as it is a more practical, easily accessible, and reproducible form of medical examination, despite its lower sensitivity in the diagnosis of COVID-19. However, there is not a sufficient number of studies in which the relationship between CXR and disease severity was investigated.[10,11]

The aim of this study is to investigate if the score of the CXR during hospitalization of COVID-19 patients is related to patients' laboratory parameters, treatments, and their need for intensive care.

MATERIAL AND METHODS

The ethics committee approval for the study was obtained from the scientific committee of our hospital, and the required permit was obtained from the Ministry of Health (May 14, 2020/116.2017.164). The study was designed as a retrospective

Corresponding author: Selma Aydoğan Eroğlu, e-mail: selmaaydogan@hotmail.com

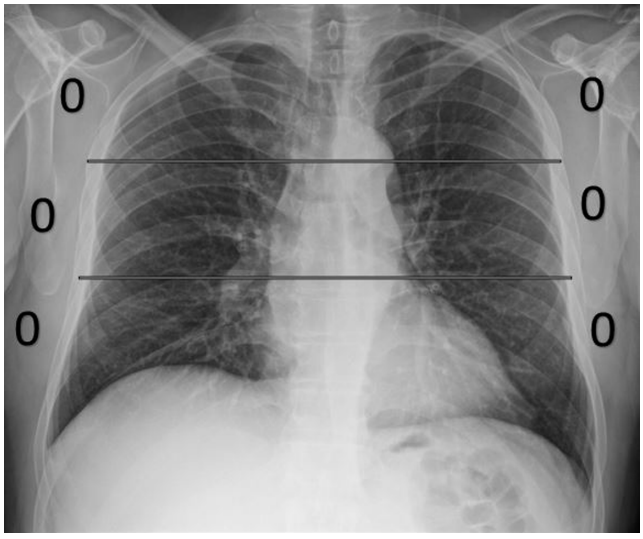

Figure 1. Example of the chest X-ray (CXR) scoring system in a patients with coronavirus disease 2019 (COVID-19) pneumonia. CXR score: 0.

observational cross-sectional study. Due to the retrospective nature of the study design, informed consent was not obtained. Patients that were diagnosed with COVID-19 on the basis of nasopharyngeal swab polymerase chain reaction (PCR)(+) results and who were hospitalized between the dates of March 15, 2020, and May 30, 2020, were included.

Research Inclusion Criteria

Being over 18 years of age and having been diagnosed with COVID-19 on the basis of nasal/oropharyngeal swab PCR (+) results and having received in-patient treatment in the pulmonology service.

Research Exclusion Criteria

An abnormal CXR was observed before the COVID-19 diagnosis, with a known medical condition, such as lung cancer, interstitial lung diseases, pleurisy, atelectasis, or pneumothorax, extensive-stage malignant diseases, and hospitalization or receiving COVID-19 treatment in another clinic.

CXRs during hospitalization were scored independently by a radiologist and a pulmonologist, both with at least 10 years of experience. A consensus was reached in cases where the radiologist and the pulmonologist disagreed in scoring, following a reevaluation. The CXR was scored by modifying the Brixia score.[12]

Modified Brixia Score

In accordance with the Brixia score, each lung was divided into 3 zones resulting in a total of 6 zones for both lungs, namely the region between the apex of the lung and the upper border of the hilus, which was defined as the upper zone, the region between the upper and lower borders of hilus line, which was defined as the middle zone, and the region between the lower border of the hilus and the lower border of the lung, which was defined as the lower zone.[12] (Figure 1). In respect of each zone, a score of 0 point meant that there is no lung involvement; a score of 1 point meant that there are only interstitial infiltrates; a score of 2 points meant that there are both interstitial and alveolar infiltrates but interstitial infiltrates are more prominent in the foreground; and a score of 3 points meant that there are both interstitial and alveolar infiltrates but alveolar infiltrates are more prominent in the foreground.[12] One point was added to the score for each zone that was determined as explained above in the event meant that the CXR involvement rate was more than 50% since the CXR involvement rate is not taken into account in the Brixia score. As a result, each CXR has scored over 18 + 6 points, a maximum of 24 points (Figures 1-3).

Study Groups

Patients were divided into 2 according to CXR, and the cut-off value was obtained by the receiver operating characteristic (ROC) curve of intensive care unit (ICU) demand (Figure 4).

Data

Demographic information (age, gender) and laboratory values of the patients were acquired from the hospital data processing system. In addition, comorbidities of the patients, used treatments, discharge status, or referral status to the ICU were also noted.

Statistical Analysis

The Statistical Package for Social Sciences version 20.0 software (IBM Corp.; Armonk, NY, USA). Patients' demographics and all clinical data were summarized using descriptive analysis. Student's *t*-test used for continuous variables (i.e., age, hemogram values, biochemistry values, and C-reactive protein [CRP]) showed that they were distributed normally in both groups. The results obtained from the Student's *t*-test were reported as mean ± standard deviation (S.D.). In the event that the groups were distributed non-normally, the nonparametric Mann–Whitney *U* test was used, and the results obtained were reported as median and interquartile

Main Points

- Scoring of the modified Brixia CXR as 5 and above during hospitalization may be associated with severe disease status.
- Those patients should be transferred to the ICU early.
- CXR scores during hospitalization may enable us to have a prediction about the severity of the Covid-19 disease.

