

Investigative Radiology

The Clinical and Chest CT Features Associated With Severe and Critical COVID-19 Pneumonia --Manuscript Draft--

Manuscript Number:	IR-D-20-00127R1
Full Title:	The Clinical and Chest CT Features Associated With Severe and Critical COVID-19 Pneumonia
Article Type:	Original Article
Keywords:	COVID-19; SARS-CoV-2; acute respiratory disease; Pneumonia; severity; risk factor
Corresponding Author:	Chuanming Li, M.D the Second Affiliated Hospital of Chongqing Medical University Chongqing, China CHINA
First Author:	Kunhua Li, MS
First Author Secondary Information:	
Order of Authors:	Kunhua Li, MS Jiong Wu, MS Faqi Wu, MS Dajing Guo, MD Linli Chen, MS Zheng Fang, MS Chuanming Li, MD
Manuscript Region of Origin:	CHINA
Abstract:	<p>Objective: To investigate the clinical and CT features associated with severe and critical Corona Virus Disease 2019 (COVID-19) pneumonia.</p> <p>Materials and Methods: Eighty-three patients with COVID-19 pneumonia including 25 severe/critical cases and 58 ordinary cases were enrolled. The chest CT images and clinical data of them were reviewed and compared. The risk factors associated with disease severity were analyzed.</p> <p>Results: Compared with the ordinary patients, the severe/critical patients had older ages, higher incidence of comorbidities, cough, expectoration, chest pain and dyspnea. The incidences of consolidation, linear opacities, crazy-paving pattern and bronchial wall thickening in severe/critical patients were significantly higher than those of the ordinary patients. Besides, severe/critical patients showed higher incidences of lymph node enlargement, pericardial effusion and pleural effusion than the ordinary patients. The CT scores of severe/critical patients were significantly higher than those of the ordinary patients ($P < 0.001$). Receiver operating characteristic (ROC) curve showed that the sensitivity and specificity of CT Score were 80.0% and 82.8% respectively for the discrimination of the two types. The clinical factors of age > 50 years old, comorbidities, dyspnea, chest pain, cough, expectoration, decreased lymphocytes and increased inflammation indicators were risk factors for severe/critical COVID-19 pneumonia. CT findings of consolidation, linear opacities, crazy-paving pattern, bronchial wall thickening, high CT scores and extrapulmonary lesions were features of severe/critical COVID-19 pneumonia.</p> <p>Conclusions: There are significant differences in clinical symptoms, laboratory examinations and CT manifestations between the ordinary patients and the severe/critical patients. Many factors are related to the severity of the disease, which can help clinicians to judge the severity of the patient and evaluate the prognosis.</p>

Dear Dr. Val M. Runge,

Thank you very much for your letter and advice. We also appreciate the constructive comments of the reviewers. This letter explained the changes made to the manuscript '**The Clinical and Chest CT Features Associated with Severe and Critical COVID-19 Pneumonia**' (No. IR-D-20-00127) in response to comments by the reviewers. **A point-by-point summary of all revisions was at the end of this letter.**

We hope that the revision is acceptable, and I look forward to hearing from you soon.

With best wishes,

Yours sincerely,

We would like to express our sincere thanks to the reviewers for the constructive and positive comments.

Reviewer #1: In this submission to Investigative Radiology the authors analyzed ordinary and severe/critical cases of COVID-19 in regard to clinical symptoms, laboratory and monitoring results as well as to the pattern and extent of pulmonary changes depicted on chest CT.

The paper is written straight forward and the topic will provide new knowledge in the field.

There are some minor revisions mandatory before a decision.

Q.1: M&M (The authors excluded 7 patients from the study population. Name what specifically led to their exclusion from the study.)

Response: we have added the details of the exclusion in the revised version (page 4, para 1, line 4).

Q.2: Typo page 4: "...Chest CT..." -> "...chest CT..."

Response: Correction has been made in the revised version (page 4, para 2, line 6).

Q3: Page 7, second paragraph.

"The people with old age or poor health often suffer...."

Consider revision such as...

"People with higher age or poor state of health suffer...."

Response: This sentence has been revised according to the reviewer's suggestion (page 8, para 2, line 2).

Q4: Page 8, first paragraph

"Chest pain may result from the inflammatory stimulation to pleura".

Consider revision...

"Chest pain may result from the inflammatory affection of the pleura."

Response: This sentence has been revised according to the reviewer's suggestion (page 8, para 2, line 7).

Q5: References (Make sure to include the latest publications regarding this topic when submitting your revised manuscript.)

Response: Several latest publications regarding this topic have been added in the references (page 10, reference 5 and page 11, reference 12,13).

Q6: Tables (As you provide a lot of parameters here, I recommend highlighting the significant P-values in bold. This shows at a glance what might be relevant factors differentiating severe from ordinary cases of COVID-19.)

Response: The significant P-values have been highlighted in bold in the revised version.

Q7: Figures

A verb is missing in the description of Fig. 1A and Fig. 2A.

Also stress out what was the clinical condition of the severely affected patient in comparison to the

ordinary COVID-19 case displayed in Fig. 1.

Be more precise what is displayed in Fig. 1B and Fig. 2B (VRT? Superimposed consolidations? Distribution of consolidation... that sort of thing...)

Response: The figure legends have been revised according to the reviewer's suggestions (page 13).

Reviewer #2: This study divided cases of COVID-19 pneumonia into ordinary cases and severe/critical cases and evaluated the clinical and chest CT features associated with severe/critical diseases.

Q1. Study population (page 3): What were the indications of chest CT in patients with COVID-19 pneumonia?

Response: Acute or subacute lesions mainly includes GGO, consolidation, interlobular septal thickening and crazy-paving pattern according to Diagnosis and Treatment of Novel Coronavirus Pneumonia (trial version fifth) of China.

Q2. Study population (page 3): In defining severe/critical cases by using $\text{PaO}_2/\text{FiO}_2 \leq 300$ mmHg, is there any condition of PEEP or CPAP ≥ 5 cmH₂O as in the Berlin definition of ARDS?

Response: According to Diagnosis and Treatment of Novel Coronavirus Pneumonia (trial version fifth) of China, the diagnostic criteria of severe/critical patients do not include the content of PEEP or CPAP ≥ 5 cmH₂O.

Q3. CT examinations and imaging evaluation (page 4): I could not find any description about "spider web sign" in references of 9 and 10. Please describe the definition of this sign.

Response: This is a new sign that we found and named. Its definition was described in detail in the revised version (page 4, para 2, line 9-12).

4. CT examinations and imaging evaluation (page 4): In calculating the CT score, were all abnormalities described above considered? Please clarify.

Response: All abnormalities were considered in the calculating of the CT scores. We have made it clear in the revised version (page 4, para 2, line 13).

5. Factors associated with severe/critical COVID-19 pneumonia (page 7): Why was multivariate analysis not performed?

Response: In this study univariate analysis was performed and many factors (19 factors) showed statistical significance. As the sample size of this study is relatively small^{1,2}, we have not been able to conduct multivariate analysis.

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6. Discussion (page 7): Is there available evidence for the statement "compared with the ordinary patients ... high mortality"? If not, please modify this sentence.

Response: References of evidence have been added in the revised version (page 7, para 3, line 2).

7. Discussion (page 8, third paragraph): Reference 14 is an article about the glossary, and therefore, this reference should be corrected.

Response: Reference 14 has been corrected according to the reviewer's suggestion

8. Figures: Please describe how the lesion was segmented in the 3D-reconstructed images.

Response: Details of the lesion segmentation in the CT examinations have been added in the revised version (page 5, para 1, line 4-8).

9. Figures: Please describe CT scores for both cases.

Response: CT scores of both cases were added in the figure legends in the revised version (page 13).

The Clinical and Chest CT Features Associated with Severe and Critical COVID-19 Pneumonia

*Kunhua Li, MS, ^{#1} Jiong Wu, MS, ^{#2} Faqi Wu, MS, ³ Dajing Guo, MD, ¹ Linli Chen, MS, ¹ Zheng Fang, MS, ¹ Chuanming Li, MD, ^{*1}*

1. Department of Radiology, the Second Affiliated Hospital of Chongqing Medical University, Chongqing, China
2. Department of Radiology, Chongqing Three Gorges Central Hospital, Chongqing, China
3. Department of Medical Service, Yanzhuang Central Hospital of Gangcheng District, Jinan, China

[#] These authors contributed equally to this work.

*Corresponding author: Chuanming Li, MD, Department of Radiology, The Second Affiliated Hospital of Chongqing Medical University, No. 74 Linjiang Rd, Yuzhong District, Chongqing, 400010, China. Fax: 86 - (023) 68485111. Telephone: 86-13618302013. Email: lichuanming@hospital.cqmu.edu.cn.

