Clinical imaging characteristics of inpatients with COVID-19 in Heilongjiang Province, China: a retrospective study

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Abstract

Objectjve: To investigate the clinical, laboratory, and radiological characteristics of patients with coronavirus disease 2019 (COVID-19) in Heilongjiang Province.

Methods: The present study carried out a retrospective analysis of 59 patients with COVID-19, including 44 patients in the intensive care unit (ICU) and 15 patients in the non-intensive care unit. The characteristics of the two groups of patients were compared.

Results: ICU care group was older and the incidence was higher than that of non-ICU group. Lymphopenia, neutrophils, and increased D-dimer levels were high-risk causes of COVID-19 patients. Compared to the non-ICU care group, the incidence of pulmonary consolidation and Ground-glass opacity combined consolidation in the ICU care group was significantly higher, all lung lobes were more likely to be involved, and the number of lung lobes involved was greater and the area around the bronchi was more likely to be involved. Of the 59 patients with COVID-19 in this group, 15 received mechanical ventilation. All the intubated patients involved lung lobes, and a large number of lesions were seen in the area around the bronchial vessels.

Conclusion: Significant differences were observed in clinical symptoms, laboratory tests, and CT features between the ICU and non-ICU care groups.

Introduction

A new pneumonia caused by the 2019 novel coronavirus (2019-nCoV) broke out in Wuhan, China, in December 2019 [1]. In January 2020, Chinese scientists isolated a novel coronavirus from patients with viral pneumonia, namely severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2, previously known as 2019-nCoV) [2]. Since then, the disease has spread rapidly from Wuhan to other regions. In February 2020, the World Health Organization (WHO) named the disease caused by this virus as coronavirus disease 2019 (COVID-19). Until the submission of this article, several cases have been reported internationally across the six continents.

The 2019-nCoV pandemic has caused severe illness in infected patients, including pneumonia and acute respiratory distress syndrome, as well as death. According to the COVID-19 joint study report released by the National Health Commission of the People's Republic of China, about 80% of the patients have light and common infection, but 13.8% of the patients are severe/critical, posing them at a high risk of mortality [3]. In addition, the prevention and control of severe and critically ill patients are yet to be resolved [3]. Thus, clinicians and radiologists must be able to identify the characteristic imaging manifestations in the chest CT findings of critically ill individuals, such that they can perform specific symptomatic treatment at the earliest, prevent complications, and provide organ functional support. Compared to other methods, computed tomography (CT) is the best technique for early detection of pneumonia. In this epidemic, there are fewer reports of clinical imaging features of severe and critically ill patients. This study describes the clinical, radiological characteristics and laboratory examination data of 59 patients with COVID-19 and compares the intensive care unit (ICU) patients with non-ICU care patients. Thus, we hope that the current results could be used by clinicians in Heilongjiang Province and worldwide for the treatment plan of the infection.

Methods

Study population

The study has been approved by the Ethics Committee of the Second Affiliated Hospital of Harbin Medical University and with the Helsinki Declaration. Informed consent was obtained from all subjects, all subjects are older than 18 years. According to the 2019-nCoV pneumonia diagnosis criteria for the diagnosis and treatment of new coronavirus-caused pneumonia (trial version 6) issued by the National Health Commission of the People's Republic of China [4], the inclusion criteria were as follows: (1) real-time fluorescent Reverse Transcription-Polymerase Chain Reaction (RT-PCR) for detection of positive cDNA of new coronavirus; (2) untreated newly diagnosed patients; (3) all clinical data of patients are complete; (4) All patients underwent at least one CT scan. Exclusion criteria were as follows: (1) treated non-newly diagnosed patients; (2) missing clinical data of patients. A total of 59 COVID-19-confirmed patients between February and March 2020 were included in this study. The cohort was divided into the ICU care group (n=44) and the non-ICU care group (n=15). The clinical data of all patients were evaluated: clinical symptoms such as gender, age, fever, cough, underlying diseases (hypertension, diabetes, cardiovascular disease, chronic obstructive pulmonary disease). Laboratory examination information when the patients were admitted, including white blood cells, lymphocytes, neutrophils, D-dimer, and C-reactive protein levels, as well as imaging data, were collected.

