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Post-COVID-19 chest imaging evaluation: which patients should be prioritized for follow-up pulmonary assessment?

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Abstract

Objectives: The current study evaluated the long-term lung abnormalities based on initial and follow-up chest computed tomography (CT) images of COVID-19 patients and investigates the possible factors associated with them.

Methods: One hundred and twenty-four hospitalized COVID-19 patients who received a follow-up chest CT scan in three hospitals in Tehran between February 20, 2021 and September, 2021, were included. Based on the presence of persistent lesions in the follow-up images, patients were divided into residual and nonresidual groups, and logistic regression analysis was performed to investigate the association between different disease characteristics and long-term lung abnormalities.

Results: The most frequent abnormality in the initial imaging was ground-glass opacities which was observed in 95.3% of patients, and residual lesions were observed in 39.8% of patients at the follow-up date. Patients in the residual group were generally older, more frequently suffered from hypertension and dyspnea, and had lower oxygen saturation and lymphocyte count, and lymphopenia was more prevalent among them. Moreover, patients in the residual group had higher initial lung involvement score, and the presence of lymphadenopathy and consolidation was more frequent among them. After adjustment for age, gender, and intervals between the two imagings, logistic regression results showed that hospitalization period, dyspnea, decreased oxygen saturation, decreased lymphocyte count, lymphopenia, consolidation, lymphadenopathy, and high initial lung involvement were strongly associated with the presence of long-term abnormalities.

Conclusion: The current study revealed multiple discrepancies between residual and nonresidual groups, which can be used to better identify the patients at risk of long-term COVID-19 lung complications.

Keywords: Computed tomography, COVID-19, follow-up.

Introduction

According to the existing knowledge regarding the Coronavirus disease 2019 (COVID-19) pandemic, the vast majority of patients demonstrate a mild disease profile which is generally accompanied with the most prevalent symptoms such as fever, cough, and fatigue.[1] In more severe cases, the disease mimics acute respiratory distress syndrome (ARDS). These patients generally require hospitalization, and a portion of them may further require mechanical respiratory support.

Apart from the short-term effects on patients, as the pandemic has been extended for such a prolonged time, long-term effects of the disease gradually manifest, and more and more are being noticed.

Such long-term effects have been documented before in similar diseases such as severe adult respiratory syndrome

and Middle East respiratory syndrome outbreaks showcasing reduced respiratory function, diffusion capacity, and total lung capacity (TLC).[2,3] These long-term effects and their resulting symptoms can significantly affect the daily activities and decrease the quality of life.

Assessment and documentation of the nature and prevalence of these long-term effects are vital in future planning, monitoring, and providing early treatments to patients suffering from the outcomes of these complications.

Objectives

In the current study, we assessed the long-term effects of COVID-19 on the lung characteristics based on computed tomography (CT) scan imaging results. These data can help provide a way to assess the resolve rate of COVID-19-related lung anomalies and provide much needed data for pulmonary rehabilitation programs intended for COVID-19 patients.

Methods

All the patients for the current study were selected from COVID-19 patients who were admitted and hospitalized to Firoozabadi General Hospital, Rasool-e-Akram General Hospital, and Firoozgar General Hospital (Tehran, Iran) from February 20, 2021 to September 21, 2021.

Patients with a negative severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2)-specific reverse transcription polymerase chain reaction test result and patients with a history of lung diseases were excluded from the study.

All selected patients had undergone an additional chest CT scan imaging at least 20 days after the first imaging procedure (in our study population, the minimum and maximum CT scan interval period was 20 and 120 days, respectively).

Patients' demographic data, baseline characteristics, medical history, chest imaging, and laboratory test results were collected from the hospital digital database.

The chest CT images were obtained using a 16-row spiral CT scanning device (Siemens AG). A tube voltage of 110 kV and automatic tube current modulation (range: 90–225 mAS) were used. The thin-section CT was reconstructed by lung algorithm with a slice thickness of <5 mm (a range from 2 to 5 mm), and the matrix size was 512 × 512 for axial images.