Conflicts of interest and sources of funding: No.

Running head: Chest CT Features Associated with Severe and Critical COVID-19

Pneumonia

The Clinical and Chest CT Features Associated with Severe and Critical COVID-19 Pneumonia

Abstract

Objective: To investigate the clinical and CT features associated with severe and critical Corona Virus Disease 2019 (COVID-19) pneumonia.

Materials and Methods: Eighty-three patients with COVID-19 pneumonia including 25 severe/critical cases and 58 ordinary cases were enrolled. The chest CT images and clinical data of them were reviewed and compared. The risk factors associated with disease severity were analyzed.

Results: Compared with the ordinary patients, the severe/critical patients had older ages, higher incidence of comorbidities, cough, expectoration, chest pain and dyspnea. The incidences of consolidation, linear opacities, crazy-paving pattern and bronchial wall thickening in severe/critical patients were significantly higher than those of the ordinary patients. Besides, severe/critical patients showed higher incidences of lymph node enlargement, pericardial effusion and pleural effusion than the ordinary patients. The CT scores of severe/critical patients were significantly higher than those of the ordinary patients ($P < 0.001$). Receiver operating characteristic (ROC) curve showed that the sensitivity and specificity of CT Score were 80.0% and 82.8% respectively for the discrimination of the two types. The clinical factors of age > 50 years old, comorbidities, dyspnea, chest pain, cough, expectoration, decreased lymphocytes and increased inflammation indicators were risk factors for severe/critical COVID-19 pneumonia. CT findings of consolidation, linear opacities, crazy-paving pattern, bronchial wall thickening, high

CT scores and extrapulmonary lesions were features of severe/critical COVID-19 pneumonia.

Conclusions: There are significant differences in clinical symptoms, laboratory examinations and CT manifestations between the ordinary patients and the severe/critical patients. Many factors are related to the severity of the disease, which can help clinicians to judge the severity of the patient and evaluate the prognosis.

Key Word: COVID-19, SARS-CoV-2, acute respiratory disease, pneumonia, severity, risk factor

INTRODUCTION

Since the middle of December 2019, many cases of pneumonia with unknown cause have been found in some hospitals in Wuhan City, Hubei Province, China.¹ At present, it has been confirmed as a new type of acute respiratory infectious disease caused by coronavirus infection.² On 12 February, 2020, the International Committee on Taxonomy of Viruses announced that the official classification of the new coronavirus is severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2).³ The World Health Organization (WHO) announced the same day that the official name of the disease caused by the virus is Corona Virus Disease 2019 (COVID-19).⁴ Up to 24:00 on ~~22~~18 February 2020, ~~7704185~~ confirmed cases (including ~~10497768~~ severe cases), ~~5248~~ ~~4148~~ suspected cases and ~~240045~~ dead cases have been officially reported in China.⁵ Many cases spread all over the world, including the United States, Japan, Singapore, Thailand, South Korea, etc, which suggested that the COVID-19 poses significant threats to international health.

Although most patients have mild symptoms and good prognosis, COVID-19 can develop to severe illnesses including pneumonia, pulmonary edema, acute respiratory distress syndrome, multiple organ failure or even death.^{6,7} The successful treatment of severe and critical cases is the

key to reduce the complication and mortality. Basic disease treatment, secondary infection prevention, and timely organ function support are needed for them. Therefore, it is very important to find the related factors of disease severity in clinical practice. However, as far as we know, there is no study on the characteristics and risk factors associated with severe and critical COVID-19 pneumonia. Therefore, in this study, we compared the clinical and CT features of 58 ordinary COVID-19 cases and 25 severe/critical cases to explore the related factors of severe /critical patients.

MATERIALS AND METHODS

Our institutional review board approved this retrospective study, and the requirement for informed consent was waived.

Study Population

Ninety patients were diagnosed as COVID-19 according to the Diagnosis and Treatment of Novel Coronavirus Pneumonia (trial version fifth) of China⁸ in our hospitals from January 2020 to February 2020 in this study. The inclusion criteria were as follows: A) having an epidemiological history; B) having one of the following etiological evidences: 1) real-time reverse-transcriptase polymerase-chain-reaction detection of SARS-CoV-2 nucleic acid positive in throat swabs or lower respiratory tract; 2) the virus gene sequencing of respiratory or blood samples was highly homologous with SARS-CoV-2. C) having underwent thin-section CT at least one time. The ordinary patients all had fever or other respiratory symptoms with CT manifestations of pneumonia. The severe/critical patients met any of the following condition:1) respiratory rate ≥ 30 breaths per minute; 2) finger of oxygen saturation $\leq 93\%$ in a resting state; 3) arterial oxygen tension (PaO₂)/inspiratory oxygen fraction (FiO₂) ≤ 300 mmHg (1mmHg=0.133kPa); 4)

respiratory failure occurred and mechanical ventilation required; 5) shock occurred; 6) patients with other organ failure needed intensive care unit monitoring and treatment.⁸ The exclusion criteria were COVID-19 patients without abnormal manifestations on CT. Finally, seven patients were excluded because of no abnormal manifestations on CT and 83 patients were included. The clinical parameters included age, gender, time from illness onset to hospital admission, comorbidities (systemic hypertension, diabetes mellitus, heart disease and chronic obstructive pulmonary disease), symptoms, clinical signs and laboratory findings were collected and evaluated.

CT Examinations and Imaging Evaluation

All scans were obtained using a 16-row multidetector scanner (Siemens Sensation 16, Erlangen, Germany) with the following parameters: 120 kVp, 150 mA, 1.5 mm collimation, 1.35:1 pitch, sharp kernel (B80f), reconstruction matrix of 512×512, slice thickness of 1.0mm, and high spatial resolution algorithm. Two chest radiologists with 10 and 8 years of experience who were blinded to the clinical data evaluated the CT findings in consensus. For each of the 83 patients, the initial ~~c~~hest CT images were evaluated for the following characteristics based on the Fleischner Society Nomenclature recommendations and similar studies:^{9,10} ground-glass opacity (GGO), consolidation, nodule, reticulation, interlobular septal thickening, crazy-paving pattern, ~~“spider web sign”~~, linear opacities, subpleural curvilinear line, bronchial wall thickening, lymph node enlargement, pleural effusion and pericardial effusion. The “spider web sign” was defined as a triangular or angular GGO in the subpleural lung with the internal interlobular septa thickened like a net, the adjacent pleura was pulled and formed a spider web-like shape in the corner. To quantify the extent of lesions, a thin-section CT score was assigned on the basis of ~~the~~ all abnormal

areas involved.¹¹ Each lobe was assigned a score that was based on the following: score 0, 0% involvement; score 1, less than 5% involvement; score 2, 5% to 25% involvement; score 3, 26% to 49% involvement; score 4, 50% to 75% involvement; and score 5, greater than 75% involvement.

There was a score of 0–5 for each lobe, with a total possible score of 0–25. The software of the Pulmonary Infection Assistant Diagnosis (V1.7.0.1, Dexin Medical Imaging Technology Co., Ltd, Xian City, Shaanxi Province, China) was applied to acquire the 3D-visualization of CT-VRT by automatically segment the whole lung and pulmonary lesions, then further precisely manual correction was made.

Statistical Analysis

All statistical analyses were performed by using SPSS statistical software (version 20.0, IBM) and MedCalc software (version 15.2.2, MedCalc Software). Categorical variables were described as frequency rates and percentages, and quantitative variables were described using mean (SD) or median (interquartile range, IQR) values. The χ^2 test and Fisher exact test were used for categorical variables. Quantitative variables were tested for normality using Shapiro-Wilk tests. Normally distributed data were analyzed by independent sample t test; otherwise, the Mann-Whitney U test was used. Receiver operating characteristic (ROC) analysis was used to determine the clinical value of CT scores in distinguishing the ordinary and severe/critical types and find the corresponding cutoff value. For logistic regression analysis, quantitative variables were transformed into categorical variables according to their normal ranges or the cutoff values provided by ROC analysis. Then a univariate logistic regression analysis was performed to identify the clinical and CT features associated with severe/critical COVID-19 pneumonia cases. *P* values < 0.05 were considered as statistically significant.

RESULTS

Characteristics and Clinical Manifestations

The most common symptoms in 83 patients with COVID-19 pneumonia were fever, cough, expectoration and myalgia. Less common symptoms were headache, dyspnea, abdominal pain/diarrhea, pharyngeal discomfort and chest pain. (Table 1).