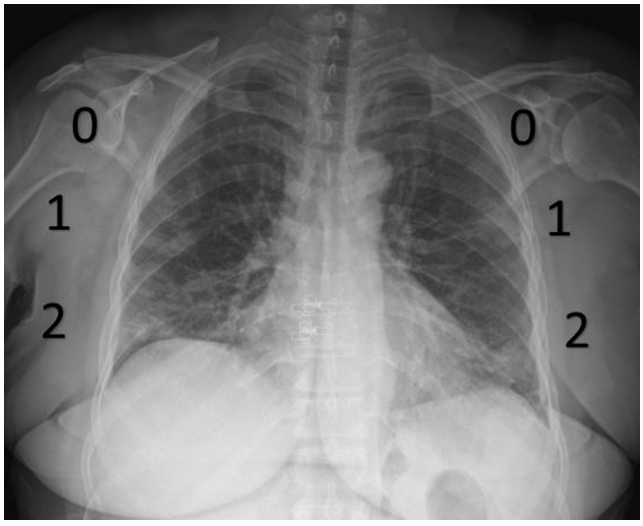

Figure 2. Example of the chest X-ray (CXR) scoring system in patients with coronavirus disease 2019 (COVID-19) pneumonia. CXR Score: 6.

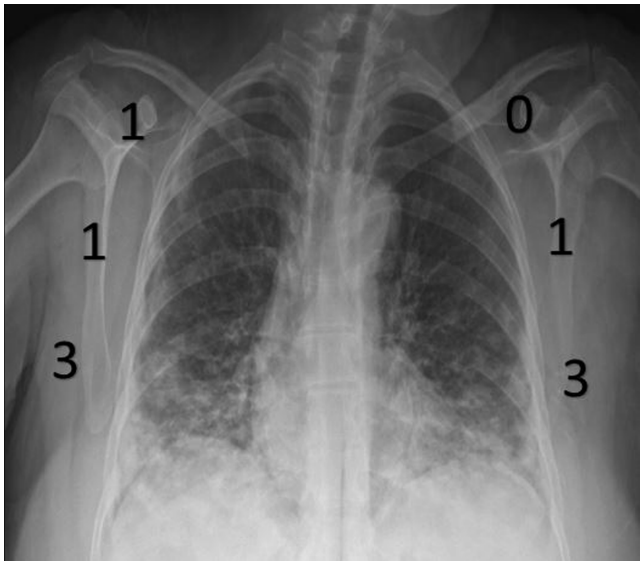

Figure 3. Example of the chest X-ray (CXR) scoring system in patients with coronavirus disease 2019 (COVID-19) pneumonia. CXR Score: 9.

range. Dichotomous values (gender and presence of comorbid diseases) were compared using the chi-squared test. If *n* was below 5, the Fisher's exact test was used, and values were reported as numbers and percentages. The ROC curve and the area under the ROC curve (AUC), and inflammatory markers (i.e., CRP, neutrophil to lymphocyte ratio [NLR], percent of lymphocyte), lactate dehydrogenase [LDH] were used to determine the optimal cut-off values in order to define the poor prognostic CXR scores (during the follow-up period after having required ICU treatment). The correlation was done by Spearman's rho test for CXR score and the inflammatory markers on the day of hospital admission in patients with COVID-19. *P* values of less than 0.05 were accepted as statistically significant.

RESULTS

A total of 338 patients diagnosed with COVID-19 hospitalized during the period that followed the criteria were included in the study (Figure 4). The patients' median (25%-75%) age was determined as 52 years (40-62). The CXR scores of the patients were non-normally distributed, and the median CXR score was determined as 4 (2-6). Of the 301 patients, 39 patients had to be transferred to ICU after hospitalization. The median CXR scores of the patients hospitalized in the pulmonology service and transferred to the ICU (25-75%) were calculated as 3 (2-6) and 9 (7-17), respectively ($P < .001$).

The threshold value of the ROC curve modified Brixia CXR score for patients that had to be transferred to ICU was calculated as 5 with 90% specificity and 80% sensitivity (AUC: 0.93 [CI 95%, 0.89-0.97] $P < .001$) (Figure 5). The cases were divided into 2 groups according to the threshold value of the modified Brixia CXR score. Accordingly, patients with a modified Brixia CXR score below 5 were included in the first group, and the ones with a modified Brixia CXR score of 5 and above were included in the second group. The ICU hospitalization rate was found as 27.15 (95% CI: 8.12-90.76) ($P < .001$) in COVID-19 patients ($n = 185$, 61.5%) included in the second group.

The demographic data, comorbidities, complete blood count (CBC), and biochemistry results of both groups were compared (Table 1). Diabetes mellitus (DM) ($P < .001$),

