Research Square

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Predictive Parameters for the Worsening Clinical Course of Mild COVID-19 Pneumonia

Cho Rom Hahm
Department of Internal Medicine, Seoul Medical Center https://orcid.org/0000-0002-6027-2185
Young Kyung Lee
Department of Radiology, Seoul Medical Center https://orcid.org/0000-0001-6953-0972
Dong Hyun Oh
Department of Internal Medicine, Seoul Medical Center https://orcid.org/0000-0002-9990-6042
Mi Young Ahn
Department of Internal Medicine, Seoul Medical Center https://orcid.org/0000-0002-7312-8502
Jae-Phil Choi
Department of Internal Medicine, Seoul Medical Center https://orcid.org/0000-0003-4805-7930
Na Ree Kang
Department of Internal Medicine, Seoul Medical Center https://orcid.org/0000-0002-9994-7741
Jungkyun Oh
Department of Hospital Medicine, Seoul Medical Center https://orcid.org/0000-0002-7716-8042
Hanzo Choi
Emergency Medicine, Myong Ji St. Mary's Hospital https://orcid.org/0000-0001-9201-5223
Suhyun Kim (sammy7597@naver.com)
Department of Internal Medicine, Seoul Medical Center https://orcid.org/0000-0002-7802-5967

Research Article

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Abstract

Background: This study aimed to determine parameters for worsening oxygenation in mild COVID-19 pneumonia.

Methods: This retrospective cohort study included confirmed COVID-19 pneumonia in a single public hospital in South Korea from January to April 2020. Parameters were compared between the two groups on the basis of clinical course: the desaturation group was defined as those with oxygen saturation ≤ 94% on ambient air, or received oxygen or mechanical ventilation (MV) throughout the clinical course versus the nonevent group who were without any respiratory event up to 28 days. The severity and extent of viral pneumonia from an initial single chest CT were calculated using artificial intelligence (AI) algorithms and measured visually by a radiologist.

Results: We included 136 patients with 32 (23.5%) in the desaturation group, of whom two needed MV and one died. Initial vital signs and duration of symptoms showed no difference between the two groups, however, univariate logistic regression analysis revealed that a variety of parameters at admission were associated with an increased risk of a desaturation event. In a sex-, age-, and comorbid illness-matched case-control study, ferritin ≥ 280 μg/L (OR 3.600, 95% CI 1.142-11.346; p=0.029), LDH≥ 240 U/L (OR 3.600, 95% CI 1.142-11.346; p=0.029), pneumonia burden (OR 1.010, 95% CI 1.002-1.019; p=0.021), and extent (OR 1.194, 95% CI 1.017-1.401; p=0.030) by AI, and visual severity scores (OR 1.146, 95% CI 1.005-1.307; p=0.042) were the predictive parameters for worsening clinical course with desaturation.

Conclusion: Our study presents initial CT parameters measured by AI or visual severity scoring as well as serum markers of inflammation at admission as the best parameters for predicting worsening oxygenation in the COVID-19 pneumonia cohort. Initial chest CT scans may help clinicians diagnose viral pneumonia and evaluate the prognosis in mild COVID-19.

Introduction

Coronavirus disease (COVID–19) has now become a pandemic since the first case of severe acute respiratory syndrome coronavirus 2 (SARS-CoV–2) in Wuhan, China [1]. The symptoms vary widely, from asymptomatic disease to pneumonia, to life-threatening complications and ultimately death. Sometimes it shows rapid progression of respiratory failure soon after the onset of dyspnoea and hypoxemia [2]. It is important to unravel the risk factors associated with hypoxemia and identify at an early stage patients who are susceptible to severe or critical illness upon infection.

Older patients and those with pre-existing respiratory or cardiovascular conditions, diabetes, hypertension, and cancer appear to be at the greatest risk for poor outcomes or severe complications [1, 3–5]. Leucocytosis, low lymphocyte count, serum levels of D-dimer, lactate dehydrogenase (LDH), ferritin, cardiac troponin, and higher concentrations of proinflammatory cytokines were reported to be risk factors associated with severe and fatal COVID–19 in hospitalised patients [1, 6, 7]. Typical imaging features of COVID–19 were established to help early screening and evaluation of the severity and extent of disease.

CT involvement scores can assist in evaluation of the severity and extent of the disease [8]. Previous studies estimating risk factors included mostly people with severe and fatal diseases at presentation, and data are lacking for subclinical or mild COVID–19 patients. We explored potential risk factors associated with worsening oxygenation in a retrospective cohort of mild patients with COVID–19 pneumonia.