Image analysis

All CT images were analyzed and diagnosed by two radiologists trained in novel coronavirus. Both radiologists have more than five years of diagnostic experience. Two doctors independently diagnosed all patient images and reached consensus. In case of disagreement between the two radiologists, a third trained radiologist with more than ten years of diagnostic experience was consulted to reach a consensus. The imaging features (Ground-glass opacity, consolidation, reticular pattern, nodular opacity), lesion distribution (unilateral/bilateral, upper/middle/lower lobe, central/peripheral/bronchial blood vessel surrounding), and the degree of involvement (focal/multifocal/diffuse, number of lung lobes) were abnormal. The radiographic images and CT scans using descriptors were defined by the Fleischner Society Naming Committee [5]. Ground-glass opacity is defined as a hazy area showing increased lung opacity with indistinct margins of pulmonary vessels on a radiograph but with preserved bronchial and vascular margins on the CT. Consolidation is defined as a homogeneous increase in parenchymal attenuation that obscures vessel margins and airway walls. The reticular pattern is defined as small linear opacities forming a net pattern. Nodular opacity is defined as a well- or poorly-defined rounded opacity, measuring up to 3 cm in diameter. The features of lesion distribution include unilateral/bilateral and upper/middle/lower lobe. The extent of lesion involvement was divided into focality, multifocality, and diffuse. Focality is defined as an abnormal single lesion, and multifocality is defined as more than one lesions; if it is diffusely distributed, it involves one or more lungs. Also, it is necessary to assess whether the lesion occurs centrally (<4 cm from the hilum) or is peripheral or involves the bronchi. The presence of pleural effusion, laterality, and any other lung findings such as mediastinal lymphadenopathy, were recorded.

Statistical analysis

SPSS 19.0 statistical software was used for analysis. Continuous variables were expressed as median (IQR) and compared using the Mann–Whitney U test. Categorical variables were expressed as the number of cases (n) and percentage/rate (%); χ^2 test or Fisher's exact test was applied to compare the ICU and non-ICU care groups. $P<0.05$ was considered statistically significant.

Results

A total of 59 patients that were confirmed cases of COVID-19 in Heilongjiang Province were included in this study. The general clinical data of the patients are shown in Table 1. The median age of the patients was 64.0 (interquartile range (IQR) 56–72) years. The common complications in the patient group included cardiovascular disease (44%), hypertension (42%), diabetes (15%), and rare complications of the chronic obstructive disease (3%), malignancy (2%), and chronic liver disease (2%). Compared to the non-ICU care patients, ICU care patients were older (median age: 67 *vs*. 56); $P = 0.037$) and more likely to have cardiovascular disease (52% *vs*. 20%; $P = 0.030$). The most common clinical symptoms in this study were fever (41/59, 69%), cough (30/59, 51%), and muscle soreness (15/59, 25%), while less common symptoms were dyspnea (14/59, 24%), headache (8/59, 13%), abdominal pain, diarrhea (5/59, 8%), and nausea (3/59, 5%). However, compared to non-ICU care patients, the incidence of muscle soreness in the ICU care patients was reduced (18% *vs*. 47%; $P = 0.042$).

Table 1. Demographics and baseline characteristics of two groups of patients infected with 2019-nCoV.

	All patients (n=59)	ICU care (n=44)	No ICU care (n=15)	*P* value
Characteristics				
Age (y)	64.0(56.0-72.0)	66.5(57.3-75.8)	56.0(50.0-68.0)	0.037
Gender				0.552
Male	29(49%)	23(52%)	6(40%)	
Female	30(51%)	21(48%)	9(60%)	
Exposure history				0.516
Contact with infected patients	42(71%)	30(68%)	12(80%)	
Unknown history	17 (29%)	14(32%)	3(20%)	
Any comorbidity				
Diabetes	9(15%)	6(14%)	3(20%)	0.680
Hypertension	25(42%)	20(45%)	5(33%)	0.412
Cardiovascular disease	26(44%)	23(52%)	3(20%)	0.030
COPD	2(3%)	1(2%)	1(7%)	0.447
Malignancy	1(2%)	1(2%)	0(0%)	--
Chronic liver disease	1(2%)	0(0%)	1(7%)	--
Signs and symptoms				
Fever	41(69%)	31(70%)	10(67%)	0.785
Highest temperature, °C				0.412
<37.3	18(31%)	14(32%)	4(27%)	
37.3–38.0	25(42%)	16(36%)	9(60%)	
38.1–39.0	15(25%)	13(30%)	2(13%)	
>39.0	1(2%)	1(2%)	0(0%)	
Cough	30(51%)	20(45%)	10(67%)	0.205
Myalgia or fatigue	15(25%)	8(18%)	7(47%)	0.042
Headache	8 14%)	4(9%)	4(27%)	0.184
Diarrhoea, bellyache	5(8%)	4(9%)	1(7%)	0.624
Dyspnoea	14(24%)	9(20%)	5(33%)	0.316
Nausea	3(5%)	1(2%)	2(13%)	0.156