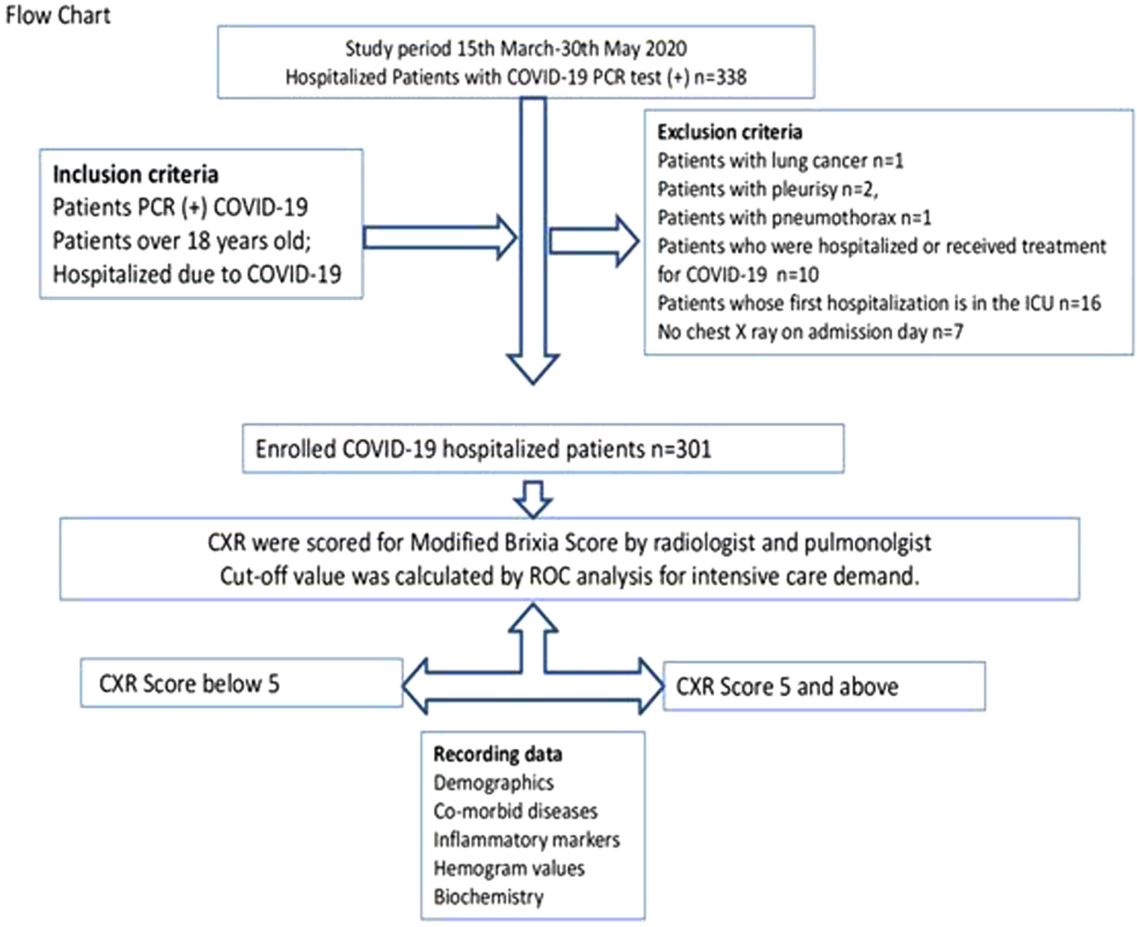

Figure 4. Flow chart.

hypertension (HT) ($P < .003$), and coronary artery disease (CAD) ($P < .04$) were found to be significantly higher in the second group compared to the first group. Additionally, leukocyte, platelet, and neutrophil counts were found to be significantly higher in the second group compared to the first group, contrary to the lymphocyte percentage, which was found to be significantly higher in the first group compared to the second group ($P < .001$ in each group) (Table 1). The

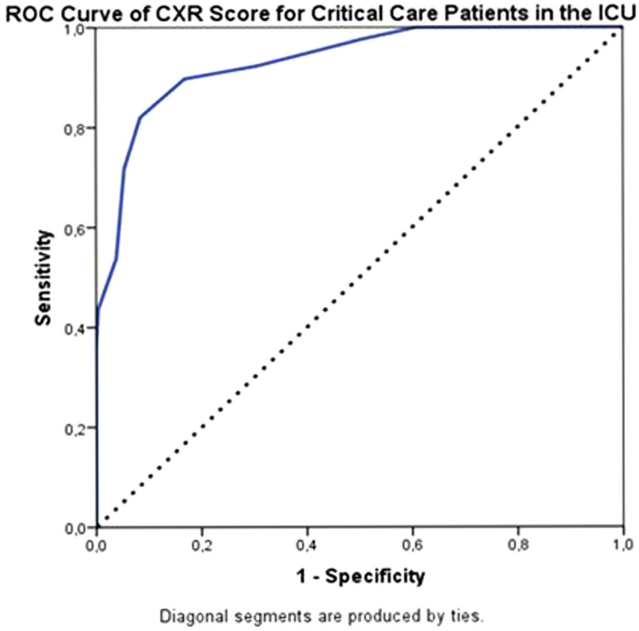

Figure 5. Receiver operating characteristic (ROC) curve of the chest X-ray (CXR) scores of the coronavirus disease 2019 (COVID-19) patients hospitalized in the pulmonology service and transferred to the intensive care unit (ICU). The area under the curve (AUC) is 0.93 (95% CI, lower limit: 0.89, upper limit: 0.97) ($P < .001$).