All of the obtained chest CT images were reviewed by two general radiologists with a clinical experience range of 4–10 years using a radiologic picture archiving and communication-system workstation.

Initial and follow-up chest CT images of all patients were carefully evaluated for the following anomalies: ground-glass opacities, consolidation, pleural effusion, lymphadenopathy, traction bronchiectasis, parenchymal bands, honeycombing/ reticulation, and air trapping. Images were reviewed using a window width of 1500 Hounsfield units (HU) and a window level of −600 HU and mediastinum using 300–350 and 30–40 HU for width and level, respectively.

Disease involvement in each lobe of the lungs was categorized using a custom scoring system (RUL, RML, and RLL standing for the right upper lobe, right middle lobe, and right lower lobe, respectively, for the right lung and LUL and LLL for the left lung). No involvement was designated as 0, and 0%–25%, 25%–50%, 50%–75%, and 75%–100% involvements were designated as 1, 2, 3, and 4, respectively. For further evaluation of the study population, patients were divided into residual and nonresidual groups based on the presence of traction bronchiectasis, reticulation/honeycombing, air trapping, and parenchymal bands in follow-up chest CT scans.

Statistical analysis

The Student's *t*-test and the χ^2 or Fisher's exact test were used for analysis of continuous and categorical variables. Furthermore, the paired *t*-test and McNemar test were used for analysis of paired continuous and categorical data. Simple and multiple logistic regressions were used to estimate crude and adjusted odds ratio (OR). All statistical analyses were performed using the SPSS version 22.0 software (IBM Corp., Armonk, N.Y., USA). A "P-value" less than 0.05 was considered significant.

Ethical considerations

This study was approved by the Scientific Advisory and Ethical Committees of Iran University of Medical Sciences (Registration number: IR.IUMS.REC.1399.034). The study was conducted in accordance with the Declaration of Helsinki. All participants signed an informed consent form.

Results

A total of 124 COVID-19 patients were enrolled in the current study. Patients were consisted of 60 (48.4%) males and 64 (51.6%) females with an age range of 17–87 years (mean ± standard deviation: 54.29 ± 16.41). The mean hospitalization period was 10.30 ± 7.26 (range: 2–38) days, and the mean interval between initial and follow-up chest CT imaging procedure was 45.40 ± 18.07 (range: 20–120)

days. A complete list of available data is provided in Supplementary Table 1.

Overall, chest CT image analysis revealed that the most prevalent initial lung abnormalities were ground-glass opacities and consolidation, which were observed in 118 (95.2%) and 39 (39.5%) patients, respectively. Further analysis of follow-up chest images revealed that lesions corresponding to persistent or residual damage to lung tissue were present in 47 (37.9%) patients and were consisted of traction bronchiectasis (3/124, 2.4%), reticulation/honeycombing (4/124, 3.2%), air trapping (15/124, 12.1%), and parenchymal bands (38/124, 30.6%) [Supplementary Table 2]. Based on the presence of these lesions in patient follow-up chest CT scans, the study population was divided into nonresidual and residual groups.

Analysis of patient's demographic data revealed that patients in the residual group were generally older (59.98 ± 14.10 vs. 50.82 ± 16.83 years; P = 0.002) and more frequently suffered from hypertension (49% vs. 26%; P = 0.009) [Table 1].

Furthermore, these patients more frequently showed symptoms of dyspnea (74.5% vs. 39%; P < 0.001) and had lower peripheral oxygen saturation (89.33 ± 6.24 vs. 92.89 ± 3.35; P < 0.001). Furthermore, asymptomatic disease presentation was more prevalent in the nonresidual group (7 [9.1%] vs. 0; 40 P = 0.041) [Table 2].