Data are median (IQR), n (%), or n/N (%), where N is the total number of patients with available data. *P* values comparing Group1 and Group2 are from χ test, Fisher's exact test, or Mann-Whitney U test. 2019-nCoV=2019 novel coronavirus. COPD=Chronic obstructive pulmonary disease.

The laboratory examination results of 59 patients are summarized in Table 2. White blood cell count (<4 × 109/L; 11/59, 19%) and lymphocyte count (<1.0 ×109/L; 26/59, 44%) was low in some patients. Compared to the non-ICU care patients, the ICU care patients are more likely to have lymphopenia (52% *vs*. 20%; *P* = 0.003), with higher levels of neutrophils and D-dimers (median 3.5 (IQR 2.6−5.2) *vs*. median 1.7 (IQR 0.8−3.1), *P* = 0.003; median 364.6 (IQR 3.5−1475.0) *vs*. median 0.5 (IQR 0.4−6.5), *P* = 0.000, respectively) and lower hemoglobin levels (median 100.5 (IQR 86.0−115.0) *vs*. median 128.0 (IQR 122.0−136.0), *P* < 0.001).

Table 2. Laboratory findings of two groups of patients infected with 2019-nCoV.

Laboratory Findings	All patients (n=59)	ICU care (n=44)	No ICU care (n=15)	*P* value
White blood cell count($\times10^{9}$/L)	5.5(4.3-7.1)	5.2(4.1-7.0)	5.8(4.6-7.0)	0.334
<4	11(19%)	9(20%)	2(13%)	0.894
4-10	42(71%)	30(68%)	12(80%)	
>10	6(10%)	5(11%)	1(7%)	
Neutrophil count($\times10^{9}$/L)	3.2(1.9-4.8)	3.5(2.6-5.2)	1.7(0.8-3.1)	0.003
Lymphocyte count($\times10^{9}$/L)	1.1(0.6-1.5)	0.9(0.6-1.3)	1.6(0.9-2.3)	0.004
<1.0	26(44%)	23(52%)	3(20%)	0.030
≥1.0	33(56%)	21(48%)	12(80%)	
Haemoglobin, g/L	104.0(92.0-122.0)	100.5(86.0-115.0)	128.0(122.0-136.0)	0.000
Platelet count($\times10^{9}$/L)	189.0(145.0-260.0)	194.5(142.0-264.5)	189.0(152.0-255.0)	0.734
<100	11(19%)	9(20%)	2(13%)	0.712
≥100	48(81%)	35(80%)	13(87%)	
Prothrombin time, s	12.4(12.0-13.3)	12.6(12.0-13.4)	12.0(11.9-13.0)	0.458
Activated partial thromboplastin time, s	30.9(28.0-33.3)	31.0(27.0-33.9)	30.5(29.0-31.8)	0.651
D-dimer, mg/L	6.1(1.5-1090.0)	364.6(3.5-1475.0)	0.5(0.4-6.5)	0.000
C-reactive protein, mg/L	8.4(2.0-30.9)	9.9(0.3-180.7)	8.0(0.2-77.9)	0.807
Alanine aminotransferase, U/L	37.6(30.2-45.0)	37.8(25.9-46.7)	36.7(34.4-40.7)	0.862
Aspartate aminotransferase, U/L	26.5(21.2-33.3)	26.5(19.3-35.0)	26.1(23.8-33.3)	0.708
≤40	51(86%)	36(82%)	15(100%)	0.100
>40	8(14%)	8(18%)	0(0%)	
Creatinine, µmol/L	57.1(44.7-89.9)	55.7(42.0-83.0)	89.9(57.0-133.0)	0.008
≤133	53(90%)	41(93%)	12(80%)	0.165
>133	6(10%)	3(7%)	3(20%)	
Creatine kinase, U/L	116.0(34.6-175.3)	130.1(34.8-200.0)	113.9(31.5-167.7)	0.676
≤185	45(76%)	32(73%)	13(87%)	0.483
>185	14(24%)	12(27%)	2(13%)	