Table 1. Comparison of Demographic Data and Laboratory Parameters According to Modified Brixia Chest X-Ray (CXR) Score (<5 and ≥5)

	All *n* = 301		CXR Score <5 *n* = 185		CXR Score ≥ 5 *n* = 116		
Values	***N***	**Values**	***N***	**Values**	***N***	**Values**	***P***
Male (*n*, %)	163	54.2%	92	49.7	71	61.2	.052
Age (*n*, years)	301	52 (40-62)	185	48 (35-58)	116	56 (48-70)	<.001
Comorbid diseases							
Hypertension (n, %)	71	23.6%	33	17.8%	38	32.8%	.003
Diabetes Mellitus (n, %)	55	18.3%	21	11.4%	34	29.3%	<.001
COPD (n, %)	12	4.0%	6	3.2%	6	5.2%	.41
Coronary Heart Diseases (n, %)	22	7.3%	9	4.9%	13	11.2%	.04
Asthma (n, %)	24	8.0%	13	7.0%	11	9.5%	.44
Congestive heart failure	6	2.0%	3	1.6%	3	2.6%	.68
Hemogram values							
Leucocytecount,109 L	301	5.8 (4.6-7.3)	185	5.5 (4.2-6.6)	116	6.6 (5.5-8.0)	.001
Erythrocytecount, 1012 L	301	4.7 (4.4-5.1)	185	4.7 (4.5-5.1)	116	4.6 (4.3-5.0)	.011
Hemoglobin, g/dL	300*	13.2 (12.3-14.4)	185	13.3 (12.4-14.6)	115	13.2 (12.0-14.2)	.082
Hematocrit, %	301	40.2 (37.1-43.0)	185	40.7 (37.7-43.5)	116	39.6 (36.7-42.3)	.032
MCV, fL	301	86.0 (83.2-89.0)	185	85.7 (83.1-89.3)	116	86.3 (83.5-89.4)	.56
Platelet count,109 L	301	252 (202-353)	185	242 (197-303)	116	302 (209-424)	<.001
Lymphocytecount, 109 L	301	1.45 (1.12-1.84)	185	1.49 (1.20-1.86)	116	1.30 (1.00-1.78)	.012
Lymphocyte, %	301	28.01 (21.1-35.2)	185	30.9 (24.47-37.15)	116	23.17 (16.18-29.59)	<.001
Eosinophilcount, 109 L	301	0.06 (0.02-0.14)	185	0.06 (0.02-0.14)	116	0.07 (0.01-0.14)	.55
EOS, %	301	1.29 (0.45-2.52)	185	1.36 (0.53-2.74)	116	1.17 (0.25-2.34)	.086
Neutrophilcount, 109 L	301	3.85 (2.88-5.15)	185	3.33 (2.57-4.65)	116	4.74 (3.59-5.96)	<.001
NEU, %	300*	68.13 (60.62-76.70)	184	64.46 (56.44-73.45)	116	74.01 (67.24-82.45)	.001
Biochemistry							
Urea, mg/dL	301	28 (23-38)	185	27 (22-34)	116	35 (27-44)	<.001
Creatinine, mg/dL	300*	0.70 (0.59-0.85)	184	0.68 (0.56-0.83)	116	0.73 (0.63-0.86)	.052
Sodium, mmol/L	299*	139 (137-140)	183	139 (137-140)	116	139 (136-140)	.51
Chloride, mmol/L	289*	101 (99-104)	177	102 (99-104)	112	99 (98-104)	.021
Potassium, mmol/L	296*	4.3 (4.0-4.7)	182	4.3 (4.0-4.6)	114	4.4 (4.1-4.8)	.019
Bilirubine (direct),mg/dL	273*	0.17 (0.14-0.20)	158	0.16 (0.13-0.2)	115	0.19 (0.14-0.23)	<.001
Bilirubine (Total), mg/dl	271*	0.60 (0.47-0.81)	156	0.58 (0.46-0.77)	115	0.63 (0.51-0.87)	.040
ALT, U/L	299*	30 (18-46)	183	28 (16-42)	116	35 (22-55)	.001
AST, U/L	300*	37 (27-55)	184	33 (26-42)	116	51 (34-73)	<.001

*Analyses were done by excluding cases with missing data and this was shown in all tables in the manuscript as signed with an asterisk. ALT, alanineaminotransferase; AST, aspartate aminotransferase; LDH, lactate dehydrogenase; GGT, gamma-glutamyl transferase; MCV, mean corpuscular volume.

percentage of neutrophils was found to be significantly higher in the second group compared to the first group, whereas the erythrocyte and lymphocyte counts and the hematocrit percentage were found to be significantly higher in the first group compared to the second group ($P = .001$, $P < .01$, $P = .012$, $P < .05$, respectively) (Table 1). Urea, potassium, direct bilirubin, total bilirubin, alanine aminotransferase (ALT), aspartate aminotransferase (AST), LDH, and gamma-glutamyl transferase (GGT) levels were found to be significantly higher in the second group compared to the first group ($P < .001$, $P = .019$, $P < .001$, $P = .040$, $P = .001$, $P < .001$, $P < .001$, $P < .001$, respectively) (Table 1).