Table 1. Comparison of past medical history and epidemiological data of residual and non-residual patients

Study groups	Non-residual (n=77)	Residual (n=47)	p-value
Age	50.82±16.83	59.98±14.10	0.002
Duration of hospitalization (n=127)	8.87±5.54	12.70±9.02	0.012
Interval between two imaging (days)	41.95±14.85	51.06±21.35	0.012
Gender (male)	38(49.4%)	22(46.8%)	0.78
Smoking history	10(13%)	1(2.1%)	0.051
Comorbidities (overall)	50(64.9%)	35(74.5%)	0.27
COPD	0	2(4.3%)	0.14
Cardiac Disease	9(11.7%)	7(14.9%)	0.6
Cancer	7(9.1%)	2(4.3%)	0.48
Liver Disease	6(7.8%)	0	0.08
Kidney Disease	7(9.1%)	1(2.1%)	0.26
Hypertension	20(26%)	23(48.9%)	0.009
diabetes	20(26%)	14(29.8%)	0.64
CVA	2(2.6%)	0	0.52
Hypothyroidism	5(6.5%)	0	0.15

Abbreviations: COPD, Chronic obstructive pulmonary disease; CVA, Cerebrovascular Accident.

Table 2. Comparison of initial symptoms of residual and non-residual patients

Study groups	Non-residual (n=77)	Residual (n= 47)	p-value
Fever	39(50.6%)	24(51.1%)	0.96
Cough	40(51.9%)	29(61.7%)	0.29
Fatigue	32(41.6%)	12(25.5%)	0.07
Nausea/Vomiting	10(13%)	4(8.5%)	0.44
Abdominal pain	7(9.1%)	4(8.5%)	0.99
Loss of appetite	4(5.2%)	2(4.3%)	0.99
Diarrhea	6(7.8)	4(8.5%)	0.99
Headache	9(11.7%)	3(6.4%)	0.53
Dyspnea	30(39%)	35(74.5%)	<0.001
Taste disturbance	5(6.5%)	0	0.15
Asymptomatic	7(9.1%)	0	0.041
Oxygen Saturation	92.89±3.35	89.33±6.24	<0.001

Laboratory test results also showed differences between the study groups, where lymphocyte cell count (1.05 ± 0.42 vs. 1.40 ± 0.90 for residual and nonresidual groups respectively; $P = 0.005$) was lower in the residual group compared to the nonresidual group. Moreover, lymphopenia was more frequent in the residual group (37 [82.2%] vs. 48 [64%]; $P = 0.033$) [Supplementary Table 3].

Evaluation of treatment regiments in the study groups showed that a higher proportion of patients in the residual group received piperacillin-tazobactam (21.3% vs. 3.9%; 51 $P = 0.005$), levofloxacin (25.5% vs. 5.2%; $P = 0.001$), and azithromycin (19.1% vs. 6.5%; $P = 0.031$). In contrast, the use of co-amoxiclav was more frequent in the nonresidual group (18.2% vs. 4.3%; $P = 0.025$) [Supplementary Table 4].

Moreover, prednisolone use was also more frequent in the residual group (10.6% vs. 1.3%; $P = 0.029$). Differences in antiviral drug administration were also assessed between the study groups, and the data results revealed that a higher proportion of patients in the residual group received lopinavir/ritonavir (29.8% vs. 14.3%; $P = 0.037$) and oseltamivir (31.9% vs. 14.3%; $P = 0.019$), while more patients in the nonresidual group received sofosbuvir (29.9% vs. 6.4%; $P = 0.002$) [Supplementary Table 5].

Comparing the initial and follow-up lung imaging features between the study group showed that patients in the residual group had significantly higher lobe involvement score in all measured lobes (RUL, RML, RLL, LUL, and LLL; $P < 0.01$ in all comparisons) in the first chest CT scan.

Furthermore, consolidation was more pronounced in the residual group ($P < 0.001$), and lymphadenopathy was also much more frequent in these patients (27.7% vs. 2.6% for residual and nonresidual groups, respectively; $P < 0.001$) [Table 3].