Data are median (IQR) or n/N (%), where N is the total number of patients with available data. p values comparing Group1 and Group2 are from χ^{2}, Fisher's exact test, or Mann-Whitney U test. 2019-nCoV=2019 novel coronavirus.

All patients (59/59; 100%) showed abnormal CT findings (Table 3). The main features of the imaging examination were Ground-glass opacity (58/59; 98%; Figure 1A), consolidation (37/59; 63%), and Ground-glass opacity combined consolidation (36/59; 61%; Figure 1B). Compared to the non-ICU care patients, the incidence of consolidation and Ground-glass opacity combined consolidation in patients with ICU care was higher (73% *vs*. 33%, $P = 0.006$; 70% *vs*. 33%, $P = 0.011$, respectively). Next, 40/59 (68%) patients showed involvement of all lung lobes in ICU group (Figure 1C) as compared to the non-ICU care patients, while the incidence of all lung lobes (75% *vs*. 47%, $P = 0.043$) and the number of lung lobes was higher in patients with ICU care (median 5 (IQR 5-5) *vs*. median 4 (IQR 2−5), $P = 0.012$). 43/59 (73%) were multifocal, 15/59 (25%) were diffuse, and only 1/59 (2%) was focal. A significant difference was detected between the degree of lung involvement in ICU and non-ICU care patients ($P = 0.032$). 23/59 (39%) patients had abnormal density shadows around the bronchi, including 21/44 (48%) ICU care patients and 2/15 (13%) non-ICU care patients. The incidence of bronchovascular involvement in patients with ICU care was significantly higher than that in non-ICU care patients (48% *vs*. 13%, $P = 0.040$), which might be observed by difficulty in breathing and needing mechanical ventilation (Figure 1D). Unilateral or bilateral pleural effusions were seen in 7/59 (12%) patients, of which, 6 were in the ICU care group (6/44, 14%) and 1 was in the non-ICU care group (1/15, 7%). In addition, mediastinal lymphadenopathy (short axis >1 cm) was observed in 13/59 cases (22%), fibrous cord shadow in 22/59 cases (37%), and arterial plaque in 32/59 (54%).

15/59 (25%) of the patients included in this study were intubated with respiratory failure. These intubated patients (100%) had Ground-glass opacity, showed bilateral lung involvement, and involved more than three lung lobes. Compared to the non-mechanically ventilated patients, 15 patients requiring mechanical ventilation were more likely to have abnormal lung changes in the area around the bronchi (53% *vs*. 34%) and showed diffuse distribution (47% *vs*. 18%).

Table 3. CT diagnosis characteristics of two groups of patients infected with 2019-nCoV.

