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TANAFFOS

Predicting Severity of Novel Coronavirus (COVID-19) Pneumonia based upon Admission Clinical, Laboratory, and Imaging Findings

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Background: The purpose of this study was to investigate the prognostic factors in hospitalized COVID-19 pneumonia patients according to the baseline clinical, laboratory, and imaging manifestations.

Materials and Methods: In this retrospective study on the SARS-CoV-2 laboratory-confirmed cases, clinical and laboratory data were collected from 156 hospitalized patients during August to October, 2020. Baseline chest CT was assessed, and the CT severity score was then calculated. Data were compared between the two groups of patients with moderate and severe/critical conditions.

Results: Of the 156 participants with the age range of 25-95 years (56.87±16.88), 70 and 86 patients were in the moderate and severe/critical groups, respectively. Most patients had typical imaging features on chest CT. Compared to the moderate group, the severe/critical group were older and were mainly suffering from underlying comorbidities. The rate of confusion on admission (P=0.008) and pulse rate≥100 (p=0.04) were significantly higher in the severe/critical group. According to the CT manifestations, consolidation, central and diffuse peripheral and central distribution, patchy/segmental morphology, crazy paving pattern, pleural effusion, aorta, and coronary artery calcification were more likely to emerge in the severe/critical group ($p<0.05$). In contrast, round/nodular morphology mainly appeared in the moderate group (p= 0.002). The chest CT severity scores were 10.24±7.91 and 6.13±4.42 in the severe/critical and moderate groups, respectively, indicating statistically significant values.

Conclusion: The clinical, laboratory, and chest CT findings can be used for the prognosis of COVID-19 pneumonia. Predicting the outcomes for the patients on admission can play a critical role in decision making.

Key words: Respiratory infections; Pneumonia; COVID-19; Prognosis

INTRODUCTION

Coronaviruses are enveloped viruses with the most extended positive ribonucleic acid genome. Under the electron microscope, the glycoprotein on the surface has a projection, which seems as a halo or corona around the virus. Rhinoviruses are the second most common cause of the common cold. Moreover, they were in charge of two critical outbreaks worldwide (namely severe acute respiratory syndrome (SARS-CoV) and the Middle East respiratory syndrome (MERS-CoV), both of which are zoonotic diseases and can be transmitted to humans in contact with animal reservoirs (1). In December 2019, there

was a deadly outbreak of mysterious pneumonia in Wuhan, China, which quickly captured the world's attention. The scientists pointed their fingers at a novel coronavirus and introduced it as a new member of this family. The virus was named severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) by the World Health Organization (WHO). COVID-19, a shortened form of Coronavirus Disease of 2019, is induced by SARS-CoV-2 (2) and spreads extremely rapidly among individuals across the globe. On March 11, 2020, the WHO announced the COVID-19 outbreak a pandemic (3). The leading cause of death among the patients infected by the virus is respiratory failure, septic shock, multiple organ failure, and cardiac arrest (4). Many studies have revealed that older age, lymphocytopenia, aggressive pulmonary radiographic infiltration, and the presence of comorbidities are associated with poor outcomes in patients (5,6). Furthermore, older age, High D-Dimer level, high lactate dehydrogenase (LDH) level, high Sequential Organ Failure Assessment (SOFA) score, cardiac injury, and hyperglycemia may increase the likelihood of in-hospital deaths (7,8). Although the reverse transcription-polymerase chain reaction (RT-PCR) test is the most common diagnostic test to detect the infected patients, many studies have documented that the sensitivity of the computerized chest tomography (CT) is higher than RT-PCR, and the patients may exhibit lung abnormalities on their chest CT regardless of the RT-PCR results. Accordingly, a chest CT is highly recommended in screening patients with typical clinical features (5,9,10). The typical features of COVID-19 pneumonia in chest imaging can be used in the early screening of highly suspected cases and even in estimating the severity and prognosis of the disease. The typical chest CT imaging illustrates Ground Glass Opacities (GGO), mixed GGO and consolidation, and vascular enlargement. Lesions are more likely to be bilateral, lower lung predominance, and have peripheral and posterior distribution (11).

This study evaluated the prognostic factors in hospitalized COVID-19 pneumonia patients regarding the clinical and laboratory findings on admission and baseline chest CT manifestations.

MATERIALS AND METHODS

This study was approved by the Ethics Committee of the Tabriz University of Medical Sciences. Informed consent was waived regarding the retrospective nature of this study since the study would bring no risk to the patients or have no effect on the subjects' rights or safety.