Using logistic regression analysis, the most prominent findings in the adjusted analysis (adjusted for age, gender, and interval period between the two imaging) of the initial chest imaging that showed a considerable association with the presence of long-term abnormalities were lymphadenopathy (OR: 13.82 [95% confidence interval (CI): 2.64–72.25], $P = 0.002$), consolidation (OR: 4.08 [95% CI: 1.83–9.60], $P = 0.001$), lymphopenia (OR: 3.28 [95% CI: 1.18–9.11], $P = 0.023$), and dyspnea (OR: 3.69[95%CI: 1.58–8.60], $P = 0.003$).A complete list of analyzed disease findings is provided in Table 4.

Table 3. Comparison of initial chest CT scan abnormalities between residual and non-residual patients

Study groups	Non-residual (n=77)	Residual (n=47)	p-value
GGO			0.07
Negative	6(7.8%)	0	
Peripheral	28(36.4%)	13(27.7%)	
Central	4(5.2%)	1(2.1%)	
Both	39(50.6%)	33(70.2%)	
Consol			<0.001
Negative	57(74%)	18(38.3%)	
Peripheral	8(10.4%)	13(27.7%)	
Central	1(1.5%)	3(6.4%)	
Both	11(14.3%)	13(27.7%)	
RUL score	1.00±0.93	1.70±1.02	<0.001
RML score	1.00±1.03	1.79±1.08	<0.001
RLL score	1.87±1.24	2.74±1.21	<0.001
LUL score	0.97±1.04	1.79±1.02	<0.001
LLL score	1.68±1.33	2.83±1.24	<0.001
FTS	1.86±3.52	3.68±3.50	0.006
ITS	6.52±4.40	10.85±4.47	<0.001
PE	3(3.9%)	3(6.4%)	0.67
LAP	2(2.6%)	13(27.7%)	<0.001

Abbreviations: RUL, Right upper lobe; RML, Right middle lobe; RLL, Right lower lobe; LUL, Left upper lobe; LLL, Left lower lobe; P-bands, parenchymal bands; NI, No involvement; FTS, Follow-up total score; ITS, Initial total score; PE, Pleural effusion; LAP, lymphadenopathy.

Table 4. Association between disease findings and the presence of long-term lung abnormalities based on logistic regression analysis

	Crude OR			Adjusted OR (adjusted for age, gender and imaging interval)		
	OR	P-value	CI 95%	OR	P-value	CI 95%
Age	1.04	0.003	1.01-1.06	1.04	0.002	1.01-1.07
Duration of hospitalization	1.08	0.008	1.02-1.14	1.11	0.002	1.04-1.18
Hypertension	2.73	0.01	1.27-5.87	1.44	0.43	0.58-3.59
Dyspnea	4.57	<0.001	2.05-10.17	3.69	0.003	1.58-8.60
Oxygen Saturation	0.84	<0.001	0.76-0.93	0.87	0.006	0.78-0.96
Lymphocyte count	0.48	0.02	0.26-0.89	0.39	0.01	0.19-0.80
Lymphopenia	2.60	0.037	1.06-6.39	3.28	0.023	1.18-9.11
Sofosbuvir	0.16	0.005	0.05-0.55	0.14	0.003	0.04-0.52
Lopinavir/Ritonavir	2.55	0.04	1.04-6.22	2.10	0.15	0.76-5.81
Oseltamivir	2.81	0.022	1.16-6.82	2.50	0.078	0.90-6.91
Consolidation	4.59	<0.001	2.11-10	4.08	0.001	1.83-9.60
Initial total score	1.23	<0.001	1.12-1.35	1.22	<0.001	1.11-1.35
Lymphadenopathy	14.34	<0.001	3.07-67.07	13.82	0.002	2.64-72.25

Discussion

COVID-19 is still considered a global threat as new variants continuously emerge resulting in new waves of infection.[4] Although the pulmonary complications may be the most apparent, as a result of its wide range of organ involvement,[5] short-term and long-term complications of COVID-19 are quite diverse encompassing audio vestibular, cardiovascular, dermatological, gastrointestinal, hematological, neurological, skeletomuscular, pulmonary, and immune systems[6] with some complications even occurring together.[7,8]