Imaging Findings	All patients (n=59)	ICU care (n=44)	No ICU care (n=15)	*P* value
Parenchymal opacities				
Consolidation	37(63%)	32(73%)	5(33%)	0.006
GGO	58(98%)	43(98%)	15(100%)	0.746
GGO and consolidation	36(61%)	31(70%)	5(33%)	0.011
Reticular opacities	13(22%)	7(16%)	6(40%)	0.073
Nodular opacities	11(19%)	8(18%)	3(20%)	0.574
Laterality				0.265
Bilateral	4(7%)	2(5%)	2(13%)	
Unilateral	55(93%)	42(95%)	13(87%)	
Involvement range of lung lobes				
All lung lobe	40(68%)	33(75%)	7(47%)	0.043
Right upper lobe	51(86%)	38(86%)	7(47%)	0.673
Right middle lobe	49(83%)	39(89%)	10(67%)	0.104
Right lower lobe	54(92%)	42(95%)	12(80%)	0.099
Left upper lobe	51(86%)	39(89%)	12(80%)	0.407
Left lower lobe	52(88%)	41(93%)	11(73%)	0.062
Number of lung lobes mean	5(4-5)	5(5-5)	4(2-5)	0.012
Distribution				
Central and peripheral	9(15%)	8(18%)	1(7%)	0.424
Central	12(20%)	11(25%)	1(7%)	0.160
Peripheral	53(90%)	39(89%)	14(93%)	0.518
Peribronchovascular	23(39%)	21(48%)	2(13%)	0.040
Extent				0.032
Single shot	1(2%)	0(0%)	1(7%)	
Multiple	43(73%)	30(68%)	13(87%)	
Diffuse	15(25%)	14(32%)	1(7%)	
Pleural effusion	6(10%)	3(7%)	3(20%)	0.165
Arterial plaque	22(37%)	15(34%)	7(47%)	0.384
Fiber rope	32(54%)	27(61%)	5(33%)	0.060
Mediastinal lymphadenopathy	13(22%)	10(23%)	3(20%)	0.569

Data is n/N (%), where N is the total number of patients with available data. Abbreviations: CT, computed tomography; GGO, ground-glass opacity;

Discussion

COVID-19 is a new outbreak that may have a profound impact on public health. With the increase in the number of confirmed cases of COVID-19, the number of severe and critical cases in Heilongjiang Province is rising continuously. This might be caused by lung tissue inflammation, which in turn, causes organ dysfunction is even life-threatening. In addition, patients with severe/critically ill patients have poor prognosis and higher mortality than ordinary patients [6, 7]. A recent assessment showed that the fatality rate of severe pneumonia is 30–50%, leading to severe complications and increasing the medical burden [8]. Thus, the early identification of such cases based on changes observed in chest radiography and clinical features is crucial. In the present study, the clinical and imaging characteristics of COVID-19 patients in the ICU care group were determined by comparing the ICU care and non-ICU care patients.

The most common clinical symptoms in this group of patients with COVID-19 were fever and cough. We found that the ICU care group was older than the non-ICU care group, and the ICU care patients were more likely to have cardiovascular disease. Also, it can be seen that older people or people with poor health conditions have a great chance of worsening pneumonia, which might be due to the weakened immune function [9].

Strikingly, due to climate conditions, Heilongjiang Province has a high incidence of cardiovascular disease. The association between COVID-19 and cardiovascular disease is rarely observed in other studies, which might be attributed to the specific geographical environment of Heilongjiang Province. Studies on SARS-CoV and Middle East Respiratory Syndrome(MERS)-CoV infections demonstrated that the risk of exacerbation in patients increases markedly with age and the presence of underlying diseases [10-12], which was consistent with the conclusions of this study. There is no difference in the male to female ratio between the two groups, indicating that gender is not a high-risk cause of disease severity, which is consistent with recent reports [13]. Compared to the ICU care group, the incidence of muscle soreness was significantly higher in the non-ICU care group. This clinical symptom is rare in other related studies and may be related to regional environmental characteristics. Taken together, these clinical manifestations can help the clinicians in determining the severity of the disease in clinical practice. Other symptoms in our COVID-19 patients were similar to other coronavirus infections, including dyspnea, headache, abdominal pain, diarrhea, and nausea. For example, SARS and MERS may belong to the same attributed infection, and also indicate that the 2019-nCoV target cells are located in the lower respiratory tract [14-16].

The present study identified multiple laboratory index differences between non-ICU care groups and ICU care groups, including lymphocyte, neutrophil, and D-dimer levels. Compared to the non-ICU care group, the ICU care group is prone to lymphopenia, which is consistent with the latest reported results [17, 18]. Lymphopenia of patients in the ICU care group indicates that a large number of immune cells are consumed and immune function is suppressed, the damage of lymphocytes may be the key to the deterioration of the patient's condition, and the decrease in the number of lymphocytes could be a critical indicator in evaluating the severity of the disease [19]. Increased neutrophil and D-dimer levels in patients in the ICU care group may be related to cytokine storms caused by the viral invasion, which is supported by recent studies [9, 20]. Notably, patients with high D-dimers for the first time are predictive of poor prognosis [20], which is consistent with the opinion of this study.

