Novel Coronavirus Pneumonia (COVID-19) Progression Course in 17 Discharged Patients: Comparison of Clinical and Thin-Section CT Features During Recovery

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Summary: Most patients showed initial radiographic deterioration in the 2nd week followed by radiographic improvement in the 3rd and 4th week. The progression course of CT pattern was later than the clinical parameters within the first two weeks.

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Abstract

Background. To retrospectively analyze the evolution of clinical features and thin-section CT imaging of novel coronavirus pneumonia (COVID-19) in 17 discharged patients.

Methods. Serial thin-section CT scans of 17 discharged patients with COVID-19 were obtained during recovery. Longitudinal changes of clinical parameters and CT pattern were documented in all patients during 4 weeks since admission. CT score was used to evaluate the extent of the disease.

Results. There was a marked improvement of fever, lymphocytes count, C-reactive protein and erythrocyte sedimentation rate within the first two weeks since admission. However, the mean CT score rapidly increased from the 1st to 3rd week, with a top score of 8.2 obtained in the 2nd week. During the 1st week, the main CT pattern was ground-glass opacities (GGO,76.5%). The frequency of GGO (52.9%) decreased in the 2nd week. Consolidation and mixed patterns (47.0%) were noted in the 2nd week. Thereafter, consolidations generally dissipated into GGO and the frequency of GGO increased in the 3rd week (76.5%) and 4th week (71.4%). Opacities were mainly located in the peripheral (76.5%), subpleural (47.1%) zones of the lungs, and presented as focal (35.3%) or multifocal (29.4%) in the 1st week and became more diffuse in the 2nd (47.1%) and 3rd week (58.8%), then showed reduced extent in 4th week (50%).

Conclusions. The progression course of CT pattern was later than the clinical parameters within the first two weeks since admission; however, there was a synchronized improvement in both clinical and radiologic features in the 4th week.

Key Words: COVID-19, novel coronavirus pneumonia, viral pneumonia, computed tomography

Introduction

In late December 2019, a new pneumonia of unknown cause broke out in Wuhan city, China [1,2], and the infection has spread rapidly in China and worldwide [3-6]. On 7th of January 2020, a novel coronavirus (SARS-COV-2) was identified as the cause via deep sequencing analysis of the respiratory tract samples [2,4]. SARS-COV-2 possess a strong ability to infect humans, with the capability of human-to-human transmission [7,8]. The number of patients is increasing rapidly. By March 7, 2020, more than 8,0000 cases of pneumonia were reported in China, including 3073 cases of death (the mortality rate is round 3.8 %).

The epidemiological and clinical characteristics of the initial novel coronavirus pneumonia (COVID-19) population in Wuhan have been recently published [9-12]. The common presentation of these patients was as a rapidly progressing lower respiratory tract illness with fever and cough. The diagnosis of COVID-19 mainly depends on the results of viral nucleic acid, which possesses a high specificity but a poor sensitivity. According to a recent publication, half of the patients were diagnosed as COVID-19 without fever in the early stage [12], and even with negative nucleic acid tests at first few times [13]. Therefore, combining imaging features with clinical and laboratory findings can help make an early diagnosis of COVID-19. At present, a limited number of reports have focused on chest imaging findings of COVID-19 [13-16]. The common CT findings of patients with COVID-19 in those reports include bilateral ground-glass opacities or areas of consolidation of the peripheral lung, which bear some resemblance to SARS-CoV [17–19] and MERS-CoV [20,21]. In a recent report of 81 patients, CT findings across different timepoints throughout the disease course has been described[16].However, the longitudinal progression of thin-section CT imaging changes in

patients with COVID-19 and its correlation with changes in clinical parameters remains unclear.

Hence, this study aimed to analyze the serial thin-section CT changes of 17 discharged patients with COVID-19, and to compare the progression trend of imaging pattern and clinical parameters.