Twenty-five (30.1%) of them were severe/critical cases, and 58 (69.9%) of them were ordinary cases. Compared with the ordinary group, the severe/critical patients were significantly older (mean age, 53.7 years [SD, 12.3] vs 41.9 years [SD,10.6]; $P < 0.001$) and had more comorbidities of diabetes mellitus and chronic obstructive pulmonary disease. No difference was observed in the proportion of men and women between the two groups. The median time from illness onset to hospital admission in severe/critical patients (8 days [6-12]) was significantly longer than those of the ordinary patients (6 days [3-8.5]) ($P = 0.006$). Compared with the ordinary patients, severe/critical patients had higher body temperature and higher incidences of cough, expectoration, dyspnea and chest pain (Table 1). No significant differences of heart rate, respiratory rate and arterial pressure were found between the two groups.

Laboratory Parameters

Compared with the ordinary patients, the severe/critical patients had increased neutrophil ratio, C-reactive protein and procalcitonin, while decreased lymphocyte ratio and lymphocyte count (Table 2). White blood cell count and neutrophil count were numerically increased in severe/critical group, but the difference did not reach statistical significance. The oxyhemoglobin saturation of the severe/critical patients was significantly lower than that of the ordinary patients.

Chest CT Findings

The common chest CT features of both groups included GGO (81/83, 97.6%), linear opacities (54/83, 65.1%), consolidation (53/83, 63.9%), interlobular septal thickening (52/83, 62.7%) and crazy-paving pattern (30/83, 36.1%) (Table 3). The occurrence rates of consolidation, linear opacities, crazy-paving pattern and bronchial wall thickening in severe/critical patients were significantly higher than those of the ordinary patients (Fig.1, Fig.2). Besides, severe/critical patients showed higher incidences of lymph node enlargement, pericardial effusion and pleural effusion than ordinary patients. The CT scores of the severe/critical patients were significantly higher than those of the ordinary patients ($P < 0.001$). The number of lung lobes involvement for severe/critical group was significantly higher than that of the ordinary group. For ROC analysis, the area under the ROC curve (AUC) of CT score was 0.87 (95% CI: 0.78, 0.94; $P < 0.001$) for the ordinary and severe/critical patients discrimination. When the cutoff value of CT score was 7, the sensitivity and specificity were 80.0% and 82.8% respectively.

Factors Associated with Severe/critical COVID-19 Pneumonia

Table 4 showed the results of univariate logistic regression analyses in relationship to severe/critical COVID-19 pneumonia. The clinical factors of age > 50 years old, comorbidities, dyspnea, chest pain, cough, expectoration, decreased lymphocytes and increased inflammation indicators were risk factors for severe/critical COVID-19 pneumonia. CT findings of consolidation, linear opacities, crazy-paving pattern, bronchial wall thickening, high CT scores (>7) and extrapulmonary lesions were imaging features of severe/critical COVID-19 pneumonia.

DISCUSSION

Compared with the ordinary patients, the severe/critical patients have poor prognosis and

high mortality^{12,13}. Studying the clinical and imaging characteristics of them is helpful to deepen our understanding of the mechanism of severe/critical conditions and promote its clinical diagnosis and treatment. The objective of this study was to identify clinical and CT features associated with severe/critical COVID-19 pneumonia by comparing severe/critical patients with ordinary patients.

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In this study, we found that the severe/critical patients were older and had more underlying diseases than the ordinary cases. The people with ~~higher age or poor state of health-old age or poor health-often~~ suffer from serious diseases, which may be the result of their weakened immune function.⁶ There was no difference in the ratio of men and women between the two groups, indicating that gender was not a risk factor for disease severity.¹⁴³ Compared with the ordinary group, the severe/critical group had higher incidences of chest pain and dyspnea. Chest pain may result from the inflammatory ~~affection of the pleura-stimulation to pleura~~. Dyspnea is related to the severe damage to alveoli in the severe/critical group. The high body temperature may indicate that the immune system of severe/critical patients were highly activated. The occurrence of these symptoms could help clinicians identify the disease severity in clinical practice.

In our study, there were multiple laboratory indicator differences between the ordinary and severe/critical group. The decrease of lymphocytes in the severe/critical patients indicates that a large number of immune cells are consumed and the immune function is inhibited. Damage to lymphocytes may be critical in the exacerbations of patients, and the decreased lymphocytes could be used as an important index in the evaluation of disease severity.¹⁵³ The increased values of neutrophil ratio, C-reactive protein and procalcitonin in severe/critical group may be related to cytokine storm induced by virus invasion and comorbid with other kinds of infections, which was

supported by the recent studies.⁶ Timely prevention of infection may help reduce complication and mortality.

Chest CT can accurately evaluate the type and extent of lung lesions. In this study we found that the most common CT findings were GGO, consolidation, crazy-paving pattern and “spider web sign” for both groups of COVID-19 pneumonia. Compared with ordinary groups, consolidation was significantly more frequent in severe/critical patients, which indicates that the alveoli are completely filled by inflammatory exudation.^{4,6} This usually means that the virus diffuses into the respiratory epithelium, leading to necrotizing bronchitis and diffuse alveolar damage.^{13,6,17,8,6} Severe/critical patients showed more lymph node enlargement, pericardial effusion and pleural effusion. These extrapulmonary lesions may indicate the occurrence of severe inflammation. Although GGO is the most common CT feature of COVID-19 pneumonia, no statistical incidence difference was observed between our two groups. The CT scores of the severe/critical group were significantly higher than those of the ordinary group. It can accurately distinguish the severe/critical patients from the ordinary patients (AUC = 0.87), which is helpful for the judgment of clinical condition and has important clinical value. To sum up, CT can evaluate the severity of the disease, which is of great significance for the diagnosis and follow-up of COVID-19 pneumonia.

This study has several limitations. Firstly, the data of the two groups were not balanced, and the sample size of the severe/critical group was relatively small. Further studies with more patients especially severe/critical patients are warranted. Secondly, because most patients remain in the hospital at the time of submission, it is difficult to assess the risk factors for poor outcomes. Finally, none of the patients had a lung biopsy or autopsy to reflect the histopathological changes.

In conclusion, in this study we found that the clinical factors of age > 50 years old, comorbidities, dyspnea, chest pain, cough, expectoration, decreased lymphocytes and increased inflammation indicators may be risk factors for severe/critical COVID-19 pneumonia. CT findings of consolidation, linear opacities, crazy-paving pattern, bronchial wall thickening, high CT scores and extrapulmonary lesions may be features of severe/critical COVID-19 pneumonia. CT plays an important role in the diagnosis and disease severity evaluation of this disease.

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FIGURE 1. Chest CT of a 44-year-old man with ordinary COVID-19 pneumonia (CT score = 5). (A) An axial CT image showed ~~M~~ multiple small regions of subpleural GGO with superimposed inter- and intralobular septal thickening. (B) ~~3D-visualization of CT-VRT 3D-postconstruction~~ showed the extent of ~~lesions-GGO~~ with scattered pattern.

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FIGURE 2. ~~Chest CT findings of severe/critical COVID-19 pneumonia (CT score =18), a Chest CT of a~~ 60-year-old man with ~~dyspnea and pleural effusion-severe/critical COVID-19 pneumonia~~. (A) An axial CT image showed ~~D~~ diffuse large regions of crazy-paving pattern (GGO with superimposed inter- and intralobular septal thickening) with partial consolidation and bronchial wall thickening. (B) ~~3D-3D-visualization of CT-VRT postconstruction~~ showed the diffuse extent of ~~GGO and consolidation~~ lesions.

TABLE 1. Baseline Characteristics between Severe/critical Group and Ordinary Group

Parameter	Total (n=83)	Severe/critical Group (n=25)	Ordinary Group (n=58)	P Value
Age (y)	45.5(12.3)	53.7(12.3)	41.9(10.6)	< 0.001
Onset of symptoms to hospital (d)*	7.00 (4.75-9.00)	8.00 (6.00-12.00)	6.00 (3.00-8.50)	0.006
Sex				
Male	44 (53.0%)	15 (60%)	29 (50.0%)	0.402
Female	39 (47.0%)	10 (40%)	29 (50.0%)	
Comorbidities	15 (18.1%)	11 (44.0%)	4 (6.9%)	< 0.001
Hypertension	5 (6.0%)	2 (8.0%)	3 (5.2%)	0.635
Diabetes mellitus	7 (7.8%)	7 (28.0%)	0 (0.0%)	< 0.001
COPD	5 (6.0%)	4 (16.0%)	1 (1.7%)	0.027
Heart disease	1 (1.2%)	1 (4.0%)	0 (0.0%)	0.301
Symptoms and Signs				
Fever	72 (86.7%)	22 (88.0%)	50 (86.2%)	1.000
Cough	65 (78.3%)	24 (96.0%)	41 (70.7%)	0.010
Expectoration	15 (18.1%)	9 (36.0%)	6 (10.3%)	0.013
Myalgia	15 (18.1%)	5 (20.0%)	10 (17.2%)	1.000
Headache	9 (10.8%)	3 (12.0%)	6 (10.3%)	1.000
Dyspnea	9 (10.8%)	7 (28.0%)	2 (3.4%)	0.004
Abdominal pain/Diarrhea	7 (8.4%)	2 (8.0%)	5 (8.6%)	1.000
Pharyngeal discomfort	6 (7.2%)	2 (8.0%)	4 (6.9%)	1.000
Chest pain	5 (6.0%)	4 (16.0%)	1 (1.7%)	0.027
Temperature (°C)	37.8 (0.7)	38.0(0.9)	37.6 (0.6)	0.048
Heart rate (beats per minute)	90 (12)	92 (14)	89 (11)	0.437
Respiratory rate	20 (20-22)	21 (19.5-24.5)	20 (20-22)	0.165
Median arterial pressure (mmHg)	93.3(86.0-101.0)	91.0(84.3-100.5)	93.3 (87.2-103.3)	0.204

Data are n (%), mean (SD), median (IQR). COPD= chronic obstructive pulmonary disease. * One patient who came to the hospital for health examination without symptom was not included in statistics.