The treatments received by, and the inflammatory markers of, both groups were compared (Table 2). Use of favipiravir, oseltamivir, another antibiotic added to azithromycin, or of a broad-spectrum antibiotic other than azithromycin was found to be significantly higher in the second

Table 2. Comparison of Treatments and Inflammatory, Thrombotic and Cardiac Markers According to Modi Brixia Chest X-Ray (CXR) Score (<5 and ≥ 5)

	All *n* = 301		CXR score <5 *n* = 185		CXR score ≥ 5 *n* = 116		*P*
Values	***N***	**Values***	***N***	**Values**	***N***	**Values***	
Used treatment							
Hydroxychloroquine (n, %)	300	99.7%	184	99.5%	116	100.0%	>.99*
Oseltamivir (n, %)	220	73.1%	122	65.9%	98	84.5%	<.001
Azithromycin (n, %)	275	91.4%	166	89.7%	109	94.0%	.20
Favipiravir (n, %)	63	20.9%	11	5.9%	52	44.8%	<.001
Antibiotic additional to Azithromycin (n, %)	90	29.9%	34	18.4%	56	48.3%	<.001
NLR	301	2.66 (1.85-3.99)	185	2.27 (1.64-3,06)	116	3.59 (2.4 4-4.94)	<.001
D-dimer, µg/L	251*	0.60 (0.40-1.10)	154	0.5 (0.3-0.8)	97	0.9 (0.6-1.3)	<.001
Troponin, µg/L	261*	3.0 (1.7-6.4)	152	2.3 (1.5-4.2)	109	5.7 (2.8-9.1)	<.001
CRP, mg/dL	292*	22 (6-69)	178	9 (3-32)	114	62 (16-92)	<.001
Procalcitonin, µg/L	248*	0.068 (0.049-0.116)	146	0.057 (0.042-0.08)	102	0.105 (0.061-0.18)	<.001
Ferritin, mL/ng	246*	148 (61-348)	149	92.1 (48,6-227.4)	97	286.0 (139.4-576.3)	<.001
PT, %	301	96 (83-101)	185	96 (82-103)	116	96 (86-100)	.77
INR	254*	1.03 (0.99-1.11)	149	1.03 (0.98-1.12)	105	1.03 (1.00-1.11)	.42

*Analyses were done by excluding cases with missing data and this was shown in all tables in the manuscript as signed with an asterisk. NLO, neutrophiltolymphocyteratio; CRP, C-reactive protein; PT, prothrombin time; INR, international normalized ratio.

group compared to the first group ($P < .001$ in each group) (Table 2). D-dimer, troponin, NLR, procalcitonin, CRP, and ferritin levels were found to be significantly higher in the second group compared to the first group ($P < .001$ in each group) (Table 2).

The correlation between the modified Brixia CXR score and the cardiac and inflammatory markers and LDH was examined (Table 3). A positive correlation was found between the CXR score and the leukocyte and neutrophil percentages, D-dimer, CRP, procalcitonin, troponin, ferritin, LDH levels, and NLR, and the highest correlation among the foregoing was found with the LDH levels. On the other hand, a negative correlation was found between the CXR score and the lymphocyte levels ($P < .001$).

Table 3. The Correlations of Modified Brixia Chest X-Ray (CXR) Score and İnflammatory Markers on Admission to the Hospital

Variables	***R***	***P***
Leucocyte	0.351	<.001
Lymphocyte percent	−0.349	<.001
Neutrophil percent	0.443	<.001
Eosinophil percent	−0.108	.062
D-dimer	0.405	<.001
Troponin	0.442	<.001
C-reactive protein	0.530	<.001
Pro-calcitonin	0.420	<.001
LDH	0.502	<.001
Ferritin	0.473	<.001
Neutrophil to lymphocyte ratio	0.410	<.001

Correlation analysis of nonparametric Spearman's rho test.

DISCUSSION

In the current study, the CXR taken during hospitalization of each COVID-19 patient was scored according to modified Brixia scoring, and the threshold value for ICU transfer was found as 5 and above. It has been demonstrated that in patients with a CXR score of 5 and above during hospitalization, the severity of the disease and ICU transfer rate increased significantly in the following days, and the odds ratio for ICU need was 27 times higher. Additionally, it was determined that mean age and comorbidities (HT, DM, CAD) were higher in the second group that includes the patients with a CXR score of 5 and above compared to the first group that includes the patients with a CXR score below 5. Additionally, the use of ribavirin, favipiravir, and broad-spectrum antibiotics were also determined to be higher in the second group compared to the first group. On the other hand, leukocyte, neutrophil, CRP, D-dimer, procalcitonin, troponin, LDH, ferritin levels were found to be significantly higher in the second group compared to the first group, with the exception of lymphocyte levels which were found to be significantly higher in the first group compared to the second group.

It has been demonstrated that as a result of our study, the rate of transfer to ICU increases significantly in patients with a CXR score of 5 and above. A thorough review of the literature revealed only one other study. The patients were divided