From a broad perspective, the CT manifestations of COVID-19 pneumonia are similar to other viral pneumonia. The imaging findings of viral pneumonia include reticular pattern and patchy or diffuse Ground-glass opacity, with or without consolidation [21]. In influenza pneumonia, lobular septal thickening and grid-like density shadows are observed frequently, while pleural effusion is rare [21]. Despite similarities, some of our patients' imaging findings are different from those of the traditional seasonal flu.

In this study, all patients with COVID-19 had abnormal chest CT findings. Additionally, Ground-glass opacity (98%) and consolidation (63%) are the most common imaging findings in the current study, which is consistent with the results of the recent COVID-19 studies [22]. This phenomenon may be related to exudative inflammation caused by alveolar and interstitial edema of the lung due to virus invasion, and CT is mainly manifested as Ground-glass opacity [23]. An autopsy report of patients with COVID-19 pneumonia deaths shows that the Ground-glass opacity corresponds to the gray-white alveolar lesions seen by the naked eye, suggesting that the virus mainly causes inflammatory reactions characterized by deep airway and alveolar damage [24]. Herein, we found that compared to the non-ICU care group, the incidence of consolidation and Ground-glass opacity combined consolidation in patients in the ICU care group was higher ($P = 0.006$; $P = 0.011$), indicating that the alveoli of critically ill patients were filled with inflammatory exudation. This means that the virus has spread to the respiratory tract, leading to necrotic bronchitis and diffuse alveolar damage [25, 26], which is consistent with the results of recently published studies [27-29]. 40/59 (68%) patients displayed imaging abnormalities involving all lung lobes (5) as compared to 7/15 (47%) of non-ICU care patients, while 33/44 (75%) of all ICU care patients were involved; the difference between the two groups was statistically significant ($P = 0.043$). In addition, we found that the degree of involvement of lung lesions was statistically significant between the two groups ($P = 0.032$). These chest imaging features may help clinicians to predict the patients' clinical development early.

In this group of patients, 15 patients needed mechanical ventilation. Compared to non-mechanical ventilation patients, CT abnormalities in the lungs of patients requiring mechanical ventilation were primarily distributed around the bronchial blood vessels, and diffuse distribution was likely to occur, which would render patients to be prone to dyspnea. Some other studies demonstrated that the distribution of abnormal lesions during CT examination may be the decisive factor for the clinical course of patients with COVID-19 [22, 30]. The other imaging features in this study included bilateral lung involvement in 93% of the patients, and most patients (90%) had lung lesions in the peripheral area without emphysema or pulmonary nodules; these imaging abnormalities and distribution patterns are consistent with results published previously [31, 32]. Among the patients in this study, only 7 (12%) patients had pleural effusion, including 6 (14%) in the ICU care group and 1 (7%) in the non-ICU care group. Furthermore, pleural effusion is a rare imaging manifestation in patients with COVID-19, and the incidence rate in the ICU care group is higher than that in the non-ICU care group, which is consistent with the results of the study by Junhua et al. [33].

Nevertheless, the present study has some limitations. (1) In the current study, none of the patients underwent lung biopsy or autopsy, which might have established a correlation between imaging and histopathology. (2) The sample size of the non-ICU care group is relatively small. Collecting standardized data for larger populations will help explore clinical manifestations and high-risk factors. (3) As most patients are still in the hospital at the time of submission of this manuscript, it is difficult to assess the risk factors for poor prognosis.

Conclusion

In summary, elderly patients with cardiovascular disease, fever and cough, may worsen the patient's condition. Lymphopenia, neutrophils, and elevated D-dimer levels are also indicators of COVID-19 disease progression. In addition, the imaging findings of severe cases of COVID-19 mainly include consolidation and Ground-glass opacity combined consolidation, which putatively involves all lung lobes and the area around the bronchi. Since several patients are currently in the critical stage, we hope that the results of this study would be beneficial for disease control, diagnosis, treatment, and prognosis in the Heilongjiang Province and worldwide and reduce the mortality rate.