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TABLE 2. Laboratory Findings between Severe/critical Group and Ordinary Group

Parameter	Total (n=83)	Severe/critical Group (n=25)	Ordinary Group (n=58)	P Value
White blood cell count ($\times 10^9/L$)	5.30 (4.20-6.80)	5.50 (4.10-7.70)	5.27 (4.20-6.30)	0.634
Increased	9 (10.8%)	4 (16.0%)	5 (8.6%)	0.544
Decreased	10 (12.0%)	4 (16.0%)	6 (10.3%)	0.720
Neutrophil ratio (%)	71.52 (11.31)	80.08 (9.51)	67.84 (10.00)	< 0.001
Increased	25 (30.1%)	16 (64.0%)	9 (15.5%)	< 0.001
Decreased	1 (1.2%)	0 (0.0%)	1 (1.7%)	1.000
Lymphocyte ratio (%)	20.59 (9.39)	13.20 (6.27)	23.78 (8.72)	< 0.001
Decreased	40 (48.2%)	20 (80.0%)	20 (34.5%)	< 0.001
Monocyte ratio (%)	7.17 (2.93)	6.16 (4.00)	7.60 (2.23)	0.100
Increased	15 (18.1%)	6 (24.0%)	9 (15.5%)	0.542
Decreased	7 (8.4%)	6 (24.0%)	1 (1.7%)	0.003
Neutrophil count ($\times 10^9/L$)	3.61 (2.67-5.56)	4.36 (2.87-6.48)	3.50 (2.64-4.46)	0.218
Increased	17 (20.5%)	7 (28.0%)	10 (17.2%)	0.265
Decreased	5 (6.0%)	2 (8.0%)	3 (5.2%)	0.635
Lymphocyte count ($\times 10^9/L$)	1.05 (0.75-1.32)	0.70 (0.44-0.95)	1.23 (0.93-1.42)	< 0.001
Decreased	44 (53.0%)	22 (88.0%)	22 (37.9%)	< 0.001
Monocyte count ($\times 10^9/L$)	0.39 (0.27-0.53)	0.34 (0.15-0.51)	0.42 (0.29-0.53)	0.045
Increased	12 (14.5%)	2 (8.0%)	10 (17.2%)	0.448
Decreased	2 (2.4%)	2 (8.0%)	0 (0.0%)	0.088
C-reactive protein (mg/L)	16.70 (3.58-60.87)	89.20 (47.88-134.64)	9.59 (2.07-29.89)	< 0.001
Increased	50 (60.2%)	23 (92.0%)	27 (46.6%)	< 0.001
Procalcitonin (ng/mL)	0.048 (0.032-0.085)	0.086 (0.054-0.215)	0.038 (0.028-0.068)	< 0.001
Increased	44 (53.0%)	21 (84.0%)	23 (39.7%)	< 0.001
Oxyhemoglobin saturation (%)	97.00 (95.10-98.00)	95.10 (92.90-97.45)	97.00 (96.00-98.00)	0.002
Decreased	16 (19.3%)	11 (44.0%)	5 (8.6%)	0.001

Data are n (%), mean (SD), median (IQR). Increased means over the upper limit of the normal range and decreased means below the lower limit of the normal range.

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TABLE 3. CT Features between Severe/critical Group and Ordinary Group

Parameter	Total (n=83)	Severe/critical Group (n=25)	Ordinary Group (n=58)	P Value
CT score	5 (4-8)	11 (8-15.5)	5 (2.5-5)	< 0.001
GGO	81 (97.6%)	25 (100.0%)	56 (96.6%)	1.000
Linear opacities	54 (65.1%)	23 (92.0%)	31 (53.4%)	0.001
Consolidation	53 (63.9%)	22 (88.0%)	31 (53.4%)	0.003
Interlobular septal thickening	52 (62.7%)	19 (76.0%)	33 (56.9%)	0.099
Crazy-paving pattern	30 (36.1%)	14 (56.0%)	16 (27.6%)	0.013
Spider web sign	21 (25.3%)	4 (16.0%)	17 (29.3%)	0.201
Bronchial wall thickening	19 (22.9%)	16 (64.0%)	3 (5.2%)	< 0.001
Subpleural curvilinear line	17 (20.5%)	8 (32.0%)	9 (15.5%)	0.088
Nodule	6 (7.2%)	3 (12.0%)	3 (5.2%)	0.359
Reticulation	4 (4.8%)	3 (12.0%)	1 (1.7%)	0.079
Lymph node enlargement	7 (8.4%)	7 (28.0%)	0 (0.0%)	< 0.001
Pleural effusion	7 (8.4%)	7 (28.0%)	0 (0.0%)	< 0.001
Pericardial effusion	4 (4.8%)	4 (16.0%)	0 (0.0%)	0.007
Frequency of lobe involvement				
Right upper lobe	62 (64.7%)	23 (92.0%)	39 (67.2%)	0.017
Right middle lobe	61 (73.5%)	22 (88.0%)	39 (67.2%)	0.049
Right lower lobe	78 (94.0%)	25 (100.0%)	53 (91.4%)	0.316
Left upper lobe	71 (85.5%)	24 (96.0%)	47 (81.0%)	0.150
Left lower lobe	80 (96.4%)	25 (100.0%)	55 (94.8%)	0.550
Upper lobe	74 (89.2%)	24 (96.0%)	50 (86.2%)	0.351
Lower lobe	80 (96.4%)	25 (100.0%)	55 (94.8%)	0.550
Bilateral lung disease	79 (95.2%)	25 (100.0%)	54 (93.1%)	0.310
Number of lobes involved	5 (4-5)	5 (5-5)	5 (3-5)	0.003

Data are n (%) and median (IQR). GGO = ground-glass opacity.

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TABLE 1. Baseline Characteristics between Severe/critical Group and Ordinary Group

Parameter	Total (n=83)	Severe/critical Group (n=25)	Ordinary Group (n=58)	P Value
Age (y)	45.5(12.3)	53.7(12.3)	41.9(10.6)	< 0.001
Onset of symptoms to hospital (d)*	7.00 (4.75-9.00)	8.00 (6.00-12.00)	6.00 (3.00-8.50)	0.006
Sex				
Male	44 (53.0%)	15 (60%)	29 (50.0%)	0.402
Female	39 (47.0%)	10 (40%)	29 (50.0%)	
Comorbidities				
Hypertension	5 (6.0%)	2 (8.0%)	3 (5.2%)	0.635
Diabetes mellitus	7 (7.8%)	7 (28.0%)	0 (0.0%)	< 0.001
COPD	5 (6.0%)	4 (16.0%)	1 (1.7%)	0.027
Heart disease	1 (1.2%)	1 (4.0%)	0 (0.0%)	0.301
Symptoms and Signs				
Fever	72 (86.7%)	22 (88.0%)	50 (86.2%)	1.000
Cough	65 (78.3%)	24 (96.0%)	41 (70.7%)	0.010
Expectoration	15 (18.1%)	9 (36.0%)	6 (10.3%)	0.013
Myalgia	15 (18.1%)	5 (20.0%)	10 (17.2%)	1.000
Headache	9 (10.8%)	3 (12.0%)	6 (10.3%)	1.000
Dyspnea	9 (10.8%)	7 (28.0%)	2 (3.4%)	0.004
Abdominal pain/Diarrhea	7 (8.4%)	2 (8.0%)	5 (8.6%)	1.000
Pharyngeal discomfort	6 (7.2%)	2 (8.0%)	4 (6.9%)	1.000
Chest pain	5 (6.0%)	4 (16.0%)	1 (1.7%)	0.027
Temperature (°C)	37.8 (0.7)	38.0(0.9)	37.6 (0.6)	0.048
Heart rate (beats per minute)	90 (12)	92 (14)	89 (11)	0.437
Respiratory rate	20 (20-22)	21 (19.5-24.5)	20 (20-22)	0.165
Median arterial pressure (mmHg)	93.3(86.0-101.0)	91.0(84.3-100.5)	93.3 (87.2-103.3)	0.204

Data are n (%), mean (SD), median (IQR). COPD= chronic obstructive pulmonary disease. * One patient who came to the hospital for health examination without symptom was not included in statistics.