Methods

Study design and participants

This retrospective, single-centre study, recruited patients from January 30th to April 15th, 2020 in a public teaching hospital that also served as a COVID–19 dedicated hospital in Seoul, South Korea. We reviewed patients with COVID–19 pneumonia who were previously discharged or had been hospitalised for at least 28 days or more. Ethical approval was provided by the institutional ethics review board of our hospital (2020–04–024). According to hospital protocol, all patients with confirmed COVID–19 were admitted to the hospital and routinely underwent non-contrast CTs. The inclusion criteria were patients aged ≥18 years who (a) were positive for nucleic acid detection of SARS-CoV–2, (b) underwent a chest CT within 24 hours of admission, and (c) showed evidence of viral pneumonia in the initial chest CT scan. The presence of ground-glass opacity (GGO) or consolidation in the bilateral peripheral posterior lungs on chest CT scans without any other specified causes or pathogen in a COVID–19 confirmed patient was categorised as CT-documented COVID–19 pneumonia [9]. The exclusion criteria were (a) patients with symptom onset more than 14 days; (b) normal findings on initial chest CT; and (c) lung abnormalities other than viral pneumonia.

The clinician's decision dictated treatment. Multidisciplinary teams screened for signs of acute deterioration and the need for intensive care unit (ICU) admission daily using an in-hospital electronic-medical-record monitoring system.

Data collection and definitions

Demographic characteristics of the patients, laboratory and radiological data were reviewed. The need for oxygen devices such as nasal oxygen supply, high-flow oxygen therapy, or respiratory support such as invasive MV were assessed.

For classification of the clinical course with poor oxygenation throughout the initial 28 day hospitalisation, we grouped patients into the desaturation group and the nonevent group. The desaturation group was defined as having any of the following criteria for admission or transfer to the ICU: (1) desaturation event with peripheral oxygen saturation of haemoglobin (SpO_2) on room air with rest ≤ 94% in at least two consecutive measurements or (2) respiratory failure requiring high-flow oxygen therapy or MV.

According to the “Diagnosis and Treatment Program of Pneumonia of COVID–19”, severe cases were defined as having any of the following criteria: (1) respiratory rate ≥ 30 breaths/min; (2) resting blood oxygen saturation ≤ 93%; or (3) partial pressure of arterial blood oxygen/fraction of inspired oxygen ≤ 300 mmHg. Critical patients needed to meet one of the following conditions: (1) respiratory failure requiring MV, (2) shock, or (3) other organ failure requiring ICU monitoring or treatment [10]. We defined “mild COVID–19 patients” as those who did not meet any of the severe or critical criteria on admission.

Chest CT acquisition

Chest CTs were performed using a 64-detector row CT scanner (SOMATOM Sensation 64, Siemens Healthcare, Erlangen, Germany) on admission (low-dose (reference mAs, 40) with automatic exposure control; slice thickness, 1.0 mm; and reconstruction interval, 3.0 mm). Axial images were reconstructed with a sharp reconstruction kernel at a 3 mm slice thickness. The CTs were performed with the patient in the supine position at full inspiration without contrast medium. Axial images were reconstructed with a sharp reconstruction kernel at a 3 mm slice thickness.

Quantitative CT analysis

CT images of each patient were uploaded in a free software for artificial intelligence (AI)-driven automatic CT analysis of COVID–19 pneumonia (MEDIP v1.2.0.0, MEDICALIP Co. Ltd., Korea), released on a website (http://medicalip.com/mobile/shop/covid19.php) on March 18, 2020. The deep learning software automatically generated a volumetric mask of the lung and pneumonia. The CT parameters from the automatic quantitative software were: the total lung volume (cm^3), the pneumonia volume (cm^3), pneumonia extent, and the mean lung densities of the total lung and the pneumonia.

An experienced thoracic radiologist (Y. K.L), blinded to the clinical data and laboratory indicators, evaluated the visual severity scores of the CT images. The CT severity score is adapted from a method previously used in patients after SARS [11]. The extent of lung lesions was scored from 0 to 5 in each lobe and summed up (0, normal; 1, 1–5% involvement; 2, 6–25% involvement; 3, 26–50% involvement; 4, 51–75%; 5, 76–100% involvement). The CT severity score was defined as the sum of the individual scores in the five lobes, which ranged from 0 to 25 points.

Statistical analysis

Continuous variables were represented as mean and standard deviation (SD) or median and interquartile ranges (IQR). A one-sample Kolmogorov-Smirnov test was performed to check the normality of all variables. To compare the two groups, the Mann-Whitney U test was used for continuous variables, and the chi-square or Fisher’s exact test was used for categorical variables. Correlation analysis was performed to identify associations between continuous variables. Univariate logistic regression analysis was performed to identify the clinical variables associated with desaturation events. Finally, a propensity

score matching analysis was performed to minimise the effect of potential confounding factors that could affect the worsening clinical course of COVID–19 pneumonia patients. We selected 26 sex-, age-, and underlying- disease-matched patients from each group to perform a case-control study at a ratio of 1:1, and a univariate logistic regression analysis was also performed with matched data.

All statistical analyses were performed using SPSS statistical software version 23.0 (IBM Corp., Armonk, NY, USA) and R software version 3.6.2 0 (R Foundation for Statistical Computing, Vienna, Austria). *P*-values were based on a two-sided significance level of 0.05.