In the current study, we observed that in a follow-up of 124 COVID-19 patients, 47 (37.9%) patients showed evidence of persistent or residual lung lesions. These patients, compared to patients with apparent disease resolve, were older, and hypertension was more prevalent among them. They also more frequently suffered from dyspnea and had lower oxygen saturation, platelet, and lymphocyte count. Based on the chest CT scan results, they had a higher initial lung involvement score, and as a treatment regimen, lopinavir/ritonavir and oseltamivir were more frequently administered to them, while sofosbuvir administration was more frequent among the nonresidual group patients.

It is important to note that in the current study, pulmonary functional test results were not available; however, it can be assumed that the existence of persisting lesions also may result in decreased pulmonary function indices such as TLC and diffusing capacity of the lungs for carbon monoxide as reported by Orzes *et al.*[9]

In our study population, only 38 patients (38/128, 30.6%) showed completely resolved radiologic findings in follow-up chest CT scan images. Other studies have reported similar results although with a high degree of variation with a range from as low as 9% to as high as 64.7% of the study population.[10-12] Such variation in results can be caused by various factors such as different initial and follow-up intervals, difference in SARS-CoV-2 variant dominance, and difference in the study population disease severity.

Based on our results, advanced age and hypertension were more prevalent in the residual group. Old age and hypertension have been linked to a severe disease course and are known risk factors for COVID-19 mortality.[13-15] Our results also suggest that these patients are more likely to develop persistent or residual pulmonary lesions and should be prioritized for post-COVID pulmonary monitoring and rehabilitation programs From the early days of the COVID-19 pandemic, lymphopenia has been known to be an indicator for disease severity and mortality.[16,17] In a study conducted by Zou *et al.*, lymphopenia was found to be associated with ARDS, which is the cornerstone of severe COVID-19.[18] Our results suggest that lymphopenia may also be associated with persistent lung damage as it was significantly more prevalent in the residual group. The exact association between COVID-19 and lymphopenia is still not well understood, although multiple mechanisms such as direct binding of SARS-CoV-2 to lymphocytes,[19] effect of granulocytic myeloid-derived suppressor cells,[20] and

lymphocyte apoptosis have been proposed.[21] Further studies regarding the association between COVID-19, lymphopenia, ARDS, and lung damage are vital for short- and long-term COVID-19 management.

During the pandemic, a wide variety of drugs have been tested with various degrees of effectiveness against COVID-19. Lopinavir/ritonavir has been widely used from the early days of the pandemic with mixed results ranging from effective to redundant[22-24] and even a possible prolonging effect on viral RNA shedding.[25] Oseltamivir, although generally more favorable, has also garnered mixed results,[26,27] and similarly has been reported to cause prolonged viral shedding.[28]

In the current study, both of these drugs were more frequently administered to patients in the residual group. To the best of our knowledge, no evidence regarding the association of fibrotic lung lesions and administration of these drugs exists; however, the possibility of prolonged viral shedding and subsequent lung tissue damage should not be overlooked.

In contrast, a significantly higher number of patients receiving sofosbuvir did not show any sign of persistent or residual lesions in the follow-up images. *In vitro* studies suggest that sofosbuvir can effectively bind to vital SARS-CoV-2 proteins.[29,30]

Moreover, several studies have already reported a relatively good effectiveness of sofosbuvir against COVID-19.[31,32] Although the purpose of this study was not to evaluate the effectiveness or adverse effects of specific treatment options, the current result and the existing evidence suggest that the use of lopinavir/ritonavir and oseltamivir should be avoided as more effective treatment options with less possible adverse effects are already available. Larger studies investigating the association of certain treatment options with the presence of long-term COVID-19-related chest abnormalities should be considered.