into groups according to their CXR scores and investigated in terms of whether there was a difference between the groups regarding the rate of transfer to ICU or disease severity. In that study, patients were divided into 2 groups in terms of their CXR scores, which were calculated based on a scoring system over a total of 6 points. As a result, patients who were found to have low CXR scores (0-1) were categorized under one group, and patients who were found to have high CXR scores (2-6) were categorized under another group. These groups were then compared in terms of whether there was a difference between their demographic data, comorbidities, hospitalization rate, and rate of transfer to the ICU.[13] The risk of hospitalization in patients with a CXR score of 2 and above was found to be significantly higher compared to the patients with a CXR score below 2. Additionally, the risk of invasive ventilation in patients with a CXR score of 3 and above was found to be significantly higher compared to patients with a CXR score below 3.[13] In another study, the patients were divided into 2 groups on the basis of whether there was any involvement in their CXRs and were then compared in terms of whether there was a difference between their laboratory data, comorbidities, and complaints. However, they were not compared in terms of disease severity, which was a parameter investigated within the scope of this study.[14] On the other hand, in several other studies conducted by radiologists, the infiltration characteristics present in the patients' CXRs were examined and scored. It was investigated in these studies whether there was a correlation between the severity of the disease (oxygen need, rate of transfer to ICU, or mortality rate) and the CXR score.[10,11,15] In one such study by Yasin et al., including COVID-19 PCR (+) patients, the scored CXRs of these patients were over a total of 8 points, a CXR score between 6 and 8 points was found to be associated with mortality.[11] In another such study by Cozzi et al., conducted on 234 patients that were admitted to the emergency ward, the scored CXRs of these patients were over a total of 48 points calculated using a scoring system called RALE (radiographic assessment of lung edema), and they demonstrated that a RALE score of 15 points or more was associated with an increased risk of ICU admission.[10] In another study conducted with 158 patients, whose CXRs were scored using RALE, a CXR score of 5 and above was found to be associated with serious illness and poor prognosis (ICU admission, intubation, death).[15] The results of this study are compatible with the results of all the aforementioned studies. In these studies, detailed laboratory data, comorbidities, and treatments patients received were not evaluated.[10,11,15]

In our study, the incidence of HT, DM, and CAD was determined to be significantly higher in patients with a modified Brixia CXR score of 5 or more. In comparison, in a very comprehensive study that was conducted in China, patients were divided into 2 groups on the basis of the severity of disease, as the group of patients whose condition is serious and the group of patients whose condition is not serious, which was determined according to oxygen saturation, PaO_2 (partial pressure arterial oxygen)/FiO_2(fraction of inspired oxygen) ratio and respiratory rate.[16] In the said study, HT, DM, and CAD were found to be significantly higher in the group of patients whose condition is serious.[16] In another study that was also conducted in China, in which the patients with COVID-19 receiving in-patient treatment in the ICU were investigated, it was found that 4 comorbidities, including HT, DM, CAD, and cerebrovascular disease, were observed more frequently in patients hospitalized in the ICU.[17] On the other hand, there are a few studies as a result of which no relationship was detected between the radiological score or the disease severity and comorbidities,[18] which is contrary to the findings of this study. The results of this study are consistent with the results of the first 2 studies.

It has been demonstrated in previous studies that the prognosis of COVID-19 worsens with the male gender and increasing age.[16,19] In addition, it was demonstrated in some studies that the CXR score also worsens with the male gender and increasing age.[13,20] In a study conducted on 783 COVID-19 patients in Italy, the age, gender, and highest CXR scores of the patients were recorded, and a significant correlation was found between the CXR score and age. In addition, the CXR scores of men between the ages of 50 and 80 were found to be significantly higher than the CXR scores of women of the same age range.[20] In another study conducted with young adults between the ages of 31 and 45, patients were divided into 2 groups on the basis of their CXR scores. The ones with a CXR score of 0-1 (low score) were included in one group, and the ones with a CXR score of 2-6 (high score) were included in the other group. It was observed that the patients of male gender and older patients had higher CXR scores compared to the patients of female gender and younger patients.[13] In parallel with the results of the above study, it was also shown in this study that the patients who had a CXR score of 5 or more were older. It was also observed that most of the patients who had a CXR score of 5 or more were of the male gender, even though the difference between the CXR scores of patients of different genders was borderline significant.

In our study, a significant decrease was detected in the lymphocyte, eosinophil, and hematocrit values of in-patients with high CXR scores, contrary to the leukocyte, neutrophil, NLR, platelet, CRP, D-dimer, procalcitonin, and troponin values, in which a significant increase was observed. In particular, CRP, procalcitonin, NLR, neutrophil, and D-dimer values were found to be higher than normal. Despite the fact that there was a significant difference between both groups in other parameters, the laboratory values of the patients in both groups were within normal limits. In addition to the studies conducted to predict the severity of the disease on the basis of laboratory parameters, there are also many meta-analyses in which many studies, including a very large number of cases, have been reviewed.[21-25] It has been shown in these meta-analyses that high leukocyte, neutrophil, procalcitonin, D-dimer, and troponin levels, as well as low lymphocyte levels, are associated with poor prognosis in COVID-19.[21-23] High levels of leukocyte, neutrophil, NLR, procalcitonin are important as indicators of systemic inflammation and secondary bacterial infections. The level of ferritin, as an acute-phase reactant, is also expected to rise. The elevation in D-dimer and troponin levels is another parameter that indicates disease severity as an indicator of increased intravascular coagulation and myocardial damage. Additionally, it was also found in our study that the LDH, urea,

AST, ALT, GGT, and bilirubin values were higher in the group of patients with a CXR score of 5 and above, compared to the group of patients with a CXR score of less than 5. Especially, AST and LDH values were found to be higher than normal levels. The elevation in these parameters is also important, as these parameters are among the markers that indicate tissue and organ damage. There are studies and meta-analyses in which it has been demonstrated that these markers elevate in severe COVID-19 cases.[24,26] The results of this study are in line with the results of all these aforementioned studies. Marcello et al. have found a positive correlation between the CXR score and the CRP and LDH values, and a negative correlation with oxygen saturation.[27] In another study, a positive correlation was found between the CXR score and the CRP and LDH levels, whereas a negative correlation was found with the lymphocyte count.[28] In our study, a positive correlation was detected between the modified Brixia CXR score and the inflammatory and cardiac markers (leukocyte, neutrophil, procalcitonin, CRP, ferritin, D-dimer, and troponin levels) and the LDH level, whereas a negative correlation was found with the lymphocyte count. It was the LDH level that showed the highest correlation with the CXR score. Unexpectedly, it was the group of patients with a CXR score of 5 and above that was found to have a higher number of platelets. Nevertheless, the platelet counts were within normal limits in both groups.