TABLE 2. Laboratory Findings between Severe/critical Group and Ordinary Group

Parameter	Total (n=83)	Severe/critical Group (n=25)	Ordinary Group (n=58)	P Value
White blood cell count ($\times 10^9/L$)	5.30 (4.20-6.80)	5.50 (4.10-7.70)	5.27 (4.20-6.30)	0.634
Increased	9 (10.8%)	4 (16.0%)	5 (8.6%)	0.544
Decreased	10 (12.0%)	4 (16.0%)	6 (10.3%)	0.720
Neutrophil ratio (%)	71.52 (11.31)	80.08 (9.51)	67.84 (10.00)	<0.001
Increased	25 (30.1%)	16 (64.0%)	9 (15.5%)	<0.001
Decreased	1 (1.2%)	0 (0.0%)	1 (1.7%)	1.000
Lymphocyte ratio (%)	20.59 (9.39)	13.20 (6.27)	23.78 (8.72)	<0.001
Decreased	40 (48.2%)	20 (80.0%)	20 (34.5%)	<0.001
Monocyte ratio (%)	7.17 (2.93)	6.16 (4.00)	7.60 (2.23)	0.100
Increased	15 (18.1%)	6 (24.0%)	9 (15.5%)	0.542
Decreased	7 (8.4%)	6 (24.0%)	1 (1.7%)	0.003
Neutrophil count ($\times 10^9/L$)	3.61 (2.67-5.56)	4.36 (2.87-6.48)	3.50 (2.64-4.46)	0.218
Increased	17 (20.5%)	7 (28.0%)	10 (17.2%)	0.265
Decreased	5 (6.0%)	2 (8.0%)	3 (5.2%)	0.635
Lymphocyte count ($\times 10^9/L$)	1.05 (0.75-1.32)	0.70 (0.44-0.95)	1.23 (0.93-1.42)	<0.001
Decreased	44 (53.0%)	22 (88.0%)	22 (37.9%)	<0.001
Monocyte count ($\times 10^9/L$)	0.39 (0.27-0.53)	0.34 (0.15-0.51)	0.42 (0.29-0.53)	0.045
Increased	12 (14.5%)	2 (8.0%)	10 (17.2%)	0.448
Decreased	2 (2.4%)	2 (8.0%)	0 (0.0%)	0.088
C-reactive protein (mg/L)	16.70 (3.58-60.87)	89.20 (47.88-134.64)	9.59 (2.07-29.89)	<0.001
Increased	50 (60.2%)	23 (92.0%)	27 (46.6%)	<0.001
Procalcitonin (ng/mL)	0.048 (0.032-0.085)	0.086 (0.054-0.215)	0.038 (0.028-0.068)	<0.001
Increased	44 (53.0%)	21 (84.0%)	23 (39.7%)	<0.001
Oxyhemoglobin saturation (%)	97.00 (95.10-98.00)	95.10 (92.90-97.45)	97.00 (96.00-98.00)	0.002
Decreased	16 (19.3%)	11 (44.0%)	5 (8.6%)	0.001

Data are n (%), mean (SD), median (IQR). Increased means over the upper limit of the normal range and decreased means below the lower limit of the normal range.

TABLE 3. CT Features between Severe/critical Group and Ordinary Group

Parameter	Total (n=83)	Severe/critical Group (n=25)	Ordinary Group (n=58)	<i>P</i> Value
CT score	5 (4-8)	11 (8-15.5)	5 (2.5-5)	< 0.001
GGO	81 (97.6%)	25 (100.0%)	56 (96.6%)	1.000
Linear opacities	54 (65.1%)	23 (92.0%)	31 (53.4%)	0.001
Consolidation	53 (63.9%)	22 (88.0%)	31 (53.4%)	0.003
Interlobular septal thickening	52 (62.7%)	19 (76.0%)	33 (56.9%)	0.099
Crazy-paving pattern	30 (36.1%)	14 (56.0%)	16 (27.6%)	0.013
Spider web sign	21 (25.3%)	4 (16.0%)	17 (29.3%)	0.201
Bronchial wall thickening	19 (22.9%)	16 (64.0%)	3 (5.2%)	< 0.001
Subpleural curvilinear line	17 (20.5%)	8 (32.0%)	9 (15.5%)	0.088
Nodule	6 (7.2%)	3 (12.0%)	3 (5.2%)	0.359
Reticulation	4 (4.8%)	3 (12.0%)	1 (1.7%)	0.079
Lymph node enlargement	7 (8.4%)	7 (28.0%)	0 (0.0%)	< 0.001
Pleural effusion	7 (8.4%)	7 (28.0%)	0 (0.0%)	< 0.001
Pericardial effusion	4 (4.8%)	4 (16.0%)	0 (0.0%)	0.007
Frequency of lobe involvement				
Right upper lobe	62 (64.7%)	23 (92.0%)	39 (67.2%)	0.017
Right middle lobe	61 (73.5%)	22 (88.0%)	39 (67.2%)	0.049
Right lower lobe	78 (94.0%)	25 (100.0%)	53 (91.4%)	0.316
Left upper lobe	71 (85.5%)	24 (96.0%)	47 (81.0%)	0.150
Left lower lobe	80 (96.4%)	25 (100.0%)	55 (94.8%)	0.550
Upper lobe	74 (89.2%)	24 (96.0%)	50 (86.2%)	0.351
Lower lobe	80 (96.4%)	25 (100.0%)	55 (94.8%)	0.550
Bilateral lung disease	79 (95.2%)	25 (100.0%)	54 (93.1%)	0.310
Number of lobes involved	5 (4-5)	5 (5-5)	5 (3-5)	0.003

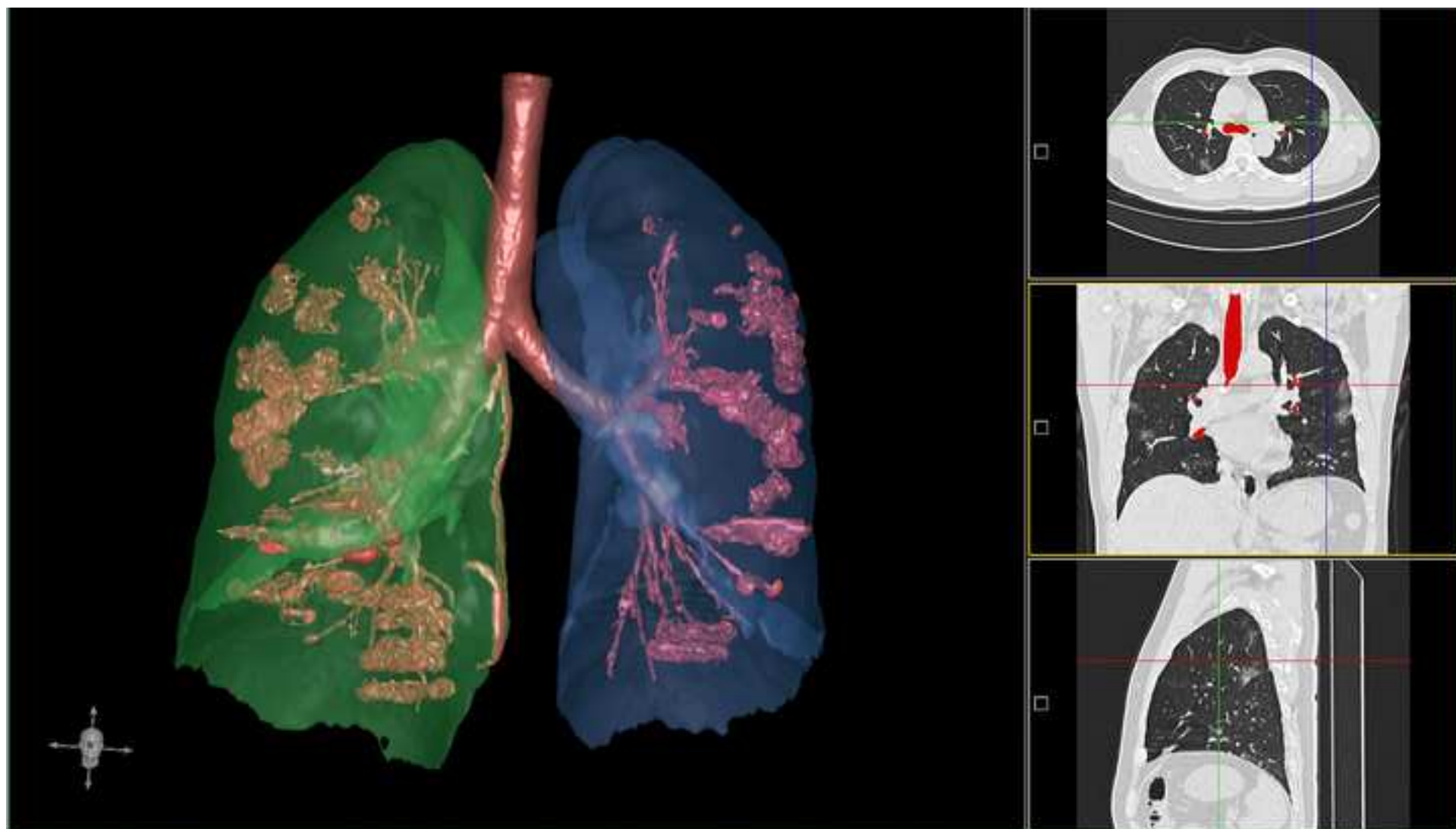
Data are n (%) and median (IQR). GGO = ground-glass opacity.