This retrospective single-center study on the SARS-CoV-2 laboratory-confirmed cases was conducted in the Radiology Research Center of the Tabriz University of Medical Sciences. The cases were defined as confirmed positive by RT-PCR assay of nasal and pharyngeal swab specimens if the initial test results or the repeated tests were performed on the patients with an initially negative test; however, highly suspected cases were clinically and epidemiologically positive. All admitted patients who were confirmed cases with lung involvement on the chest CT (n=156) were included in this study from August to October 2020 (Figure 1).

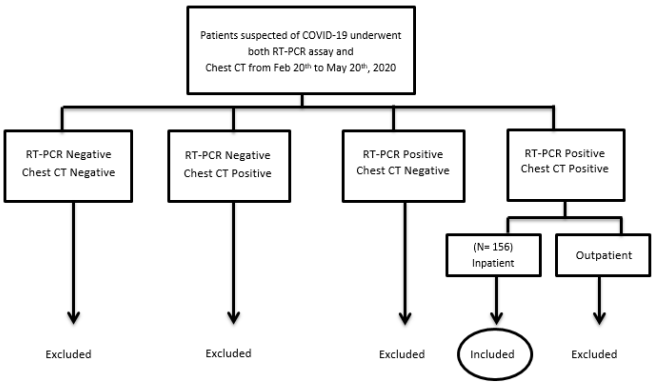

Figure 1. Flow-chart for patient inclusion.

The patients' data, including patient demographic information, epidemiologic features, clinical characteristics, and laboratory data, were collected from the hospital database at the time of admission as the symptoms of patients may vary over time during hospitalization (12). The baseline chest CT examinations were performed on admission on all patients during a deep inspiration breath-hold, with no contrast administration on a GE Bright speed

eight slice Scanner. The scanner parameters were 120 kVp, 100 mAs, and 1.35 pitch, and the images were reconstructed with a high spatial resolution algorithm with a 2.5 mm slice thickness and 1.5 mm intervals. A radiologist reviewed the chest CT scans while blinded to all clinical information and follow-up scans. For each of the patients, the images were described according to the "Fleischner Society guidelines: glossary of terms for thoracic imaging" (13). The description was as follows: Lesion density (namely GGO, consolidation, mixed GGO, and consolidation); axial distribution (namely the outer side of one-third of the lung as peripheral and the inner side of two-third of the lung as central (peribronchovascular)); morphology (namely patchy/segmental and round/nodular opacities); crazy paving pattern (i.e., interlobular and intralobular septal thickening within GGO background); vascular enlargement (i.e., dilatation of pulmonary vessels around lesions); pleural and pericardial effusion; solid nodules; lymphadenopathy; cardiomegaly (i.e., cardiothoracic ratio >50%); aorta and coronary artery calcification; and pulmonary artery diameter measured at the right branch separation level.

Moreover, the chest CT severity score (CT-SS) was calculated in this study according to Yang et al. (2020) for COVID-19, indicating the disease extension and quantifying the lung involvement (14). The score was used in this study in a similar approach and was calculated on the baseline CT scan of each patient. To estimate this score, both lungs were divided into 20 sections as follows: The general pattern of lungs consists of 18 segments (10 in the right and 8 in the left lung). Two subdivisions were added as follows: First, the posterior apical segment of the left upper lobe was divided into the apical and posterior regions. Second, the anteromedial basal segment of the left lower lobe was divided into the anterior and basal regions. Finally, the lung opacities in each of the 20 regions were subjectively marked on the chest CT by using scores '0, 1, and 2' for parenchymal opacity of 0%, <50%, or ≥50%, respectively. The CT-SS is defined as the summation of the individual scores in the 20 regions of the lungs, which may range from 0 to 40. Finally, clinical outcomes, including length of stay, intubation, discharge, and mortality rates, were gathered. Then the participants were assigned into two moderate and severe/critical groups according to the Chines clinical guidelines for COVID-19 issued by the National Health Commission (15). The patients with fever and respiratory symptoms along with pneumonia manifestations on the chest CT were assigned into the moderate group. The following criteria placed the patient in the severe/critical group: 1) shortness of breath, respiratory rate (RR) ≥30 times/min, 2) oxygen saturation ($SatO_2$) ≤93% at rest, 3) PaO_2/FiO_2 (Alveolar oxygen partial pressure / Fraction of inspiration O_2) ≤300 mmHg, 4) respiratory failure requiring mechanical ventilation, 5) shock, and 6) other organ failures requiring the Intensive Care Unit (ICU) admission.