Materials and Methods

Patients and Clinical characteristics

This retrospective study was approved by the Institutional Review Board. The requirement for informed patient consent was waived by the Ethics Committee for the emerging infectious disease. Between December 20th, 2019 and February 2nd, 2020, 17 patients with confirmed COVID-19 who underwent at least three serial chest CT scans were retrospectively included. Throat swab samples were collected for confirmation of COVID-19 by the RT-PCR as previously described [9-10]. All the patients showed improvement both clinically and on thin-section CT imaging on discharge. The standard for survive and discharge of patients was according to the guideline of Diagnosis and Treatment of Pneumonia Caused by SARS-COV-2 (trial sixth version) published by the China Ministry of Health [22], which include: temperature returning to normal for more than 3 days, both the clinical and chest imaging showing significant improvement, and two consecutive respiratory pathogen nucleic acid tests turning negative (the interval at least 24 hours). Three readers (X.H.,Y.C., M.D.) recorded the clinical parameters of the patients during treatment.

CT Image Acquisition

CT was performed using the following CT scanners: SOMATOM Definition AS+, Siemens Healthineers, Germany. CT scan parameters were as described in our previous study[16]. All follow-up scans were obtained by using the same scanner used to obtain the initial scans. Of 17

cases, four scans were available in 14 cases, and three scans in 3 cases.

Image Interpretation

The initial images and follow-up chest CT scans obtained from 17 patients were reviewed by three experienced radiologists (H.S., N.J., Y.C.). All Digital Imaging and Communications in Medicine (DICOM) images were analyzed from the CT studies without access to clinical findings of the patients. After separate evaluations, disagreements wherever found were solved by discussion and consensus. On each CT scan, lung segment involved, the location of lesion categorized as central, peripheral or both; and the distribution of opacities classified as being predominantly subpleural, peribronchovascular or random were recorded. The extent of lesion involvement was categorized as focal, multifocal, diffuse**.** The predominant pattern was categorized as ground glass opacities, consolidation, reticular and mixed pattern. In addition, the margin definition, interlobular/septal thickening , crazy paving (thickened interlobular septa and intralobular lines superimposed on a background of ground-glass opacity)[23], air bronchogram, bronchiolectasis, cavitation, calcifications, thickening of the adjacent pleura , evidence of pulmonary fibrosis , tree-in-bud, pleural effusion and lymphadenopathy were also documented.

The extent of pulmonary abnormalities on thin-slice CT was also evaluated. A semi-quantitative CT scoring system was used to quantitatively estimate the pulmonary involvement of all these abnormalities on the basis of the area involved, as previously reported by Ooi et al[24]. After evaluation, the scans were classified according to the time from the admission to 1, 2, 3, and 4 weeks.

Statistical Analysis

The analyses were performed using SAS (SAS, version 9.4, SAS Institute, Cary, NC, USA). Distribution normality was assessed using the Kolmogorov-Smirnov test. Normally, non-normally distributed data and categorical variables were expressed as the mean ± standard deviation, median (interquartile range) and frequency (percentage), respectively. Differences between weeks were analyzed by generalized linear mixed models (for categorical data) or linear mixed models (for continuous data without/with square root transformation). A P value <0.05 (two-tailed) was considered to be statistically significant.

Results

Clinical and laboratory findings

Clinical characteristics and laboratory findings in all patients on admission are summarized in Table 1. The 17 patients included 6 men and 11 women, who ranged in age from 27 to 60 years old (mean age, 40.0±10 years old). Seven (41.2%) of 17 cases were health care workers (nurses) who had close contact with confirmed case of COVID-19 in the hospital.

The most common symptom at onset was fever (14/17,82.4%), among which 12 (85.7%) patients had a temperature of＞38℃. The laboratory findings showed leukopenia in 9 patients (52.9%), and lymphocytopenia in 8 (47.1%) patients. Levels of C-reactive protein (CRP, 11.7mg/L) and erythrocyte sedimentation rate (ESR, 34mm/h) were increased. 3 (17.6%) patients had elevated alanine transaminase (ALT), and 4 (23.5%) had elevated aspartate transaminase (AST). The initial CT scans were acquired during a mean of 4 days (range, 1-7 days) and 2 days (0-5 days) from the onset of symptoms and admission, respectively. The mean time length between the very first and the last scan was 21.2 days. The median stay was 23 days [IQR 18–30.5].