In our study, the use of oseltamivir, favipiravir, and a broad-spectrum antibiotic other than azithromycin was determined to be significantly higher in the group with a CXR score of 5 and above. During the first months, hydroxychloroquine was administered to the patients with a mild course, in accordance with the COVID-19 guidelines in our country, whereas favipiravir was administered to the patients with hypoxia and with a more severe course or with progressed CXR despite the hydroxychloroquine treatment. Despite the fact that the patients were not referred to ICU during the period the study was conducted, administering favipiravir treatment was a parameter, which alone indicated the severity of the disease. Additionally, azithromycin treatment was administered to all patients who were found to have pneumonia on the basis of CT, taking the atypical pneumonia factors into consideration. In cases where the presence of secondary bacterial infection was considered due to prominent leukocytosis and elevated CRP levels and the intense consolidation appearance in CT, another broad-spectrum antibiotic was administered.

The first limitation of this study is that it was conducted as a single-centered and retrospective study. Nevertheless, the results obtained on the basis of our data are of the nature that would assist physicians during the pandemic period. Another limitation of this study is that a nasal swab test for influenza could not be administered to the patients included in this study. The very first COVID-19 case in our country was detected during a period when the rate of influenza was on the decline. Nonetheless, the Ministry of Health recommended the use of oseltamivir during the months of March and April in its COVID-19 guide. Patients were administered the COVID-19 and influenza treatments concurrently. There were no patients in this study who had both COVID-19 and influenza since the first COVID case in our country was not seen earlier than March 11, and even if there were any cases that were missed, they are thought to be limited in number.

In conclusion, it has been demonstrated that as a result of this study, scoring of the modified Brixia CXR as 5 and above during hospitalization is associated with severe disease status as determined by worsening laboratory results and transfer to the ICU. Despite the fact that the clinical course of patients hospitalized due to COVID-19 generally becomes clear in the forthcoming days of the disease, CXR scores during hospitalization may enable us to have a prediction about the severity of the disease.

Ethics Committee Approval: This study was approved by Ethics committee of University of Health Sciences Istanbul Sureyyapasa Chest Diseases and Thoracic Surgery Training and Research Hospital (Approval No: 14.05.2020 /116.2017.164).

Informed Consent: Verbal/Written informed consent was obtained from the patients who agreed to take part in the study.

Peer Review: Externally peer-reviewed.

Author Contributions: Supervision – S.A.E., T.Y., Z.K.; Design – S.A.E., T.Y., Z.K.; Resources – S.A.E.; Materials – S.A.E., S.C., COVID Interest Group.; Data Collection and/or Processing – S.A.E.; Analysis and/or Interpretation – S.A.E., T.Y., Z.K.; X.X.; Writing Manuscript – S.A.E., T.Y., Z.K., COVID Interest Group.; Critical Review – S.A.E., T.Y., Z.K.

COVID Interest Group: Ayşem Öztin Guven, Reyhan Yıldız, Elif Yıldırım, Özlem Soğukpınar, Sümeyye Bekir, Lale Sertçelik, Baran Gündoguş, Murat Kavas, Meltem Agca, Gül Erdal Dönmez, Makbule Akbay, Feride Yaman, Dilem Anıl Tokyay, Fatma Özbaki, Sibel Boğa, Tülin Sevim, İpek Ozmen, Huriye Berk Takir, Dildar Duman, Nagihan Durmus Kocak, Ülkü Aka Aktürk, Hilal Altinoz, Dilek Ernam, Selahattin Oztaş, Tülay Törün, Özlem Oruç, Eylem Tuncay, Sinem Güngör, ÖzlemYazıcıoğlu Moçin, Emine Aksoy, Birsen Ocaklı, Hakan Günen, Sibel Arınç, Nalan Adıguzel, Gökay Güngör.

Conflict of Interest: The authors have no conflict of interest to declare.

Financial Disclosure: The authors declared that this study has received no financial support.

REFERENCES

1. World Health Organization. Director-General's opening remarks at the media briefing on COVID-19 - 11 March 2020. Accessed April 1, 2020; March 11, 2020. (available at: https://www.who.int/dg/speeches/detail/who-director-general-sopening-remarks-at-the-media-briefing-on-covid-19---11-march-2020)
2. Coronaviridae Study Group of the International Committee on Taxonomy of Viruses. The species severe acute respiratory syndrome-related coronavirus: Classifying2019-nCoV and naming it SARS-CoV-2. *Nat Microbiol*. 2020;5:536-544.
3. World Health Organization (WHO). *COVID-19 Weekly Epidemiological Update*; January 5, 2021. (available at: https://www.who.int/publications/m/item/weekly-epidemiological-update---5-january-2021)
4. Xu J, Yang X., Yang L. et al. Clinical course and predictors of 60-day mortality in 239 critically ill patients with COVID-19: A multi center retrospective study from Wuhan, China. *Crit Care*. 2020;24(394):2-11. (doi: https://doi.org/10.1186/s13054-020-03098-9)