It is also of note to mention that a higher proportion of patients in the residual group received prednisolone and certain broad-spectrum antibiotics. This is probably due to a more severe disease course and suspicion of superinfections in the residual group patients.

There were a number of limitations regarding our study. The time period between the two chest CT scan imaging was longer in the residual group, and this may have introduced an unwanted bias into our analysis results. As this was a retrospective cohort study, the time period between the two imaging procedures was not controlled, which may have introduced an unwanted bias into our results.

Conclusions

Several studies have already shown that similar to other coronavirus-related diseases, COVID-19 can also give rise to long-term complications. Based on our results, patients with advanced age, hypertension, lymphopenia, and high initial lung involvement are at a greater risk of developing long-term lung complications, and long-term follow-up of these patients using radiological and functional lung evaluations should be considered.

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Competing interests

The authors declare that they have no competing interests.

Abbreviations

Coronavirus disease 2019: COVID-19;

Severe acute respiratory syndrome coronavirus 2: SARS-CoV-2;

Acute respiratory distress syndrome: ARDS;

Total lung capacity: TLC;

Hounsfield units: HU.

Authors' contributions

All authors read and approved the final manuscript. All authors take responsibility for the integrity of the data and the accuracy of the data analysis.

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Availability of data and materials

The data used in this study are available from the corresponding author on request.

Ethics approval and consent to participate

The study was conducted in accordance with the Declaration of Helsinki. This study was approved by the scientific advisory and ethical committees of Iran University of medical sciences (Registration number: IR.IUMS.REC.1399.034). All participants signed an informed consent form.

Consent for publication

By submitting this document, the authors declare their consent for the final accepted version of the manuscript to be considered for publication.

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Supplementary Table 1. Demographic information, comorbidities, clinical symptoms and treatment data of the study population.

Age	**54.29 ± 16.41**	**AB treatment (overall)**	**92 (74.2%)**
Duration of hospitalization (days)(n = 127)	10.30 ± 7.26	Piperacillin Tazobactam	13 (10.5%)
Interval between two imaging (days)	45.40 ± 18.07	vancomycin	15 (12.1%)
Gender (male)	60 (48.4%)	Imipenem	11 (8.9%)
Smoking history	11 (8.9%)	Ceftriaxone	36 (29%)
Comorbidities (overall)	85 (68.5%)	Teicoplanin	2 (1.6%)
COPD	2 (1.6%)	Meropenem	7 (5.6%)
Cardiac Disease	16 (12.9%)	Ciprofloxacin	5 (4%)
Cancer	9 (7.3%)	Ceftazidime	3 (2.4%)
Liver Disease	6 (4.8%)	Co-amoxiclav	16 (12.9%)
Kidney Disease	8 (6.5%)	Clindamycin	3 (2.4%)
HTN	43 (34.7%)	Cefepime	13 (10.5%)
diabetes	34 (27.4%)	Ampicillin Sulbactam	3 (2.4%)
Migraine	3 (2.4%)	Levofloxacin	16 (12.9%)
CVA	2 (1.6%)	Azithromycin	14 (11.3%)
Hypothyroidism	5 (4%)	Interferon	30 (24.2%)
Gout	2 (1.6%)	IVIG	2 (1.6%)
Fever	63 (50.8%)	Hydroxychloroquine	73 (58.9%)
Cough	69 (55.6%)	CS treatment (overall)	67 (54%)
Fatigue	44 (35.5%)	Dexamethasone	57 (46%)
Nausea/Vomiting	14 (11.3%)	Hydrocortisone	8 (6.5%)
Abdominal pain	11 (8.9%)	Prednisolone	6 (4.8%)
Loss of appetite	6 (4.8%)	Antiviral treatment (overall)	97 (78.2%)
Diarrhea	10 (8.1%)	Favipiravir	8 (6.5%)
Headache	12 (9.7%)	Ribavirin	2 (1.6%)