Treatment and Progression of clinical changes over 4 weeks

The mean time of treatment was 22 days (range, 18–31 days). Patients were treated by anti-viral drug (ganciclovir, abidol hydrochloride, oseltamivir, or interferon) and empirical antibacterial drug (moxifloxacin hydrochloride, amoxicillin, meropenem or linezolid). Abidol hydrochloride is approved in China and Russia as an antivirals drug for influenza treatment. The hexadecadrol (5mg) was given to three patients (P6, P14 and P17), and the methylprednisolone(40mg) and auxiliary ventilation were used in Patient 1 and 2. There was a marked resolution of fever within the first two week since admission (Figure1a, $p < 0.0001$) and improvement in oxygen saturation and heart rate (Figure 1b) within the first two weeks (Table 2) . There was also a trend of improvement in lymphocyte (Figure 1d), CRP and ESR (Figure1e) within the first week (Table 2). There was an initial increase of ALT level in 3rd week followed by improvement, and a slow continuous increase in AST level from 2nd week (Figure 1f, Table 2).

Imaging findings of the initial thin-section CT

As Table 3 and 4 illustrate, the initial chest CT in first week was abnormal in all patients (100%). The mean CT score was 4.3 per/ patient (ranged from 1 to 11). The predominant CT feature was poor-defined (88.2%) ground-glass opacities (GGO, 76.5%) with enlarged pulmonary vessels (70.6%) mainly involving the peripheral (76.5%) bilateral (70.6%) lung parenchyma. Of 13 patients with GGO pattern (Figure 2a), seven patients (53.8%) showed GGO plus smooth interlobular septal thickening (Figure 2b) and one presented as GGO plus irregular linear opacities. Other common findings included thickening of the adjacent pleura (41.2%, Figure 2c), crazy paving (35.3%, Figure 2b), air bronchograms (29.4%, Figure 2d) and interlobar fissure displacement (23.5%).

Progression of thin-section CT changes over 4 weeks

As Figure 3 showed, there was a marked increase of mean CT score of all patients from 1st week to 3rd week (4.3, 8.2 and 7.2 per/ patients in 1st, 2nd and 3rd week, respectively). After that, a decrease to a mean CT score of 4.2 occurred in the 4th week(p=0.0190). When analyzing the evolution of CT findings, the present study had identified three patterns of radiographic progression (Figure 3). Type 1 evolution pattern was the most common observed in 12 patients (70.6%), with initial radiographic deteriorations in the 2nd week followed by radiographic improvement in the 3rd and 4th week (Figure 4). Four patients (23.5%) had type 3 evolution pattern (static radiographic change, Figure 5). One patient (Patient 15, 5.9%) had type 2 pattern (progressive radiographic improvement, Figure 6).

The predominant abnormality of CT changes through 4 weeks are shown in table 4 and Figure 7. The frequency of ground-glass opacities decreased from 1st week (13/17, 76.5%) to the 2nd week (9/17, 52.9%), then slowly increased in 3rd week (76.5%) and 4th week (71.4%). Consolidation (29.4%) and mixed pattern (17.6%) were noted in the 2nd week and the mix pattern reached highest proportions in the 4th week on three (21.4%) of 14 scans. Opacities were mainly located in the peripheral (13/17,76.5%), subpleural (8/17,47.1%) zones of the lungs, and presented as focal (35.3%) or multifocal (29.4%) in the 1st week and became more diffuse in the 2nd (47.1%) and 3rd week (58.8%), then showed reduced extent in 4nd week(50%).

Crazy paving appearance had the highest frequency in 2nd week (76.5%), but disappeared in the 4th week($p<0.0001$). Pleural effusion appeared from 2nd week (11.8%) and peaked at 3rd week(23.5%). In the 4th week, bronchiectasis was identified in 2 patients (15.4%) and evidence of pulmonary fibrosis was seen in 3 patients (23.7%, p=0.0012). Presence of subpleural nodule was

found in one scan(P7) at 3rd week, which was dissipated on follow-up CT scans. The other findings such as air bronchogram, enlarged pulmonary vessels, thickening of the adjacent pleura and interlobe fissure displacement were observed over 4 weeks.