5. Ruan Q, Yang K, Wang W, Jiang L, Song J. Clinical predictors of mortality due to COVID-19 based on an analysis of data of 150 patients from Wuhan, China. *Intensive Care Med*. 2020;46(5):846-848. [CrossRef]
6. Francone M, Iafrate F, Masci GM et al. Chest CT score in COVID-19 patients: Correlation with diseases everity and short-term prognosis. *Eur Radiol*. 2020;30(12):6808-6817. [CrossRef]
7. Yang R, Li X, Liu H et al. Chest CT severity score: An imaging tool for assessing severeCOVID-19. *Radiol Cardiothorac Imaging*. 2020;2(2):e200047. [CrossRef]
8. Colombi D, Bodini FC, Petrini M et al. Well-aerated lung on admitting chest CT to predict adverse outcome in COVID-19 pneumonia. *Radiology*. 2020;296(2):E86-E96. [CrossRef]
9. Zhong L, Zhang S, Wang J et al. Analysis of chest CT results of coronavirus Disease 2019 (COVID-19) patients at first follow-up. *Can Respir J*. 2020;2020:5328267. [CrossRef]
10. Cozzi D, Albanesi M, Cavigli E et al. Chest X-ray in new coronavirus Disease 2019 (COVID-19) infection: Findings and correlation with clinical outcome. *Radiol Med*. 2020;125(8):730-737. [CrossRef]
11. Yasin R, Gouda W. Chest X-ray findings monitoring COVID-19 disease course and severity. *Egypt J Radiol Nucl Med*. 2020;51(1):193. [CrossRef].
12. Borghesi A, Maroldi R. COVID-19 outbreak in Italy: Experimental chest X-ray scoring system for quantifying and monitoring disease progression. *Radiol Med*. 2020;125(5):509-513. [CrossRef]
13. Toussie D, Voutsinas N, Finkelstein M et al. Clinical and chest radiography featuresdetermine patient outcomes in young and middle-aged adults with COVID-19. *Radiology*. 2020;297(1):E197-E206. [CrossRef]
14. Gatti M, Calandri M, Barba M et al. Baseline chest X-ray in coronavirus disease 19 (COVID-19) patients: association with clinical and laboratory data. *Radiol Med*. 2020;125(12):1271-1279. [CrossRef]
15. Kerpel A, Apter S, Nissan N et al. Diagnostic and prognostic value of chest radiographs for COVID-19 at presentation. *West J Emerg Med*. 2020;21(5):1067-1075. [CrossRef]
16. Yu C, Lei Q, Li W et al. Epidemiological and clinical characteristics of 1663 hospitalizedpatients infected with COVID-19 in Wuhan, China: A single-center experience. *J Infect Public Health*. 2020;13(9):1202-1209. [CrossRef]
17. 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):1061-1069. [CrossRef]
18. Huang C, Wang Y, Li X et al. Clinical features of patients infected with 2019 novelcoronavirus in Wuhan, China. *Lancet*. 2020;395(10223):497-506. [CrossRef]
19. Yazdanpanah Y. French COVID cohort investigators and study group. Impact on disease mortality of clinical, biological, and virological characteristics at hospital admission and overtime in COVID-19 patient. *J Med Virol*. 2020:1-3. [CrossRef]
20. Borghesi A, Zigliani A, Masciullo R et al. Radiographic severity index in COVID-19pneumonia: relationship to age and sex in 783 Italian patients. *Radiol Med*. 2020;125(5):461-464. [CrossRef]
21. Moutchia J, Pokharel P, Kerri A et al. Clinical laboratory parameters associated with severe or critical novel coronavirus disease 2019 (COVID-19): A systematic review and meta-analysis. *PLOS ONE*. 2020;15(10):e0239802. [CrossRef]
22. Bao J, Li C, Zhang K et al. Comparative analysis of laboratory indexes of severe and nonsevere patients infected with COVID-19. *Clin Chim Acta*. 2020;509:180-194. [CrossRef]
23. Tian W, Jiang W,Yao J et al. Predictors of mortality in hospitalized COVID-19 patients: A systematic review and meta-analysis. *J Med Virol*. 2020;92(10):1875-1883. [CrossRef]
24. Feng X, Li S, Sun Q et al. Immune-inflammatory parameters in COVID-19 cases: Asystematic review and meta-analysis. *Front Med*. 2020;7:301. [CrossRef]
25. Shang Y, Liu T, Wei Y et al. Scoring systems for predicting mortality for severe patients with COVID-19. Scoring systems for predicting mortality for severe patients with COVID-19. *EClinicalMedicine*. 2020;24:100426. [CrossRef])
26. Ghahramani S, Tabrizi R, Lankarani KB et al. Laboratory features of severe vs. non-severeCOVID-19 patients in Asian populations: A systematic review and meta-analysis. *Eur J Med Res*. 2020;25(1):30. [CrossRef]
27. Orsi MA, Oliva G, Toluian T et al. Feasibility, reproducibility, and clinical validity of a quantitative chest X-ray assessment for COVID-19. *Am J Trop Med Hyg*. 2020;103(2):822-827. [CrossRef]
28. Hui TCH, Khoo HW, Young BE et al. Clinical utility of chest radiography for severe COVID-19. *Quant Imaging Med Surg*. 2020;10(7):1540-1550. [CrossRef]