Results

Demographics and clinical courses of enrolled patients

A total of 244 patients were admitted with laboratory-confirmed COVID–19 *(Figure 1).* After excluding 97 patients with normal baseline CT scans, four patients whose symptom onset was >14 days, and seven patients with bacterial coinfection or mycobacterial disease, 136 patients were included in this study (56 men, 80 women; mean age, 44.8±17.4 years; range, 18–95 years). No patient received MV or high-flow oxygen therapy on admission, only one patient had SpO_2 on room air ≤ 93%, and two patients showed respiratory rate ≥ 30 breaths/min, there was no shock or organ failure at presentation. Most patients, except for three patients, were classified as having mild COVID–19 on admission [10].

Among the 136 patients, 32 patients (23.5%) were classified into the desaturation group, and 104 remained in the nonevent group (76.5%) during 28 days of hospitalisation. All patients in the desaturation group had oxygen desaturation ≤ 94% in at least two consecutive measurements, and 10 patients required oxygen supplementation. Only two patients in the desaturation group needed MV, while a total of five patients needed high-flow oxygen therapy before or without MV. No patient needed extracorporeal membrane oxygenation (ECMO). During hospitalisation, 10 patients were admitted to the ICU, including two patients who developed acute respiratory distress syndrome (ARDS), and one patient died declining to apply the MV in accordance with a previously signed advance directive. Among the patients in the desaturation group, time intervals for oxygen desaturation ≤ 94% were a median 2 (IQR, 1–5) days from admission and 8 (IQR 6–11) days from symptom or disease onset, respectively. The duration of oxygen support was a median 3 (IQR 1–7) days after admission and 12 (IQR 9–13) days from symptom or disease onset.

Baseline characteristics and laboratory indices between the two groups

The baseline characteristics of COVID–19 patients according to the clinical course are summarised in *Table 1.* The average interval for admission from symptom or disease onset was 6.8 days. Only 71 of 136 patients (52.2%) complained of respiratory symptoms, and only 23 of 136 patients (16.9%) had a body temperature (BT) ≥37.5℃ on admission. Intervals between symptom or disease onset and admission,

and initial symptoms showed no difference between the two groups. The first recorded vital signs were similar in the two groups.

Patients in the desaturation group were older (P <0.001), and had more underlying diseases than those in the nonevent group (40.6% vs. 22.1%, P = 0.038). Hypertension was the most common underlying disease in both groups, and dementia was more frequent (15.6% vs. 1.0%, P = 0.003) in the desaturation group than in the nonevent group. The desaturation group showed higher body mass index (BMI) and 53.1% had obesity based on a BMI ≥25 kg/m^2 (vs. 26.9%, P = 0.006).

There were numerous differences in laboratory findings between the two groups *(Table 1),* including higher serum levels of C-reactive protein (CRP), ferritin, and LDH as well as lower lymphocyte counts in the desaturation group than in the nonevent group (all P <0.05). The desaturation group had higher pneumonia severity index (PSI); (56.5 vs. 37.1, P <0.001) and MuLBSTA score (6.0 vs. 3.9, p = 0.001) than the nonevent group, the modified early warning score (MEWS) showed no difference (1.4 vs. 1.3, P = 0.737).

Relationships between CT features and worsening oxygenation

The pneumonia volume quantified using AI was significantly larger in the desaturation group (median 45.2 cm^3 vs. 10.7 cm^3, P = 0.001) as well as the extent of opacities (median 2.4% vs. 0.5%, P = 0.001). Visual severity scores of the CT images were also significantly higher in the desaturation group (8.0±5.2 vs. 4.6±3.2, P <0.001). In particular, 37.5% of the desaturation group showed a visual severity score ≥11/25 (vs. 4.8% of nonevent group); *(Table 2).*

Figure 2 shows examples of COVID–19 pneumonia lesions from each group detected by free software for AI-driven automatic CT analysis.

Predictors of worsening clinical course

We initially evaluated the results using univariate analysis *(Table 3).* Our analysis revealed that elderly patients, dementia, obesity, higher pneumonia severity scores, such as the PSI and MuLBSTA score, higher levels of initial CRP, ferritin, and LDH, and lower lymphocyte levels were associated with the *desaturation group* compared to the *nonevent group.* In addition, pneumonia volume and the extent of the CT by AI, and visual severity scores, were higher in the *desaturation group* when compared with *nonevent group (*p < 0.05).