Dyspnea	65 (52.4%)	Lopinavir/Ritonavir	25 (20.2%)
Taste disturbance	5 (4%)	Oseltamivir	26 (21%)
LOC	3 (2.4%)	Sofosbuvir	26 (21%)
Asymptomatic	7 (5.6%)	Atazanavir	12 (9.7%)
Sat O_2	91.49 ± 4.99	Sofosbuvir/Daclatasvir	5 (4%)
Leukocytosis (n = 122)	16 (13.1%)	Ledipasvir	2 (1.6%)
Lymphopenia (n = 120)	85 (70.8%)	Lopinavir	2 (1.6%)
Shift to left (n = 115)	31 (27%)	Remdesivir	19 (15.3%)

Abbreviations: COPD, Chronic obstructive pulmonary disease; HTN, hypertension; CVA, Cerebrovascular Accident; LOC, Loss of Consciousness; sat O_2, Saturation of Oxygen.

Supplementary Table 2. Descriptive information regarding the initial and follow-up imaging characteristics of the study population.

	Initial imaging	**Follow-up imaging**
Ground-glass opacities		
Negative	6 (4.8%)	57 (46%)
Peripheral	41 (33.1%)	43 (34.7%)
Central	5 (4%)	2 (1.6%)
Both	72 (58.1%)	22 (17.7%)
Consolidation		
Negative	75 (60.5%)	111 (89.5%)
Peripheral	21 (16.9%)	7 (5.6%)
Central	4 (3.2%)	1 (0.8%)
Both	24 (19.4%)	5 (4%)
RUL score		
No involvement	25 (20.2%)	87 (70.2%)
0-25 %	62 (50%)	32 (25.8%)
25-50 %	22 (17.7%)	4 (3.2%)
50-75 %	9 (7.3%)	0
75-100%	6 (4.8%)	1 (0.8%)
RML score		
No involvement	32 (25.8%)	84 (67.7%)
0-25 %	48 (38.7%)	28 (22.6%)
25-50 %	25 (20.2%)	9 (7.3%)
50-75 %	13 (10.5%)	2 (1.6%)
75-100%	6 (4.8%)	1 (0.8%)
RLL score		
No involvement	7 (5.6%)	70 (56.5%)
0-25 %	42 (33.9%)	35 (28.2%)
25-50 %	24 (19.4%)	11 (8.9%)
50-75 %	21 (16.9%)	4 (3.2%)
75-100%	30 (24.2%)	4 (3.2%)
LUL_SCORE		
No involvement	32 (25.8%)	84 (67.7%)
0-25 %	49 (39.5%)	32 (25.8%)
25-50 %	25 (20.2%)	7 (5.6%)
50-75 %	12 (9.7%)	0
75-100%	6 (4.8%)	1 (0.8%)
LLL score		
No involvement	16 (12.9%)	77 (62.1%)
0-25 %	36 (29%)	25 (20.2%)
25-50 %	22 (17.7%)	15 (12.1%)
50-75 %	18 (14.5%)	2 (1.6%)
75-100%	32 (25.8%)	5 (4%)
total score	8.16 ± 4.89	2.55 ± 3.61
Pleural effusion	6 (4.8%)	9 (7.3%)
lymphadenopathy	12 (12.1%)	10 (8.1%)
Tractional bronchiectasis	0	3 (2.4%)
Honey combing reticulation	0	4 (3.2%)
Air trapping	0	15 (12.1%)
P-bands	0	38 (30.6%)

Supplementary Table 3. Comparison of laboratory test results of residual and non-residual patients