Discussion

In our study, the age of patients was 40±6 years old, younger than previously reported [9-12]. Besides, five patients (29.4%) had underlying diseases, similar to previous studies[9,10]. There was a female gender predilection (male: female, 6:11). On the contrary, COVID-19 patients were mostly men (73%) in a previous study[9]. Such a discrepancy may be due to the different study populations and demographic features. Our study only included survived and discharged patients, while previous studies included COVID-19 patients without considering the prognosis. Fever and cough were the most common symptoms, consistent with manifestations of lower respiratory tract infection. In the present study, laboratory test showed leukopenia in 9(52.9%) patients, and lymphocytopenia in 8(47.1%) patients on admission. Both CRP and ESR levels were elevated, similar to previous betacoronavirus infections[19,20]. There was a marked resolution of fever within the first week, and improvement in oxygen saturation and heart rate within the first two weeks. There was also a trend towards improvement in lymphocyte, CRP and ESR within the first week. However, there was an initial increase of ALT level in the 3rd week followed by improvement, and a slow continuous increase of AST level from 2nd weeks in those patients. The preliminary results indicate that patients with COVID-19 may develop liver damage during hospitalization. This may due to the viral infection of liver cells [25], therapeutic medications[25,26] or immune-mediated inflammation[25] causing damage to liver tissue.

Initial chest CTs were abnormal in all patients (100%). However, Chuang et al. [15] reported three patients (14%) to have normal CT at diagnosis, which might be related to prolonged incubation period. It may also be due to variable imaging techniques, particularly slice thickness across different studies. More than half of the patients in the previous study underwent CT scan with 8 mm or 5mm slice thickness, in which subtle findings, such as small GGO in the early stage of disease may be overlooked. During the 1st week, the mean CT score was 5.4 per/patient (range, 1-11). The predominant abnormality on CT was ground-glass opacities (GGO, 82.4%) with enlarged pulmonary vessels (70.6%) that mainly involved the peripheral (76.5%) pulmonary parenchyma bilaterally (70.6%). The presence of GGO is a common finding in viral infections, which was linked to variable histopathologic changes, such as diffuse alveolar damage or interstitial (intrapulmonary or airway) inflammatory cell infiltration[27,28]. Moreover, the enlarged pulmonary vessels also indicated an inflammatory cell infiltration of the vessels. The peripheral, subpleural lung involvement bare some resemblance to SARS-CoV [17-19] and MERS-CoV [20,21]. However, in contrast, SARS-CoV infection usually presents with unifocal opacification [24]. The focal or multifocal of lesion involvement were common CT findings in our case series of COVID-19 in early stage, consistent with the report by Chuang et al. [15]. Other common CT findings included thickening of the adjacent pleura (41.2%), crazy paving (35.3%), air bronchogram (29.4%) and interlobar fissural displacement (23.5%).

A marked increase of mean CT score was noted during the 1st to 2nd week (from 4.3 to 8.2). Then, there was a slow decline in CT score (7.2) at 3rd week in 58.8% (10 of 17) of patients. Thereafter, the extent of changes rapidly decreased to a mean CT score of 4.2 in 4th week indicating resolution. When analyzing the evolution of CT finding of all patients by time, the

present study found that most patients recovering from COVID-19 showed an initial radiographic deterioration to a peak (mean time, 2nd week) followed by radiographic improvement in the 3rd and 4th week. Nevertheless, there was remarkable resolution of fever and improvement in oxygen saturation and heart rate, lymphocyte, CRP and ESR within the first two weeks. Accordingly, we may conclude that the progression course of CT pattern was later than the clinical parameters within the first two weeks. This may result from inflammatory reaction occurring earlier than the morphological changes of lung. Thereafter, the radiologic findings and clinical parameter showed a synchronization of improvement at 4th week. Although, the four patients had a static radiographic course, the CT score remained low (＜4) in those cases. Therefore, evolution course type 1, 2 or 3 with a consistent low CT score may be associated with a favorable outcome.