After matching on the propensity score, 52 patients were included in the analysis, and between-group differences for all covariates were eliminated *(Table S1).* After excluding the impact of age, underlying disease, initial symptoms and first recorded vital signs, initial pneumonia severity scoring, and complete blood count, ferritin ≥ 280 μg/L (OR 3.600, 95% CI 1.142–11.346; p = 0.029), LDH ≥ 240U/L (OR 3.600, 95% CI 1.142–11.346; p = 0.029), pneumonia volume (OR 1.010, 95% CI 1.002–1.019; p = 0.021) and

extent (OR 1.194, 95% CI 1.017–1.401; p = 0.030) by AI, and visual severity scores (OR 1.146, 95% CI 1.005–1.307; p = 0.042) were the parameters for predicting worsening clinical course with oxygen desaturation in this cohort ($P < 0.05$); *(Table 4).*

Discussion

An estimated 2.3% of COVID–19 patients require tracheal intubation currently [12]. A prominent complication of advanced COVID–19 is acute hypoxemic respiratory failure requiring oxygen and MV. It is estimated that 15–20% of infected people develop severe pneumonia and 5%–10% require critical care [12]. A recent report according to the Chinese classification showed that 14% of patients were of the severe type and 5% were of the critical type [13]. Severe illness of COVID–19 usually begins approximately 1 week after the onset of symptoms [2], while patients have variable phases of symptoms and disease onset at admission [12]. In the present study, most patients were classified as having mild COVID–19 at presentation [10], and no patient received MV or high-flow oxygen therapy on admission. In the beginning, only three patients were classified into the desaturation group. Patients in this cohort were admitted an average of 6.8 days from symptom onset, and 12.5% were asymptomatic on admission. Nevertheless, 23.5% of these mild patients proceeded to oxygen desaturation during a median 2 days from hospitalisation. This study was undertaken to determine the predictive parameters for a worsening clinical course in patients with mild COVID–19 pneumonia admitted at a relatively early phase from symptom or disease onset.

Early case series from the Korean Cohort Study showed that 21.4% of patients received oxygen therapy, with no requirement for MV [14]. In the Daegu and Gyeongbuk area, Republic of Korea, substantial community outbreaks were linked to a large religious meeting, and a retrospective study from that area (mean age of 55.4±17.1 years) showed that 13.3% of patients required ICU admission with MV use in 11.2%, ECMO in 4.1%, and a mortality rate of 5.1% [15]. The fatality rate of South Korea, which is 2.32% (to date) nationwide, is much lower than the rates reported in China or other countries [4, 6, 16–19]. Although recent data (median age of 51 years) outside Wuhan, China showed an 0.8% mortality rate [20]. Studies on COVID–19 have been limited to patients with severe or critical disease admitted to the ICU. In contrast, a recent report showed that more than 80% of COVID–19 cases were mild in China [4, 6, 13, 16–19]. In our study, most cases were mild, as evidenced by relatively low rates of ICU admission and mortality rates that would be related to younger ages (mean 44.8 ± 17.4) and lower comorbidity rates (26.5%) than that of previous reports. In metropolitan Seoul, all confirmed cases were either hospitalised at dedicated hospitals or monitored at community isolation centres. Many cases of COVID–19 were diagnosed by surveillance testing in South Korea, so that a large proportion of the patients in our cohort had mild or subclinical symptoms at the beginning of hospitalisation. The comprehensive hospital management with close monitoring led to mostly favourable outcomes, in addition to early case detection and immediate admission strategy of South Korea.

To our knowledge, markers for the prediction of worsening oxygenation among patients with initially mild COVID–19 pneumonia are not defined. In this cohort, only 16.9% showed fever based on a BT ≥37.5°C.

Most of the first recorded vital signs were within normal ranges and showed no difference between the two groups, suggesting that the worsening clinical course cannot be distinguished by initial vital signs. Apart from that, we noted that more patients in the desaturation group had higher pneumonia severity scores, and several laboratory parameters such as lymphopenia, higher ferritin and LDH, as well as older age and comorbidities such as dementia and obesity were associated with a worsening clinical course and oxygen desaturation. Feng et al. suggested that the variance of the MuLBSTA score, may have a better predictive value in COVID–19 pneumonia as with this study [10, 21]. Xie et al. suggested that traditional method such as the new early warning score (NEWS) may not help predict patients who will develop respiratory failure in COVID–19 [22]. Our data showed no difference in MEWS.

Our results also underline the importance of the integration of CT extent and severity into the management of COVID–19 pneumonia patients. Despite recent advances in molecular viral characterisation, recent evidence does not support a severity or mortality stratification based on viral load dynamics [23]. However, CT extent or CT features were recognised as important factors for predicting a worsening prognosis [23–25]. This is consistent with the results of the current study. The rapid development of AI has significantly improved automatic lung segmentation technology, making it possible to quantify the lesions automatically [25]. Quantitative analysis of CT using AI tools could provide an automatic and objective estimation of the disease burden, facilitating imaging interpretation during the pandemic [23]. This study aimed to investigate the capability of quantitative CT imaging features combined with traditional clinical biomarkers in predicting progression to worsening course in the early stages of COVID–19. We used free software and did not analyse the parameters for each lobe. We found that the AI-driven parameters of pneumonia volume and extent of the whole lung in the initial chest CT predicted the worsening oxygen saturation in mild COVID–19 pneumonia. Our study confirms the additional benefit of the visual severity scores summing the estimated extent of each lobe and the integration of clinical and laboratory parameters.