Study groups	Non-residual (n =77)	Residual (n = 47)	p-value
WBC × 10^9/L (n = 122)	7.25 ± 3.52	7.12 ± 3.07	0.83
Lymphocyte × 10^9/L (n = 120)	1.40 ± 0.90	1.05 ± 0.42	0.005
PMN × 10^9/L (n = 115)	5.37 ± 3.20	5.72 ± 2.95	0.56
Hb g/dL (n = 122)	12.48 ± 2.74	12.65 ± 2.55	0.74
Platelet × 10^9/L (n = 122)	236.65 ± 128.81	210.20 ± 99.62	0.24
Troponin ng/mL (n = 71)	4.70 ± 14.35	4.23 ± 6.43	0.88
ESR (n = 91)	44.98 ± 26.08	50.30 ± 26.26	0.34
LDH U/L (n = 101)	727.14 ± 772	622.76 ± 268.19	0.42
CRP mg/L (n = 104)	45.07 ± 42.14	54.95 ± 47.59	0.27
AST U/L (n = 117)	54.46 ± 52.38	55.47 ± 42.66	0.91
Leukocytosis (n = 122)	10 (13%)	6 (13.3%)	0.96
Lymphopenia (n = 120)	48 (64%)	37 (82.2%)	0.033
Shift to left (n = 115)	17 (24.3%)	14 (31.1%)	0.42

Abbreviations: WBC, White blood cells; HTN, hypertension; PMN, Polymorphonuclear neutrophils; Hb, Hemoglobin; ESR, Erythrocyte sedimentation rate; LDH, Lactate dehydrogenase; CRP, C-reactive protein; AST, Aspartate transaminase.

Supplementary Table 4. Comparison of antibiotic treatments administered to residual and non-residual patients

Study groups	Non-residual (n =77)	Residual (n = 47)	p-value
AB treatment (overall)	58 (75.3%)	34 (72.3%)	0.71
Piperacillin Tazobactam	3 (3.9%)	10 (21.3%)	0.005
vancomycin	8 (10.4%)	7 (14.9%)	0.46
Imipenem	5 (6.5%)	6 (12.8%)	0.33
Ceftriaxone	27 (35.1%)	9 (19.1%)	0.06
Teicoplanin	2 (2.6%)	0	0.52
Meropenem	4 (5.2%)	3 (6.4%)	0.99
Ciprofloxacin	4 (5.2%)	1 (2.1%)	0.65
Ceftazidime	3 (3.9%)	0	0.29
Co-amoxiclav	14 (18.2%)	2 (4.3%)	0.025
Clindamycin	1 (1.3%)	2 (4.3%)	0.56
Cefepime	8 (10.4%)	5 (10.6%)	0.99
Ampicillin Sulbactam	2 (2.6%)	1 (2.1%)	0.99
Levofloxacin	4 (5.2%)	12 (25.5%)	0.001
Azithromycin	5 (6.5%)	9 (19.1%)	0.031
Interferon	19 (24.7%)	11 (23.4%)	0.87
IVIG	1 (1.3%)	1 (2.1%)	0.99

Supplementary Table 5. Comparison of corticosteroid and antiviral treatments administered to residual and non-residual patients

Study groups	Non-residual (n =77)	Residual (n = 47)	p-value
Hydroxychloroquine	51 (79.7%)	22 (64.7%)	0.10
CS treatment (overall)	41 (53.2%)	26 (55.3%)	0.82
Dexamethasone	35 (45.5%)	22 (46.8%)	0.88
Hydrocortisone	6 (7.8%)	2 (4.3%)	0.71
Prednisolone	1 (1.3%)	5 (10.6%)	0.029
Antiviral treatment (overall)	57 (74%)	40 (85.1%)	0.15
Favipiravir	4 (5.2%)	4 (8.5%)	0.48
Ribavirin	0	2 (4.3%)	0.14
Lopinavir/Ritonavir	11 (14.3%)	14 (29.8%)	0.037
Oseltamivir	11 (14.3%)	15 (31.9%)	0.019
Sofosbuvir	23 (29.9%)	3 (6.4%)	0.002
Atazanavir	7 (9.1%)	5 (10.6%)	0.76
Sofosbuvir/Daclatasvir	2 (2.6%)	3 (6.4%)	0.37
Ledipasvir	2 (2.6%)	0	0.52
Lopinavir	2 (2.6%)	0	0.52
Remdesivir	9 (11.7%)	10 (21.3%)	0.15