Similar to the initial chest CT during the 1st week, the main CT pattern was GGO (9/17, 52.9%) in 2nd week, although the frequency of GGO slightly decreased. Meanwhile, consolidation and mixed pattern (47.0%) were noted in the 2nd week. Thereafter, the frequency of GGO increased in 3rd week (76.5%) and 4th week (71.4%) due to dissolution of consolidation into GGO. Furthermore, GGO plus interlobular septal thickening were the main pattern in 3rd week, while GGO plus irregular linear opacities were the main pattern in the 4th week (60%). Consolidation pattern was not observed in the 4th week, while the mixed pattern reached highest proportions. This phenomenon may be attributed to the fact that consolidations generally either resolved completely or regressed to small areas of irregular linear opacities. Opacities were mainly located in the peripheral, subpleural zones of the lungs as focal or multifocal lesions in the 1st week, and disease quickly evolved to a more extensive and diffuse picture in the 2nd week, then improved in the 3rd and 4th weeks. This trend of changes in lesion distribution was consistent with the CT score in the

present study. The crazy paving reached the highest frequency in the 2nd week (76.5%), but was not seen in the 4th week. This phenomenon suggests that the presence of crazy paving may be associated with an early period of disease. Pleural effusion appeared from the 2nd week (11.8%) and peaked at the 3rd week (23.5%). This feature is different from SARS-CoV[17-19] and other recent publications on COVID-19 [13-15], which barely present with pleural effusion. Previous studies showed that the presence of pleural effusion in patients infected with MERS-CoV or Avian flu (H5N1) was a poor prognostic factor [20,29]. Nevertheless, in three patients, pleural effusion was totally absorbed on follow-up CT scans.

In the 4th week, bronchiectasis in 2 patients (15.4%) and evidence of pulmonary fibrosis in 3 patients (23.7%) were identified. As Antonio et al [30] described, pulmonary fibrosis included parenchymal bands, traction bronchiectasis, and irregular interfaces. They found 15 (62%) of SARS patients to have evidence of fibrosis on CT after discharge. Since the natural history of COVID-19 has not been fully studied, it may be premature to define these pulmonary changes as irreversible and longer-term follow-up is needed. Lymphadenopathy, tree-in-bud, masses, cavitation and calcifications were not observed in our case series, which is in line with the previous studies on COVID-19 [15] and SARS-CoV[17-19].

Our study had several limitations. First, this study was performed at a single center with a small sample size. Second, the subjects included in our study were all discharged patients, cases of death or other outcomes were not included. Hence, natural selection bias may have occurred Thirdly, only patients with serial chest CT thin-section CT images available were included, which make the findings non-generalizable to people with milder disease who did not undergo serial CT or those with asymptomatic disease. Finally, due to the short time of follow up, the CT findings

after discharge were not documented.

In conclusion, most patients with COVID-19 showed an initial radiographic deterioration to a peak at the 2nd week since admission followed by radiographic improvement in the 3rd and 4th week. The progression course of CT pattern was later than the clinical parameters within the first two weeks, but showed synchronization of improvement in both clinical and radiologic features in the 4th week. Longer-term follow-up is required to determine whether the findings (bronchiectasis and pulmonary fibrosis) in the 4th week represent irreversible fibrosis.

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Table 1 Clinical characteristics and laboratory findings in patients with COVID-19 on admission