We experienced that hypoxemia was the first step for quick deterioration in some patients and observed that some patients are relatively asymptomatic although they have a good degree of hypoxemia for inexplicable reasons, referred to as “silent hypoxemia” in Wuhan [22]. We designed this study to identify parameters at an early stage to predict whether oxygen will decrease. This study has limitations. First, it is a single-centre retrospective study. In our hospital, the standard cutoff value for admission or transfer to the ICU and change or add-on of antiviral agents was 94% of the SpO_2 on ambient air. These criteria should be regarded as empirical, as there is no robust supporting evidence. Second, fewer patients were severe or critical compared to other studies. The majority of the desaturation group recovered without oxygen or MV, or ECMO. These favourable outcomes may not reflect the full prognosis of patients with COVID–19 in other areas. We did not analyse the factors that could affect outcomes such as regional differences, medical resources, and treatment options we applied as in a clinical trial. Nevertheless, these data, including patients with mild symptoms in a relatively early stage, are thought to be useful in predicting parameters for clinical course and triaging patients in real practice. Third, we did not analyse the CT scans at the time of deterioration or follow-up, and the features or patterns with GGO or

consolidation, though the extent and burden of the total GGO/consolidation of the initial CT proved to be one of the predictive parameters for the clinical course of mild COVID–19 pneumonia.

Our study presents initial CT parameters measured by AI or visual extent scoring as well as serum markers of inflammation such as ferritin and LDH at admission as the best parameters for predicting worsening oxygenation in mild COVID–19 pneumonia patients.

Abbreviations

COVID–19: Coronavirus disease 2019, MV: mechanical ventilation, CT: computed tomography, AI: artificial intelligence, SARS-CoV–2: severe acute respiratory syndrome coronavirus 2, LDH: lactate dehydrogenase, GGO: ground-glass opacity, ICU: intensive care unit, SpO_2: oxygen saturation of hemoglobin, SD: standard deviation, IQR: inter-quartile ranges, ECMO: extracorporeal membrane oxygenation, ARDS: acute respiratory distress syndrome, BT: body temperature, BMI: body mass index, CRP: C-reactive protein, PSI: pneumonia severity index, MuLBSTA: multilobular infiltration, hypo-lymphocytosis, bacterial coinfection, smoking history, hypertension, and age, MEWS: modified early warning score, OR: odds ratio, CI: confidence interval, NEWS: new early warning score

Declarations

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Author contributions:

S. Kim conceived and designed the study, analysed the data, and wrote the manuscript. C. R. Hahm, D. H. Oh, M. Y. Ahn, J-P Choi, N. R. Kang, and J. Oh contributed to data acquisition and analysis. H. Choi interpreted and visualized the data. Y. K. Lee evaluated the visual severity scores of the CT images and provided expert insights into this study. All authors revised the manuscript.

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Availability of data and materials:

The datasets analyzed during the current study available from the corresponding author on reasonable request.

Ethics approval and consent to participate:

The study protocol was approved by the ethics institutional review boards of participating centers (Institutional Review Board of Seoul Medical Center (2020–04–024)). Due to the retrospective design of the study and there was minimal to no risk or benefit to enrolled patients, an informed consent was waived.

Consent for publication:

Not applicable (The manuscript does not contain any individual persons'

data).

Competing interests:

The authors declare that they have no competing interests.

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Tables

Table 1. Baseline characteristics of hospitalised COVID-19 pneumonia patients according to the clinical course.

Variables	Total (n=136)	Desaturation Group (n=32)	Nonevent Group (n=104)	*P*-value†
Age (years)	44.8 ± 17.4	55.0 ± 20.0	41.7 ± 15.3	**< 0.001†**
Male, n (%)	56 (41.2)	16 (50.0)	40 (38.5)	0.305
Comorbidities, n (%)	36 (26.5%)	13 (40.6%)	23 (22.1%)	**0.038†**
Hypertension	28 (20.6)	10 (31.3)	18 (17.3)	0.088
Diabetes mellitus	12 (8.8)	5 (15.6)	7 (6.7)	0.153
Obstructive airway disease	4 (2.9)	1 (3.1)	3 (2.9)	0.663
Immunosuppressive agents	3 (2.2)	1 (3.1)	2 (1.9)	0.556
Chronic renal disease	1 (0.7)	0 (0)	1 (1.0)	0.765
Residence in a nursing home or long-term facility, n (%)	5 (3.7)	3 (9.4)	2 (1.9)	0.085
BMI (kg/m^2)	23.6 ± 4.0	25.1 ± 3.6	23.4 ± 3.3	**0.009†**
BMI ≥ 25 kg/m^2, n (%)	45 (33.1)	17 (53.1)	28 (26.9)	**0.006†**
Interval between symptom or disease onset and admission (days)	6.8 ± 4.9	6.7 ± 4.6	6.8 ± 5.1	0.941
Initial symptoms, n (%)				
Asymptomatic	17 (12.5)	4 (12.5)	13 (12.5)	0.634
General (fever, chill, myalgia)	85 (62.5)	21 (65.6)	64 (61.5)	0.421
Respiratory (sore throat, rhinorrhea, cough, sputum, dyspnoea)	71 (52.2)	12 (37.5)	59 (56.7)	0.057
Gastrointestinal	10 (7.4)	1 (3.1)	9 (8.7)	0.268
Others	32 (23.5)	5 (15.6)	27 (26.0)	0.167
First recorded vital sign				
Heart Rate (beats/min)	87.2 ± 14.2	87.8 ± 14.1	87.0 ± 14.3	0.791
Systolic blood pressure (mmHg)	128.2 ± 14.9	125.9 ± 12.6	128.9 ± 15.5	0.674