Statistical analysis of the study was performed using the IBM SPSS software version 26. The categorical variables were expressed as frequency and compared using the chi-squared test in the moderate and severe/critical groups. On the other hand, mean ± SD (Standard Deviation) was used to describe the quantitative variables. The independent-samples *t*-test was used to analyze normally distributed data; otherwise, the Mann-Whitney *U* test was used. P <0.05 was set as the significance level.

RESULTS

Of the 156 patients (74 men and 82 women; age range of 25-95 years (56.87 ± 16.88)), 70 persons (34 men and 36 women) were in the moderate group, and 86 cases (40 men and 46 women) were in the severe/critical group. Among the initial clinical findings, the cough was the most frequent presenting onset symptom (65%), followed by dyspnea (64%) (Table1). Table 1 summarizes the laboratory test results. As shown in figure 2, 80, 53, and 29% of all patients were marked for GGO, consolidation, and GGO-consolidation, respectively. Regarding lesion morphology, 65 and 51% of the patients manifested patchy/segmental

and round/nodular; however, both morphologies were observed in 18% of cases (Figure 2).

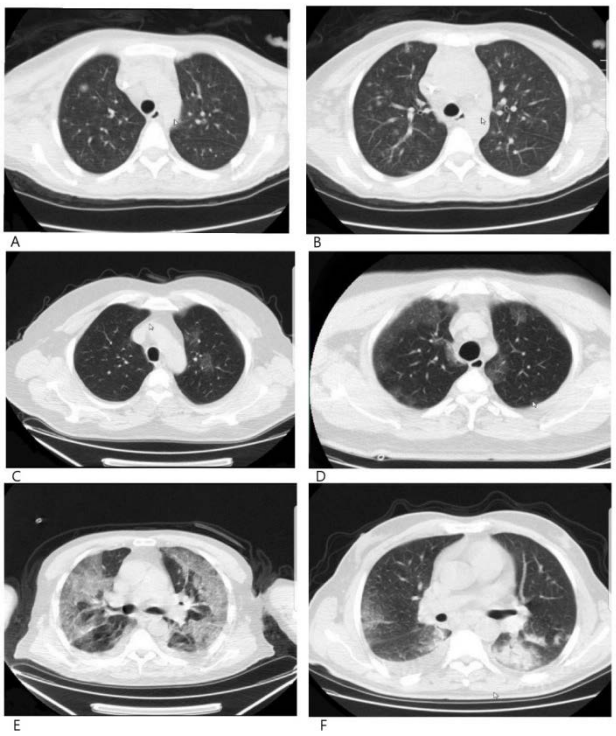

Figure 2. Patients with confirmed COVID-19, (A and B): 32-year-old woman, Moderate group, Onset symptom was fever, Baseline CT shows Ground Glass Opacity with round morphology and peribronchovascular distribution. (C): 55-year-old man, Moderate group, Patient had exposure history, Baseline CT shows Patchy Ground Glass Opacities with peribronchovascular distribution. (D): 51-year-old man, Severe/critical group, Baseline CT shows Patchy Ground Glass Opacities with the peripheral distribution. (E): 75-year-old man, Severe/critical group, Onset symptom was dyspnea, Baseline CT shows mixed Ground Glass Opacity, consolidation, and Crazy paving pattern. (F), 72-year-old man, Severe/critical group, Onset symptom was dyspnea, Baseline CT shows pleural effusion; consolidation in the left lung and peripheral Ground Glass Opacity in the right lung.

Lesion distribution was mainly peripheral (75%). In this regard, in 54% of cases, central (peribronchovascular) distribution was illustrated, and diffuse peripheral and central distribution was illustrated in the images of 31% of the participants. In 72% of studied cases, the lungs were affected bilaterally; however, the right lung was more involved (91%). COVID-19 pneumonia generally involved the lower lobe of the right lung, the lower lobe of the left lung, and the upper lobe of the right lung in 77, 71, and 65% of the cases, respectively. At the segmental level of involvement, the right lower lobe posterior segment was dominantly affected. Other chest CT findings are presented in Table (2). The following results were obtained from comparing clinical characteristics, laboratory findings, and the CT manifestations between the two moderate and severe/critical groups:

The patients in the severe/critical group were older than the moderate group. Regarding gender, no significant difference was noticed between the two groups. The medical history of hypertension, diabetes, cardiovascular disease, and chronic lung diseases was mainly positive in the severe/critical group. Considering clinical characteristics and vital signs, there was no significant difference between the two groups. The exceptions were confusion on admission (P=0.008) and pulse rate (PR) ≥ 100 (p = 0.04), which were significantly higher in the severe/critical group. Among all chest CT manifestations, consolidation, central (peribronchovascular) and diffuse peripheral and central distribution, patchy/segmental morphology, crazy paving pattern, pleural effusion, aorta, and coronary artery calcification were more likely to be observed in the severe/critical group ($p < 0.05$) (Table 2).

In contrast, round/nodular opacity mainly manifested in the moderate group (p=0.002). The vascular enlargement was mainly found in the severe/critical group, but it was not statistically significant. Another point about CT imaging was that pulmonary artery diameter had a significant difference between the two groups (P = 0.035). The CT-SS values were 10.24±7.91 and 6.13±4.42 for the severe/critical group and the moderate group, respectively, indicating a statistically significant difference. A significant positive correlation was noticed between the CT-SS and LDH levels (correlation coefficient= 0.4) and between the CT-SS and ferritin levels (correlation coefficient=0.63). There was also a negative correlation between CT-SS and lymphocyte count (correlation coefficient = 0.18).

Table 1. Laboratory and Clinical findings of patients in admission

	Moderate (N=70)	Severe/Critical (N=86)	Total (N=156)	P
Laboratory Findings				
White Blood Cell, mm^{-3}	6879 (3000-17600)	8321 (3400-30800)	7648	0.035
Lymphocyte, mm^{-3}	1626 (530-6300)	1558 (488-4400)	1590	0.648
Lactate Dehydrogenase, U/l	419 (126-1581)	490 (200-921)	454	0.145
Ferritin, ng/ml	736 (52-1207)	360 (153-1483)	545	0.065
Creatinine, mg/dl	1 (0.50-2.20)	1.3 (0.50-6.80)	1.24	0.024
Troponin, ng/ml	7.6 (0.00-30.10)	5.1 (0.00-100.00)	6.8	0.819
Alkaline Phosphatase, IU/l	202 (113-388)	290 (35-1358)	253	0.035
Magnesium, mg/dl	1.86 (1.60-2.30)	1.89 (1.20-2.10)	1.87	0.656
AST (Aspartate Aminotransferase), IU/l	33 (13-162)	36 (10-149)	35	0.581
ALT (Alanine Aminotransferase), IU/l	34 (10-246)	45 (10-452)	53	0.654
C-Reactive Protein				0.902
- Negative	18 (26%)	17 (20%)	35 (22%)	
- +	15 (21%)	20 (23%)	35 (22%)	
- ++	14 (20%)	15 (17%)	29 (19%)	
- +++	12 (17%)	12 (14%)	24 (15%)	
Clinical Findings				
Qualitative Variables				
Age group (y)				0.000
- ≤20	0(0%)	0(0%)	0(0%)	
- 21 - 40	20(29%)	12(14%)	32(21%)	
- 41 -60	35(50%)	27(31%)	62(40%)	
- 61 -80	11(16%)	33(38%)	44(28%)	
- ≥ 80	4(6%)	14(16%)	18(12%)	
Sex				0.798
- Female	36(51%)	46(53%)	82(53%)	
- Male	34(49%)	40(47%)	74(47%)	
Fever (BT≥37.3°c)	29(41%)	41(48%)	70(45%)	0.397
Cough	46(66%)	56(65%)	102(65%)	0.938
Hemoptysis	0(0%)	1(1%)	1(0%)	0.365
Myalgia	22(31%)	31(36%)	53(34%)	0.545
Fatigue	3(4%)	7(8%)	10(6%)	0.328
Diarrhea	5(7%)	7(8%)	12(8%)	0.816
Nausea or vomiting	9(13%)	13(15%)	22(14%)	0.687
Poor appetite	10(14%)	15(22%)	25(16%)	0.593
Abdominal pain	4(6%)	7(8%)	11(7%)	0.556
Sore throat	5(7%)	2(2%)	7(4%)	0.148
Runny nose	1(1%)	0(0%)	1(0%)	0.266
headache	2(3%)	8(9%)	10(6%)	0.102
Dyspnea	43(61%)	57(66%)	100(64%)	
Confusion	3(4%)	20(23%)	23(15%)	0.001
Current smoker	1(1%)	4(5%)	5(3%)	0.256
Past Medical History				
- Hypertension	18(26%)	40(47%)	58(38%)	0.008
- Diabetes	8(11%)	21(24%)	29(19%)	0.038
- Cardiovascular Disease	7(10%)	19(22%)	26(17%)	0.044
- Chronic Lung Disease	7(10%)	20(23%)	27(17%)	0.034
- Cancer	2(3%)	3(3%)	5(3%)	0.824
Quantitative Variables				
Saturation O_2 (%)	95.20±2.00	87.62±4.81	91.02±5.36	0.000
Systolic BP	136.30±24.7	135.14±24.86	135.66±24.71	0.772
Diastolic BP	83.59±14.05	81.65±15.12	82.51±14.63	0.420
Respiratory Rate	19	21	20	0.009
Pulse Rate	93	98	96	0.045
Hospital Stay (Days)	5.16±1.65	5.12±2.58	5.13±2.20	0.909