Patients No./ Sex/Age（y）	Smoking history	Symptoms	Maximal T° C	Comorbidities	Leukocyte count(10^9/L)	Lymphocyte count(10^9/L)	Serum amyloid A protein(mg/L)	CRP (mg/L)	ESR (mm/h)	ALT (U/L)	AST (U/L)
P1/male/44	Current	Fever, cough, Sputum	38.6	COPD	7.86	0.7	713.6	19.4	/	56	63
P 2/female/60	Never	Fever	39.4	Hypertension	3.49	1.07	66.8	19.3	78	30	30
P3/ male/32	Never	Weakness, Fever, cough	37.1	without	2.79	2.3	/	6.62	80	50	45
P 4/ female/32	Never	Fever, cough	37.6	without	5.01	0.89	/	5.04	14	49	20
P 5/ female/41	Never	Headache	37	without	4.66	1.23	/	＜3.41	14	49	33
P 6/ female/41	Never	Fever	38.7	without	2.68	0.7	678.2	76.1	39	32	42
P 7/ female/35	Never	Fever, pharyngalgia	38.0	without	4.47	1.05	/	＜3.41	5	29	31
P 8/ female/25	Never	Fever, cough	39.1	without	6.3	1.2	15.7	＜3.14	7	16	17
P9/ female/42	Never	Fever, cough, Sputum	37.0	without	4.36	0.95	/	＜3.41	27	19	18
P10/female/51	Never	Sore muscle,cough	36.6	without	3.41	1.69	/	4.54	14	33	23
P11/ male/33	Current	Fever, cough,	37.7	without	3.43	1.22	/	14.9	7	33	24
P12/ male/27	Never	Fever	37.2	without	6.59	1.63	46.4	14.96	13	33	32
P13/ male/31	Never	Fever	38.8	without	3.14	0.95	/	＜3.14	31	21	16
P14/ female/41	Never	Weakness, Fever, Headache	38.7	Pituitary adenoma	3.17	0.95	39.6	＜3.41	31		40
P15/ female/54	Never	Cough, shortness of breath	36.6	II DM	4.5	1.31	2.1	21	16	21	16

P16/ male/43	Current	Fever	38.2	II DM	3.45	1.12	59.8	148	58	58	148
P17/ female/48	Never	Fever	38.5	without	9.6	0.8	628.3	105	95	95	105

T, temperature; CRP, C-reactive protein, ESR, erythrocyte sedimentation rate; AST, Aspartate aminotransferase. ALT, Alanine aminotransferase, COPD, chronic obstructive pulmonary disease.

Table 2 Clinical Parameter of Patients with COVID-19 within 4 weeks since admission

Clinical parameters	At week 1	At week 2	At week 3	At week 4	*P* value
Maximal T° C	38.3±0.9	36.9±0.7	37.2±1	36.5±0.3	<0.0001*
Heart rate(bpm)	82.5±10.8	81.9±11	86.1±10.4	79.9±8	0.3622
Oxygen saturation (%)	93.1±8.9	96.6±3.1	97.8±3.7	99.4±0.9	0.1153
Leukocyte count(10^9/L)	4.6±1.9	4.7±1.4	5.4±2	5±1.4	0.6906
Lymphocyte count(10^9/L)	1.2±0.4	1.3±0.5	1.3±0.6	1.5±0.5	0.4072
CRP(mg/L)	11.7(11.8)	8.7(19.3)	3.14(9.9)	3.04(0)	0.0751
ESR(mm/h)	34(16)	30.5(23.5)	24.5(25.5)	21.5(35)	0.8511
AST(U/L)	33(24.5)	27(40)	46(28)	40.5(39)	0.8434
AST(U/L)	31(22)	22(38)	33(25)	37.5(8)	0.7104

Date are presented as the mean± SD or median (interquartile range).

T, temperature; CRP, C-reactive protein, ESR, erythrocyte sedimentation rate; AST, Aspartate aminotransferase. ALT, Alanine aminotransferase

**P*<0.05 between over 4 weeks since admission

Table 3 Longitudinal changes of the predominant CT pattern and CT Score in patients with COVID-19