Respiratory rate (breaths/min)	18.9 ± 2.7	19.5 ± 4.4	18.8 ± 1.9	0.775
Body temperature (°C)	36.9 ± 0.6	37.1 ± 0.6	36.9 ± 0.5	0.095
Oxygen saturation, SpO2 (%)	97.4 ± 1.5	96.4 ± 1.9	97.7 ± 1.2	**< 0.001†**
Severity scorings on presentation				
MEWS	1.3 ± 0.7	1.4 ± 0.9	1.3 ± 0.6	0.737
PSI	41.6 ± 21.8	56.5 ± 25.2	37.1 ± 18.6	**< 0.001†**
MuLBSTA score	4.4 ± 3.1	6.0 ± 3.4	3.9 ± 2.9	**0.001†**
Initial laboratory findings				
White blood cells (10^9/L)	5.7 ± 2.2	6.0 ± 2.6	5.6 ± 2.0	0.364
Neutrophil (10^9/L)	3.4±1.9	4.0 ± 2.5	3.2 ± 1.6	0.062
Lymphocyte (10^9/L)	1.6±0.6	1.4 ± 0.4	1.7 ± 0.7	**0.003†**
Platelet (10^9/L)	226.1 ± 70.6	210.3 ± 59.0	231.0 ± 73.3	0.146
CRP (mg/dL), median (IQR)	0.4 (0.1-1.2)	1.79 (0.35-4.28)	0.29 (0.10-0.77)	**< 0.001†**
CRP ≥ 0.4 mg/dL, n (%)	65 (47.8)	23 (71.9)	42 (40.4)	**0.002†**
Ferritin (μg/L), median (IQR)	149.2 (86.7-321.5) *(n=100)*	355.6 (195.6-744.9) *(n=27)*	106.8 (70.2-219.3) *(n=73)*	**< 0.001†**
Ferritin ≥ 280 μg/L, n (%)	29 (29.0)	16 (50.0)	13 (12.5)	**< 0.001†**
LDH (U/L), median (IQR)	245 (213-309) *(n=135)*	305 (226-340) *(n=32)*	236 (212-289) *(n=103)*	**0.006†**
LDH ≥ 240	51 (37.8)	19 (59.4)	32 (30.8)	

U/L, n (%)	0.003†

Data are presented as mean ± standard deviation, unless otherwise stated.

BMI: body mass index; MEWS: modified early warning score; PSI: pneumonia severity index; MuLBSTA score: multilobe infiltration, hypo-lymphocytosis, bacterial coinfection, smoking history, hypertension and age; CRP: C-reactive protein; LDH: lactate dehydrogenase; IQR: interquartile range

†$P < 0.05$ was considered statistically significant.

Table 2. Comparison of parameters and scores of the initial low-dose chest CT scan between the two groups.

Variables	Total (n=136)	Desaturation Group (n=32)	Nonevent Group (n=104)	*P*-value†
Quantitative CT analysis by AI				
Pneumonia volume (cm^3), median (IQR)	13.8 (3.8-46.7)	45.2 (8.5-170.6)	10.7 (3.5-38.2)	**0.001†**
Extent of opacities (%), median (IQR)	0.7 (0.2-2.2)	2.4 (0.5-6.5)	0.5 (0.2-1.7)	**0.001†**
Visually estimated CT scoring by the radiologist				
Visual severity score	5.4 ± 4.0	8.0 ± 5.2	4.6 ± 3.2	**< 0.001†**
0–5, n (%)	90 (66.2)	16 (50.0)	74 (71.2)	
6-10, n (%)	29 (21.3)	4 (12.5)	25 (24.0)	
≥ 11, n (%)	17 (12.5)	12 (37.5)	5 (4.8)	

Data are presented as mean ± standard deviation, unless otherwise stated.

CT: computed tomography; AI: artificial intelligence; IQR: interquartile range

†$P < 0.05$ was considered statistically significant.

Table 3. Univariate analysis of predictive parameters for oxygen desaturation with COVID-19 pneumonia (n=136).