Note: Laboratory Findings; Except C- Reactive Protein (number of patients with the percentage in parenthesis) other data is mean with the range in parenthesis. Clinical Findings; Qualitative variables are numbers with the percentage in parenthesis and quantitative variables are mean ± SD.

Table 2. Radiologic findings of patients in admission

Lesion type	Moderate (N=**70**)	Severe/Critical (N= 86)	Total (N=156)	P
Ground Glass Opacity	58(83%)	67(78%)	125(80%)	0.441
Consolidation	30(43%)	52(60%)	82(53%)	0.0281
Mixed	20(29%)	25(29%)	45(29%)	0.946
Distribution pattern				
Peripheral	50(71%)	67(78%)	117(75%)	0.353
Central	31(44%)	53(62%)	84(54%)	0.031
Both	13(19%)	36(42%)	49(31%)	0.002
Morphology				
Segmental/Patchy opacity	34(49%)	67(78%)	101(65%)	0.000
Round/Nodular opacity	45(64%)	34(40%)	79(51%)	0.002
Both shapes opacity	11(16%)	17(20%)	28(18%)	0.512
Calcification				
Coronary artery calcification	14(20%)	25(29%)	39(25%)	0.193
Aortic Calcification	19(27%)	41(48%)	60(38%)	0.009
Pleural effusion	3(4%)	13(15%)	16(10%)	0.027
Pericardial effusion	2(3%)	2(2%)	4(3%)	0.835
Crazy paving pattern	1(1%)	8(9%)	9(6%)	0.036
Cardiomegaly	1(1%)	2(2%)	3(2%)	0.685
Vascular enlargement	4(6%)	8(9%)	12(8%)	0.403
Solid Nodule	1(1%)	1(1%)	2(1%)	0.883
Lymphadenopathy	0(0%)	2(2%)	2(1%)	0.199
Lung region distribution				
Unilateral	21(30%)	23(27%)	44(28%)	0.704
Bilateral	49(70%)	63(73%)	112(72%)	0.653
Lobar Involvement				
RUL	41(59%)	60(70%)	101(65%)	0.145
RML	32(46%)	44(51%)	76(49%)	0.498
RLL	53(76%)	67(78%)	120(77%)	0.746
LUL	30(43%)	38(44%)	68(44%)	0.868
LLL	49(70%)	62(72%)	111(71%)	0.774
LINGULA	25(36%)	40(47%)	65(42%)	0.194
Segment involvement				
RU Apical	6(9%)	21(24%)	27(17%)	0.031
RU Anterior	24(34%)	40(47%)	64(41%)	0.217
RU Posterior	29(41%)	47(55%)	76(49%)	0.222
RML Lateral	25(36%)	39(45%)	61(39%)	0.129
RML Medial	14(20%)	25(29%)	34(22%)	0.096
RL Superior	28(40%)	50(58%)	78(50%)	0.001
RL Anterior	9(13%)	29(34%)	28(18%)	0.004
RL Posterior	36(51%)	58(67%)	9460%)	0.015
RL Medial	20(29%)	35(41%)	55(35%)	0.007
RL Lateral	30(43%)	37(43%)	67(43%)	0.006
LU Apical	5(7%)	13(15%)	18(12%)	0.212
LU anterior	15(21%)	24(28%)	39(25%)	0.246
LU Posterior	24(34%)	36(42%)	60(38%)	0.508
LINGULA Superior	15(21%)	30(35%)	45(29%)	0.028
LINGULA Inferior	19(27%)	36(42%)	55(35%)	0.032
LL Superior	25(36%)	36(42%)	61(39%)	0.006
LL Anterior	7(10%)	29(34%)	36(23%)	0.002
LL Posterior	35(50%)	52(60%)	87(56%)	0.001
LL Medial	15(21%)	33(38%)	48(31%)	0.004
LL Lateral	23(33%)	37(43%)	60(38%)	0.042
CT severity score	6.13±4.42	10.24±10.91	8.4±6.87	0.001
Pulmonary Artery Diameter	25.47±3.48	26.21±4.38	26.2±4.04	0.035