Patients No./ Sex/Age (y)	CT pattern at Week 1(No)	CT pattern at Week 2(No)	CT pattern at Week 3(No)	CT pattern at Week 4(No)	*P* value
P1/male/44	GGO (11)	GGO (18)	GGO (15)	GGO (8)	
P2/female/60	GGO (9)	Consolidation (22)	Mixed (16)	Mixed (8)	
P3/ male/32	GGO (4)	GGO (5)	GGO (4)	NP	
P4/ female/32	GGO (1)	GGO (3)	Mixed (4)	Mixed (4)	
P5/ female/41	GGO (5)	Consolidation (10)	Consolidation (11)	GGO (6)	
P6/ female/41	Consolidation (9)	GGO (14)	GGO (11)	GGO (7)	
P7/ female/35	GGO (1)	GGO (2)	GGO (4)	GGO (1)	
P8/ female/25	Consolidation (1)	Mixed (4)	GGO (2)	GGO (2)	
P9/ female/42	GGO (1)	GGO(3)	GGO (5)	GGO (3)	
P10/female/51	GGO (5)	GGO (8)	GGO (8)	GGO (6)	
P11/ male/33	Mixed (4)	Mixed (9)	GGO (5)	NP	
P12/ male/27	GGO (1)	Consolidation (3)	GGO (3)	NP	
P13/ male/31	GGO (2)	GGO (2)	Consolidation (2)	GGO (1)	
P14/ female/41	Mixed (5)	Mixed (12)	GGO (8)	Mixed (6)	
P15/ female/54	GGO (6)	Consolidation (7)	GGO (6)	GGO (4)	
P16/ male/43	GGO (7)	Consolidation (14)	GGO (13)	Resolution (0)	
P17/ female/48	GGO (1)	GGO (4)	GGO (6)	GGO (3)	
Average CT score/per patient	4.3±3.2	8.2±6.0	7.2±4.5	4.2±2.7	0.0190*

Date are presented as the mean± SD. NP, thin-section CT not performed; GGO, ground-glass opacities

*$P<0.05$ between over 4 weeks since admission

Table 4 CT Features of Patients with COVID-19 within 4 weeks since admission

CT characteristics	Features at week 1	Features at week 2	Features at week 3	Features at week 4[#]	*P* value
Lung involvement					0.0014*
Unilateral	5(29.4%)	0(0)	2(11.8%)	3(21.4%)	
Bilateral	12(70.6%)	17(100%)	15(88.2%)	10(71.4%)	
Location					0.5184
Central	0(0)	0(0)	0(0)	1(7.1%)	
Peripheral	13(76.5%)	11(64.7%)	10(58.8%)	9(63.3%)	
Both	4(23.5%)	6(35.3%)	7(41.2%)	3(21.4%)	
Predominant distribution					0.1053
Septal/subpleural	8(47.1%)	7(41.2%)	6(35.3%)	6(42.9%)	
Peribronchovasular	1 (5.8%)	0(0)	0(0)	6(42.8%)	
Both	8(47.1%)	10(58.8%)	11(64.7%)	1(7.1%)	
Random	0(0)	0(0)	0(0)	0(0)	
Extent of lesion involvement					0.2086
focal	6(35.3%)	0(0)	1(5.9%)	2(14.3%)	
multifocal	5(29.4%)	9(52.9%)	6(35.3%)	4(28.6%)	
diffuse	6(35.3%)	8(47.1%)	10(58.8%)	7(50%)	
Predominantly CT pattern					0.7344
Ground glass opacity	13(76.5%)	9(52.9%)	13(76.5%)	10(71.4%)	0.1332
GGO alone	5(38.5%)	0(0)	2(15.4%)	1(10%)	
GGO+ interlobular septal thickening	7(53.8%)	6(66.7%)	5(38.5%)	3(30%)	
GGO+irregular linear opacities	1(7.7%)	3(33.3%)	6(37.5%)	6(60%)	
Consolidation	2(11.8%)	5(29.4%)	2(11.8%)	0(0)	
Reticular	0(0)	0(0)	0(0)	0(0)	