Variable	OR	95% CI	*P*-value†
Age (years)	1.047	1.021–1.074	**< 0.001†**
Dementia (versus non dementia)	19.074	2.138–170.167	**0.008†**
BMI (kg/m^2)	3.076	1.357–6.973	**0.007†**
PSI	1.043	1.021–1.065	**< 0.001†**
MuLBSTA score	1.269	1.097–1.469	**0.002†**
Lymphocyte count (10^9/L)	0.320	0.137–0.750	**0.009†**
CRP ≥ 0.4 mg/dL (versus CRP < 0.4 mg/dL)	3.772	1.589–8.955	**0.003†**
Ferritin ≥ 280 µg/L (versus Ferritin < µg/L)	7.000	2.834–17.293	**< 0.001†**
LDH ≥ 240 U/L (versus < LDH 240 U/L)	3.288	1.450–7.460	**0.004†**
Pneumonia Volume (cm^3) by AI	1.014	1.007–1.022	**< 0.001†**
Extent of Opacities (%) by AI	1.283	1.109–1.486	**0.001†**
Visual Severity Scoring of the CT by the radiologist	1.225	1.105–1.359	**< 0.001†**

BMI: body mass index; PSI: pneumonia severity index; MuLBSTA score: multilobe infiltration, hypo-lymphocytosis, bacterial coinfection, smoking history, hypertension and age; CRP: C-reactive protein; LDH: lactate dehydrogenase; AI: artificial intelligence; CT: computed tomography; OR: odds ratio; CI: confidence interval

†$P < 0.05$ was considered statistically significant.

Table 4. Univariate analysis of predictive parameters for oxygen desaturation with COVID-19 pneumonia in matched case-control study (n=52).

Variables	OR	95% CI	*P*-value†
CRP ≥ 0.4 mg/dL (versus CRP < 0.4 mg/dL)	2.224	0.627–7.890	0.216
Ferritin ≥ 280 μg/L (versus Ferritin < μg/L)	3.600	1.142–11.346	**0.029†**
LDH ≥ 240 U/L (versus < LDH 240 U/L)	3.600	1.142–11.346	**0.029†**
Pneumonia Volume (cm^3) by AI	1.010	1.002–1.019	**0.021†**
Extent of Opacities (%) by AI	1.194	1.017–1.401	**0.030†**
Visual Severity Scoring of the CT by the radiologist	1.146	1.005–1.307	**0.042†**

CRP: C-reactive protein; LDH: lactate dehydrogenase; AI: artificial intelligence; CT: computed tomography; OR: odds ratio; CI: confidence interval

Figures

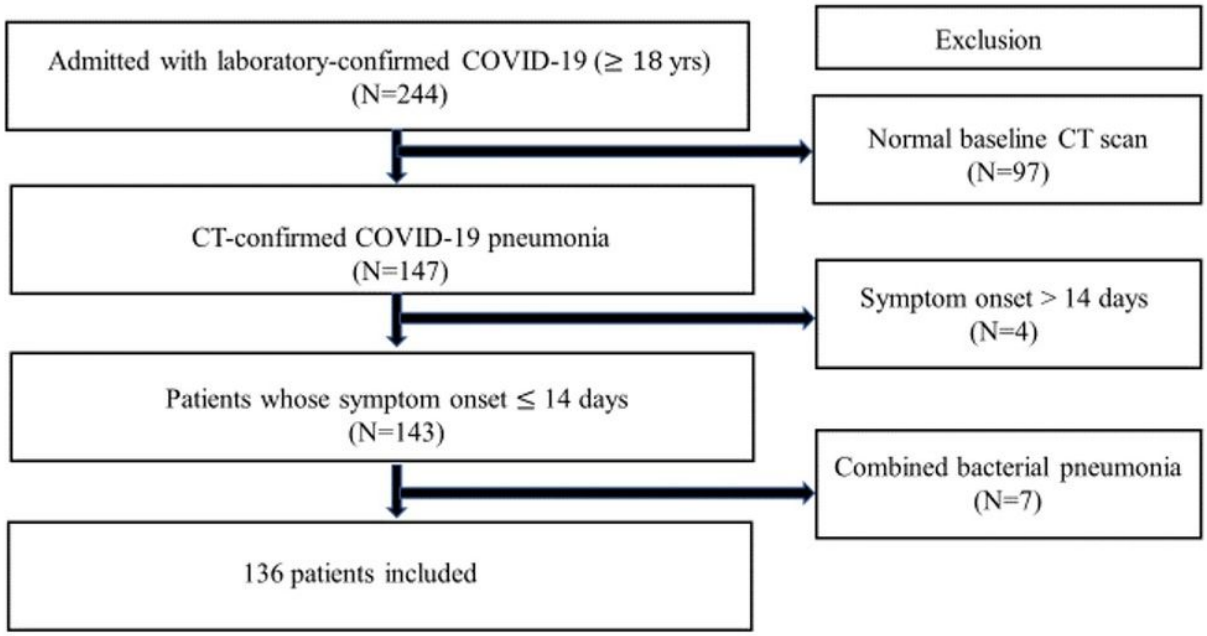
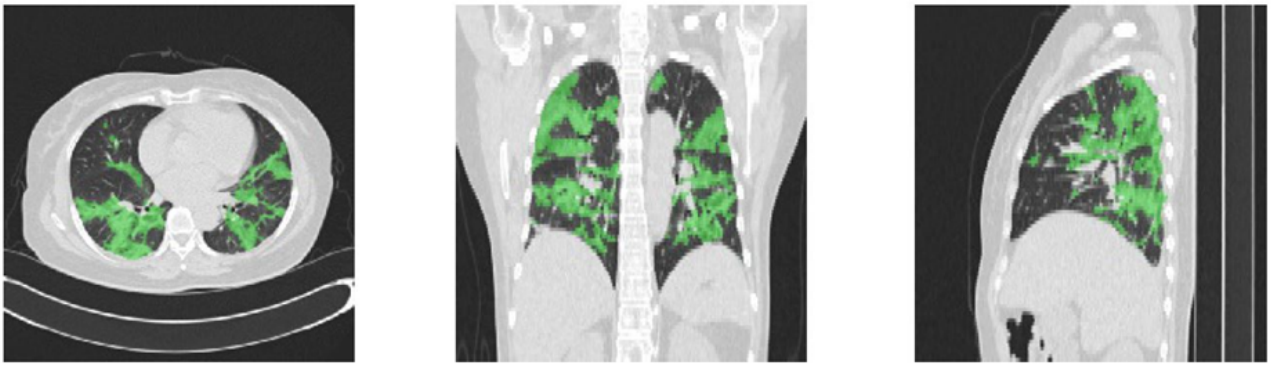