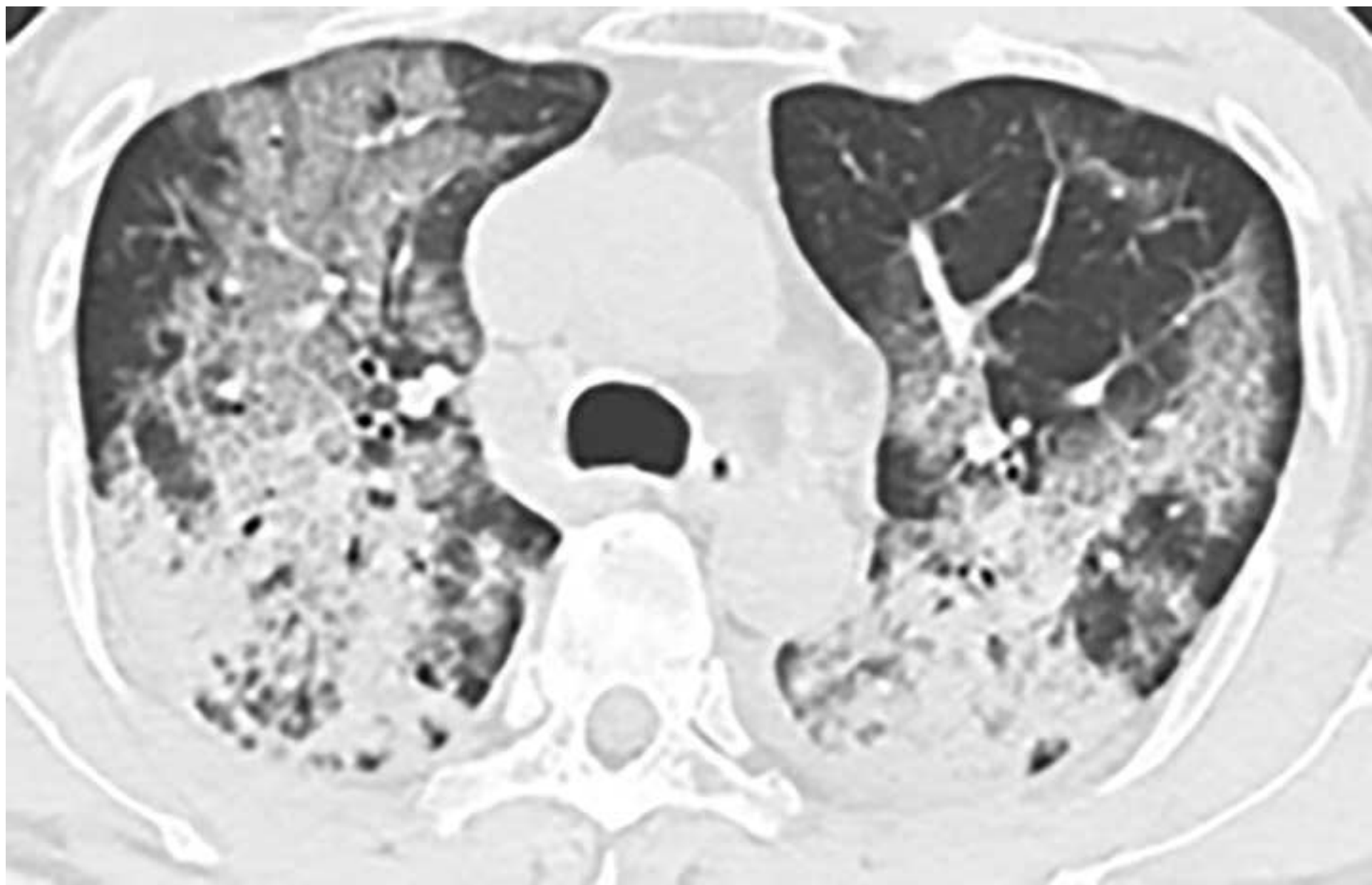
TABLE 4. Univariate Logistic Analysis of Clinical and CT features for Severe/critical COVID-19 Pneumonia

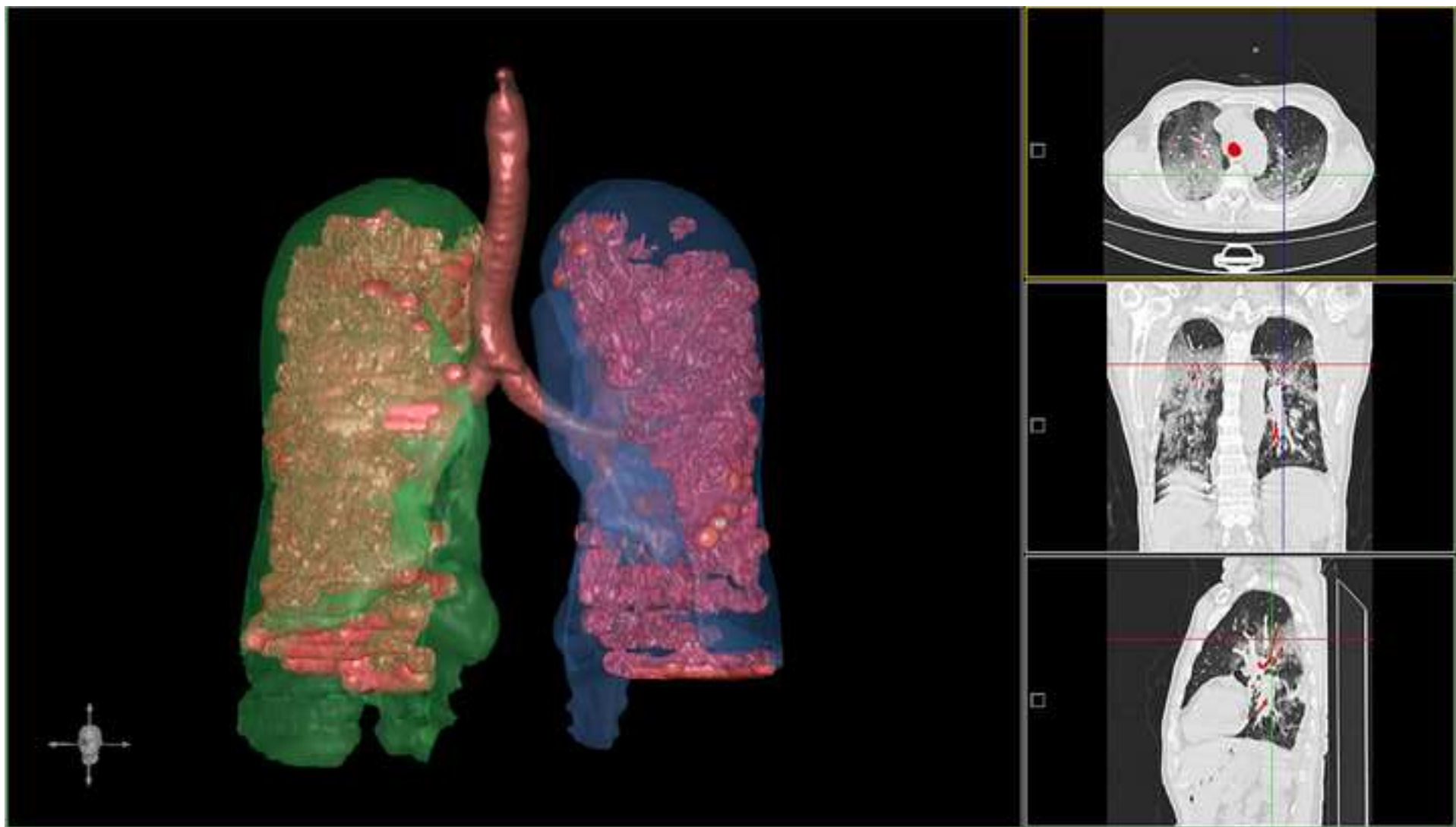
Parameter	Odds Ratio	P Value
Age > 50y	7.596 (2.664-21.659)	< 0.001
Comorbidities	10.607 (2.930-38.399)	< 0.001
Dyspnea	10.899 (2.073-57.198)	0.005
Chest pain	10.857 (1.147-102.773)	0.038
Cough	9.951 (1.245-79.554)	0.030
Expectoration	4.875 (1.505-15.789)	0.008
Neutrophil ratio increased	9.679 (3.278-28.577)	< 0.001
Lymphocyte ratio decreased	7.600 (2.481-23.284)	< 0.001
Monocyte ratio decreased	18.000 (2.035-159.193)	0.009
Lymphocyte count decreased	12.000 (3.213-44.819)	< 0.001
C-reactive protein increased	13.204 (2.847-61.237)	0.001
Procalcitonin increased	7.989 (2.426-26.305)	0.001
Oxyhemoglobin saturation decreased	8.329 (2.483-27.933)	< 0.001
CT score > 7	19.200 (5.820-63.336)	< 0.001
Consolidation	6.387 (1.720-23.719)	0.006
Crazy-paving pattern	3.341 (1.257-8.878)	0.016
Linear opacities	10.016 (2.160-46.454)	0.003
Bronchial wall thickening	32.593 (7.876-134.880)	< 0.001
Right upper lobe	5.603 (1.195-26.277)	0.029
Right middle lobe	3.573 (0.950-13.442)	0.060