Note: Except for CT severity score and pulmonary artery diameter (mean ± SD) other data is the number of patients with the percentage in parenthesis.

From another perspective, the following results were obtained from comparing the survivors and non-survivors: The non-survivors were older than the survivors, and the medical history of hypertension (p=0.01), diabetes (P=0.04), and chronic lung disease (P=0.03) was more likely in this group. Regarding clinical characteristics, a majority of the non-survivors had confusion when admitted to the hospital. Regarding the laboratory findings, increased white blood cell (WBC) count (P = 0.004), LDH (P = 0.03), ferritin (P = 0.01), and creatinine (P = 0.01), and decreased magnesium (P=0.01) were significantly higher in non-survivors. Regarding the chest CT manifestations, pericardial effusion, aorta, and coronary artery calcification were mostly observed in the non-survivors.

DISCUSSION

This study was to assess the prognosis in hospitalized COVID-19 pneumonia patients and detect the association between the baseline clinical, laboratory, and chest CT findings with the outcome. Predicting the outcomes and the mortality risk of the patients on admission may play a critical role in patient management and care planning.

The findings of this study were consistent with those of the previous studies, indicating that the patients in the severe/critical group as non-survivors mostly had underlying medical conditions and were older than the moderate group cases or survivors. One of the probable causes might be reduced immunity (8,16). Confusion on admission was also associated with poor prognosis. In the severe cases, central nervous system involvement and neurologic manifestations, mainly nonspecific symptoms such as confusion, were noticed (17).

Other findings of this study generally correspond with the early radiology research efforts (11,16,18). Bilateral involvement, peripheral distribution, GGO, and consolidation were the typical chest CT hallmarks in these patients. Furthermore, the CT involvement pattern was found to be efficient in stratifying disease severity, predicting the prognosis, and assessing the mortality risk.

The presentation of lung consolidation was significantly higher in the severe/critical group. This finding was in line with those of the previous studies (19). The finding can be associated with more severe alveolar infiltration in such patients.

Second, the round/nodular morphology was significantly more frequent in the moderate group, as opposed to patchy/segmental opacity, which was mainly noticed in the severe/critical group. This inconsistency can be justified with assuming a hypothesis on the formation of lesions. The round/nodular lesion is an area of infiltration restricted from the periphery; hence, the expansion of the lesion is limited. However, this does not apply to patchy/segmental morphology, and the lesion can expand violently. However, this hypothesis needs to be further investigated by reviewing follow-up chest CT and determining the changes in the CT findings.

Moreover, crazy paving patterns and pleural effusion were significantly higher in the severe/critical group. It can be argued that this is the result of microvascular injury and leakage from alveolar capillaries. The pathogenesis of COVID-19 can explain the vascular enlargement around lesions and the enlarged pulmonary artery diameter in the severe/critical group by micro thrombosis and vessel occlusion (20).

Furthermore, the aorta and coronary artery calcifications were significantly higher in the severe/critical group and the non-survivors. This seems to be logical by considering the association between these findings and the positive medical history of cardiovascular disease, hypertension, and diabetes.

Finally, the low serum magnesium level was noticed to be more likely in the severe/critical group. This can be related to kidney injury or drug-induced magnesium loss caused by broad-spectrum antibiotic administration in some cases (21).

The study had several limitations. First, only the patients admitted to the hospital were included, and the outpatient data were disregarded. Next, due to the retrospective nature of this study, all laboratory data were not available in the database. Finally, by evaluating the changes in follow-up scans along with the baseline chest CT, more accurate findings can be obtained and further examined in other studies.

In conclusion, clinical, laboratory, and chest CT findings can be used to detect the severity of the COVID-19

pneumonia. Predicting the outcome and mortality risk for the patients on admission can play a critical role in patient management and care planning.

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