Figure 1

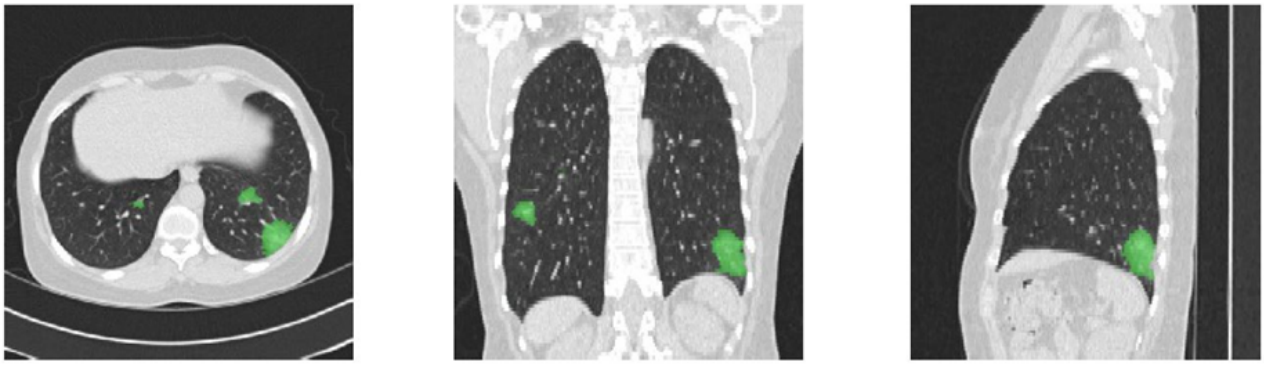
Study flow diagram.

	Volume (㎤)	Mean (HU)	Standard Deviation	Pneumonia Burden (g)	% extent (ACR)
Lung	2353.8	−647.1	246.1	–	–
Pneumonia	550.5	−348.0	193.3	382.3	23.4% (0.2)



A

	Volume (㎤)	Mean (HU)	Standard Deviation	Pneumonia Burden (g)	% extent (ACR)
Lung	3953.7	−819.9	140.0	–	–
Pneumonia	34.3	−462.2	180.1	19.6	0.9% (0.0)



B

Figure 2

COVID-19 pneumonia lesions detected by the AI system and comparison of the interpretation of the quantification CT parameters between the desaturation group (A) and nonevent group (B). The following images of two patients are illustrated. One is a 55-year-old female (A) who entered the desaturation group within 24 hours of admission. She presented with desaturation ≤ 94% within 24 h of admission and worsened rapidly, requiring high-flow oxygen therapy on the 3rd day after admission. She was discharged

on the 42nd day from admission. AI calculated a pneumonia volume of 382.3 g and pneumonia extent of 23.4%. The radiologist scored 19/25 using the visual severity score. The other image shows a 47-year-old female (B) who did not meet the desaturation group criteria during follow-up and was discharged from the hospital after the 41st day without any respiratory event. AI calculated a pneumonia volume of 19.6 g and pneumonia extent of 0.9%, and the radiologist scored 6/25 using the visual severity score.

Supplementary Files

This is a list of supplementary files associated with this preprint. Click to download.

- Supplementarytable.pdf