Data in parentheses are 95% confidence intervals. COVID-19 = Corona Virus Disease 2019.









The Clinical and Chest CT Features Associated with Severe and Critical COVID-19 Pneumonia

Abstract

Objective: To investigate the clinical and CT features associated with severe and critical Corona Virus Disease 2019 (COVID-19) pneumonia.

Materials and Methods: Eighty-three patients with COVID-19 pneumonia including 25 severe/critical cases and 58 ordinary cases were enrolled. The chest CT images and clinical data of them were reviewed and compared. The risk factors associated with disease severity were analyzed.

Results: Compared with the ordinary patients, the severe/critical patients had older ages, higher incidence of comorbidities, cough, expectoration, chest pain and dyspnea. The incidences of consolidation, linear opacities, crazy-paving pattern and bronchial wall thickening in severe/critical patients were significantly higher than those of the ordinary patients. Besides, severe/critical patients showed higher incidences of lymph node enlargement, pericardial effusion and pleural effusion than the ordinary patients. The CT scores of severe/critical patients were significantly higher than those of the ordinary patients ($P < 0.001$). Receiver operating characteristic (ROC) curve showed that the sensitivity and specificity of CT Score were 80.0% and 82.8% respectively for the discrimination of the two types. The clinical factors of age > 50 years old, comorbidities, dyspnea, chest pain, cough, expectoration, decreased lymphocytes and increased inflammation indicators were risk factors for severe/critical COVID-19 pneumonia. CT findings of consolidation, linear opacities, crazy-paving pattern, bronchial wall thickening, high

CT scores and extrapulmonary lesions were features of severe/critical COVID-19 pneumonia.

Conclusions: There are significant differences in clinical symptoms, laboratory examinations and CT manifestations between the ordinary patients and the severe/critical patients. Many factors are related to the severity of the disease, which can help clinicians to judge the severity of the patient and evaluate the prognosis.

Key Word: COVID-19, SARS-CoV-2, acute respiratory disease, pneumonia, severity, risk factor

INTRODUCTION

Since the middle of December 2019, many cases of pneumonia with unknown cause have been found in some hospitals in Wuhan City, Hubei Province, China.¹ At present, it has been confirmed as a new type of acute respiratory infectious disease caused by coronavirus infection.² On 12 February, 2020, the International Committee on Taxonomy of Viruses announced that the official classification of the new coronavirus is severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2).³ The World Health Organization (WHO) announced the same day that the official name of the disease caused by the virus is Corona Virus Disease 2019 (COVID-19).⁴ Up to 24:00 on 22 February 2020, 77041 confirmed cases (including 10968 severe cases), 4148 suspected cases and 2445 dead cases have been officially reported in China.⁵ Many cases spread all over the world, including the United States, Japan, Singapore, Thailand, South Korea, etc, which suggested that the COVID-19 poses significant threats to international health.

Although most patients have mild symptoms and good prognosis, COVID-19 can develop to severe illnesses including pneumonia, pulmonary edema, acute respiratory distress syndrome, multiple organ failure or even death.^{6,7} The successful treatment of severe and critical cases is the

key to reduce the complication and mortality. Basic disease treatment, secondary infection prevention, and timely organ function support are needed for them. Therefore, it is very important to find the related factors of disease severity in clinical practice. However, as far as we know, there is no study on the characteristics and risk factors associated with severe and critical COVID-19 pneumonia. Therefore, in this study, we compared the clinical and CT features of 58 ordinary COVID-19 cases and 25 severe/critical cases to explore the related factors of severe /critical patients.

MATERIALS AND METHODS

Our institutional review board approved this retrospective study, and the requirement for informed consent was waived.

Study Population

Ninety patients were diagnosed as COVID-19 according to the Diagnosis and Treatment of Novel Coronavirus Pneumonia (trial version fifth) of China⁸ in our hospitals from January 2020 to February 2020 in this study. The inclusion criteria were as follows: A) having an epidemiological history; B) having one of the following etiological evidences: 1) real-time reverse-transcriptase polymerase-chain-reaction detection of SARS-CoV-2 nucleic acid positive in throat swabs or lower respiratory tract; 2) the virus gene sequencing of respiratory or blood samples was highly homologous with SARS-CoV-2. C) having underwent thin-section CT at least one time. The ordinary patients all had fever or other respiratory symptoms with CT manifestations of pneumonia. The severe/critical patients met any of the following condition: 1) respiratory rate ≥ 30 breaths per minute; 2) finger of oxygen saturation $\leq 93\%$ in a resting state; 3) arterial oxygen tension (P_{aO_2})/inspiratory oxygen fraction (F_{iO_2}) ≤ 300 mmHg (1mmHg=0.133kPa); 4)

respiratory failure occurred and mechanical ventilation required; 5) shock occurred; 6) patients with other organ failure needed intensive care unit monitoring and treatment.⁸ The exclusion criteria were COVID-19 patients without abnormal manifestations on CT. Finally, seven patients were excluded because of no abnormal manifestations on CT and 83 patients were included. The clinical parameters included age, gender, time from illness onset to hospital admission, comorbidities (systemic hypertension, diabetes mellitus, heart disease and chronic obstructive pulmonary disease), symptoms, clinical signs and laboratory findings were collected and evaluated.

CT Examinations and Imaging Evaluation

All scans were obtained using a 16-row multidetector scanner (Siemens Sensation 16, Erlangen, Germany) with the following parameters: 120 kVp, 150 mA, 1.5 mm collimation, 1.35:1 pitch, sharp kernel (B80f), reconstruction matrix of 512×512, slice thickness of 1.0mm, and high spatial resolution algorithm. Two chest radiologists with 10 and 8 years of experience who were blinded to the clinical data evaluated the CT findings in consensus. For each of the 83 patients, the initial chest CT images were evaluated for the following characteristics based on the Fleischner Society Nomenclature recommendations and similar studies:^{9,10} ground-glass opacity (GGO), consolidation, nodule, reticulation, interlobular septal thickening, crazy-paving pattern, linear opacities, subpleural curvilinear line, bronchial wall thickening, lymph node enlargement, pleural effusion and pericardial effusion. The “spider web sign” was defined as a triangular or angular GGO in the subpleural lung with the internal interlobular septa thickened like a net, the adjacent pleura was pulled and formed a spider web-like shape in the corner. To quantify the extent of lesions, a thin-section CT score was assigned on the basis of all abnormal areas

involved.¹¹ Each lobe was assigned a score that was based on the following: score 0, 0% involvement; score 1, less than 5% involvement; score 2, 5% to 25% involvement; score 3, 26% to 49% involvement; score 4, 50% to 75% involvement; and score 5, greater than 75% involvement. There was a score of 0–5 for each lobe, with a total possible score of 0–25. The software of the Pulmonary Infection Assistant Diagnosis (V1.7.0.1, Dexin Medical Imaging Technology Co., Ltd, Xian City, Shaanxi Province, China) was applied to acquire the 3D-visualization of CT-VRT by automatically segment the whole lung and pulmonary lesions, then further precisely manual correction was made.