Declarations

Competing interests: The authors declare no competing interests.

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Figures

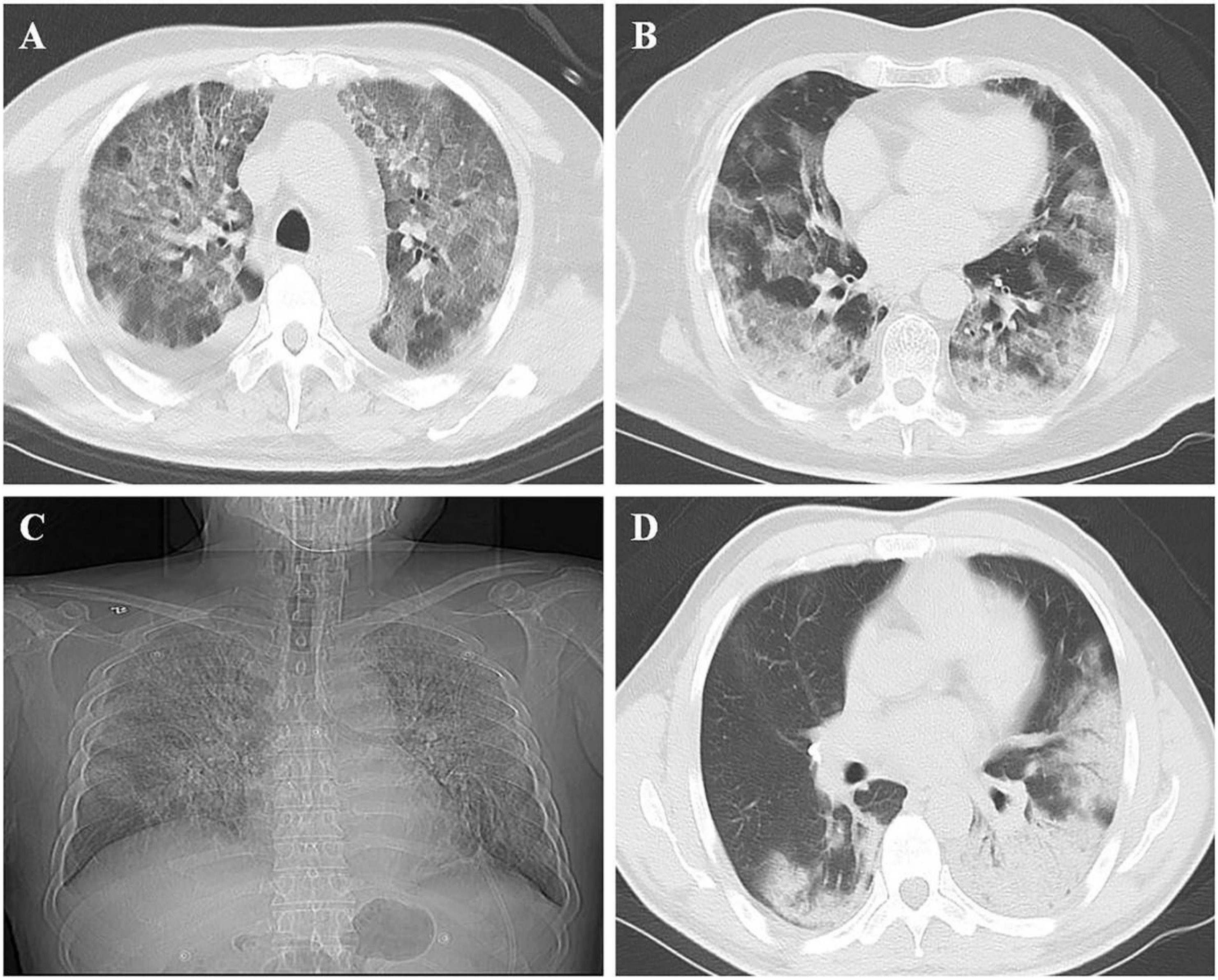

Figure 1

Chest imaging of patients with COVID-19. A: Ground-glass opacity; B: Lesion combined with Ground-glass opacity and consolidation; C: Lesion involving all lung lobe of both lungs; D: Lesion involving bronchial blood vessel surrounding area.