Statistical Analysis

All statistical analyses were performed by using SPSS statistical software (version 20.0, IBM) and MedCalc software (version 15.2.2, MedCalc Software). Categorical variables were described as frequency rates and percentages, and quantitative variables were described using mean (SD) or median (interquartile range, IQR) values. The χ^2 test and Fisher exact test were used for categorical variables. Quantitative variables were tested for normality using Shapiro-Wilk tests. Normally distributed data were analyzed by independent sample t test; otherwise, the Mann-Whitney U test was used. Receiver operating characteristic (ROC) analysis was used to determine the clinical value of CT scores in distinguishing the ordinary and severe/critical types and find the corresponding cutoff value. For logistic regression analysis, quantitative variables were transformed into categorical variables according to their normal ranges or the cutoff values provided by ROC analysis. Then a univariate logistic regression analysis was performed to identify the clinical and CT features associated with severe/critical COVID-19 pneumonia cases. *P* values < 0.05 were considered as statistically significant.

RESULTS

Characteristics and Clinical Manifestations

The most common symptoms in 83 patients with COVID-19 pneumonia were fever, cough, expectoration and myalgia. Less common symptoms were headache, dyspnea, abdominal pain/diarrhea, pharyngeal discomfort and chest pain. (Table 1).

Twenty-five (30.1%) of them were severe/critical cases, and 58 (69.9%) of them were ordinary cases. Compared with the ordinary group, the severe/critical patients were significantly older (mean age, 53.7 years [SD, 12.3] vs 41.9 years [SD,10.6]; $P < 0.001$) and had more comorbidities of diabetes mellitus and chronic obstructive pulmonary disease. No difference was observed in the proportion of men and women between the two groups. The median time from illness onset to hospital admission in severe/critical patients (8 days [6-12]) was significantly longer than those of the ordinary patients (6 days [3-8.5]) ($P = 0.006$). Compared with the ordinary patients, severe/critical patients had higher body temperature and higher incidences of cough, expectoration, dyspnea and chest pain (Table 1). No significant differences of heart rate, respiratory rate and arterial pressure were found between the two groups.

Laboratory Parameters

Compared with the ordinary patients, the severe/critical patients had increased neutrophil ratio, C-reactive protein and procalcitonin, while decreased lymphocyte ratio and lymphocyte count (Table 2). White blood cell count and neutrophil count were numerically increased in severe/critical group, but the difference did not reach statistical significance. The oxyhemoglobin saturation of the severe/critical patients was significantly lower than that of the ordinary patients.

Chest CT Findings

The common chest CT features of both groups included GGO (81/83, 97.6%), linear opacities (54/83, 65.1%), consolidation (53/83, 63.9%), interlobular septal thickening (52/83, 62.7%) and crazy-paving pattern (30/83, 36.1%) (Table 3). The occurrence rates of consolidation, linear opacities, crazy-paving pattern and bronchial wall thickening in severe/critical patients were significantly higher than those of the ordinary patients (Fig.1, Fig.2). Besides, severe/critical patients showed higher incidences of lymph node enlargement, pericardial effusion and pleural effusion than ordinary patients. The CT scores of the severe/critical patients were significantly higher than those of the ordinary patients ($P < 0.001$). The number of lung lobes involvement for severe/critical group was significantly higher than that of the ordinary group. For ROC analysis, the area under the ROC curve (AUC) of CT score was 0.87 (95% CI: 0.78, 0.94; $P < 0.001$) for the ordinary and severe/critical patients discrimination. When the cutoff value of CT score was 7, the sensitivity and specificity were 80.0% and 82.8% respectively.

Factors Associated with Severe/critical COVID-19 Pneumonia

Table 4 showed the results of univariate logistic regression analyses in relationship to severe/critical COVID-19 pneumonia. The clinical factors of age > 50 years old, comorbidities, dyspnea, chest pain, cough, expectoration, decreased lymphocytes and increased inflammation indicators were risk factors for severe/critical COVID-19 pneumonia. CT findings of consolidation, linear opacities, crazy-paving pattern, bronchial wall thickening, high CT scores (>7) and extrapulmonary lesions were imaging features of severe/critical COVID-19 pneumonia.

DISCUSSION

Compared with the ordinary patients, the severe/critical patients have poor prognosis and

high mortality^{12,13}. Studying the clinical and imaging characteristics of them is helpful to deepen our understanding of the mechanism of severe/critical conditions and promote its clinical diagnosis and treatment. The objective of this study was to identify clinical and CT features associated with severe/critical COVID-19 pneumonia by comparing severe/critical patients with ordinary patients.

In this study, we found that the severe/critical patients were older and had more underlying diseases than the ordinary cases. The people with higher age or poor state of health suffer from serious diseases, which may be the result of their weakened immune function.⁶ There was no difference in the ratio of men and women between the two groups, indicating that gender was not a risk factor for disease severity.¹⁴ Compared with the ordinary group, the severe/critical group had higher incidences of chest pain and dyspnea. Chest pain may result from the inflammatory affection of the pleura. Dyspnea is related to the severe damage to alveoli in the severe/critical group. The high body temperature may indicate that the immune system of severe/critical patients were highly activated. The occurrence of these symptoms could help clinicians identify the disease severity in clinical practice.

In our study, there were multiple laboratory indicator differences between the ordinary and severe/critical group. The decrease of lymphocytes in the severe/critical patients indicates that a large number of immune cells are consumed and the immune function is inhibited. Damage to lymphocytes may be critical in the exacerbations of patients, and the decreased lymphocytes could be used as an important index in the evaluation of disease severity.¹⁵ The increased values of neutrophil ratio, C-reactive protein and procalcitonin in severe/critical group may be related to cytokine storm induced by virus invasion and comorbid with other kinds of infections, which was

supported by the recent studies.⁶ Timely prevention of infection may help reduce complication and mortality.

Chest CT can accurately evaluate the type and extent of lung lesions. In this study we found that the most common CT findings were GGO, consolidation, crazy-paving pattern and “spider web sign” for both groups of COVID-19 pneumonia. Compared with ordinary groups, consolidation was significantly more frequent in severe/critical patients, which indicates that the alveoli are completely filled by inflammatory exudation. This usually means that the virus diffuses into the respiratory epithelium, leading to necrotizing bronchitis and diffuse alveolar damage.^{16,17} Severe/critical patients showed more lymph node enlargement, pericardial effusion and pleural effusion. These extrapulmonary lesions may indicate the occurrence of severe inflammation. Although GGO is the most common CT feature of COVID-19 pneumonia, no statistical incidence difference was observed between our two groups. The CT scores of the severe/critical group were significantly higher than those of the ordinary group. It can accurately distinguish the severe/critical patients from the ordinary patients (AUC = 0.87), which is helpful for the judgment of clinical condition and has important clinical value. To sum up, CT can evaluate the severity of the disease, which is of great significance for the diagnosis and follow-up of COVID-19 pneumonia.

This study has several limitations. Firstly, the data of the two groups were not balanced, and the sample size of the severe/critical group was relatively small. Further studies with more patients especially severe/critical patients are warranted. Secondly, because most patients remain in the hospital at the time of submission, it is difficult to assess the risk factors for poor outcomes. Finally, none of the patients had a lung biopsy or autopsy to reflect the histopathological changes.

In conclusion, in this study we found that the clinical factors of age > 50 years old, comorbidities, dyspnea, chest pain, cough, expectoration, decreased lymphocytes and increased inflammation indicators may be risk factors for severe/critical COVID-19 pneumonia. CT findings of consolidation, linear opacities, crazy-paving pattern, bronchial wall thickening, high CT scores and extrapulmonary lesions may be features of severe/critical COVID-19 pneumonia. CT plays an important role in the diagnosis and disease severity evaluation of this disease.

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FIGURE 1. Chest CT of a 44-year-old man with ordinary COVID-19 pneumonia (CT score = 5). (A) An axial CT image showed multiple small regions of subpleural GGO with superimposed inter- and intralobular septal thickening. (B) 3D-visualization of CT-VRT showed the extent of GGO with scattered pattern.

FIGURE 2. Chest CT findings of severe/critical COVID-19 pneumonia (CT score =18), a 60-year-old man with dyspnea and pleural effusion. (A) An axial CT image showed diffuse large regions of crazy-paving pattern (GGO with superimposed inter- and intralobular septal thickening) with partial consolidation and bronchial wall thickening. (B) 3D-visualization of CT-VRT showed the diffuse extent of GGO and consolidation.