Mixed	2(11.8%)	3(17.6%)	2(11.8%)	3(21.4%)	
Presence of nodule	0(0%)	0(0)	1(5.9%)	0(0)	0.2997
Margin definition					0.0558
Well-defined	2(11.8%)	0(0)	0(0)	0(0)	
Poor-defined	15(88.2%)	17(100%)	17(100%)	13 (92.8%)	
Interlobular/septal thickening	7(41.2%)	9(52.9%)	12(70.6%)	7(50%)	0.3751
Smooth	7(100%)	9(100%)	12(100%)	7(100%)	
Irregular	0(0)	0(0)	0(0)	0(0)	
Enlarged pulmonary vessels	12(70.6%)	8(47.1%)	12(70.6%)	10(71.4%)	0.3407
Bronchiolar dilatation	0(0)	0(0)	0(0)	2(14.3%)	0.0177*
Crazy paving	6(35.3%)	13(76.5%)	7(41.2%)	0(0)	<0.0001*
Air bronchogram	5(29.4%)	11(64.7%)	8(47.1%)	3(21.4%)	0.0714
Thickening of the adjacent pleura	7(41.2%)	13(76.5%)	12(70.6%)	6(42.9%)	0.0320*
Interleaf fissure displacement	4(23.5%)	4(23.5%)	5(29.5%)	2(14.3%)	0.8366
Evidence of pulmonary fibrosis	0(0)	0(0)	0(0)	3(21.4%)	0.0012*
Pleural effusion	0(0)	2(11.8%)	4(23.5%)	1(7.1%)	0.0071*
Lymphadenopathy	0(0)	0(0)	0(0)	0(0)	1.0000

Data are presented as the n (n/N %), where N is the total number of CT scans with available data.

14 CT scans were available at 4th week.

*P<0.05 between over 4 weeks since admission

Figure legends

Figure 1 Time course of clinical parameters changes in the 17 Patients with COVID-19. T, temperature: CRP, C-reactive protein, ESR, erythrocyte sedimentation rate; ALT, Alanine aminotransferase; AST, Aspartate aminotransferase.

Figure 2 Transverse thin-section CT scans in different patients with COVID-19 on admission showed (a) homogeneous ground-glass opacities, (b) ground-glass opacities associated with smooth interlobular and intralobular septal thickening (crazy paving), (c) solid nodule with halo sign and thickening of the adjacent pleura(arrow), and (d) air bronchograms (arrow) within the consolidation.

Figure 3 Line graph showing the average CT score in all patients at various time points from admission and three patterns of radiographic progression determined from serial chest CT scans. Type 1 stands for an initial radiographic deterioration to a peak level followed by radiographic improvement, with maximum difference in overall mean lung involvement greater than 25%; Type 2 is progressive radiographic improvement. Type 3 represents a static radiographic change with no discernible radiographic peak or change in overall mean lung involvement of less than 25% for more than 2 weeks.

Figure 4 Transverse thin-section serial CT scans in a 44-year-old male with COVID-19 obtained over the course of admission. (a) Scan obtained on 3rd day since admission shows patchy ground glass opacities with interlobular and intralobular septal thickening that affected bilateral, subpleural lung parenchyma of both lower lobes. (b) Scan obtained on 8th day shows that the lesions extent has increased. (c) Scan obtained on day 17 shows the previous opacifications being mildly

dissipated and the density became heterogeneous with irregular linear opacities. (d) Scan obtained on day 23 shows further resolution of the lesions.

Figure 5 Transverse thin-section serial CT scans in a 37-year-old male with COVID-19 obtained over the course of admission. (a) Scan obtained on day 2 since admission shows focal subpleural ground glass opacity along with interlobular and intralobular septal thickening (crazy paving) in the right lower lobe. (b) Scan obtained on day 9 shows a slight enlargement of the opacification. (c) Scan obtained on day 20 shows increased density of the lesions, although it was reduced in extent. (c) Scan obtained on day 29 shows ground-glass opacities with superimposed irregular linear opacities.

Figure 6 Transverse thin-section serial CT scans in a 54-year-old female with COVID-19 obtained over the course of admission. (a) Scan obtained on day 6 since admission shows flakes of consolidations in the right lower lobe. (b) Scan obtained on day 14 shows that the previous lesion was dissipated into light ground glass opacities. (c) Scan obtained on day 20 shows further resolution of the lesions.

Figure 7 (a)Stacked-bar graph shows distribution of different CT patterns of lung changes at various time points. (b) Stacked-bar graph shows distribution of different types of ground-glass opacities on thin-section CT scans at various time points.

Figure 1

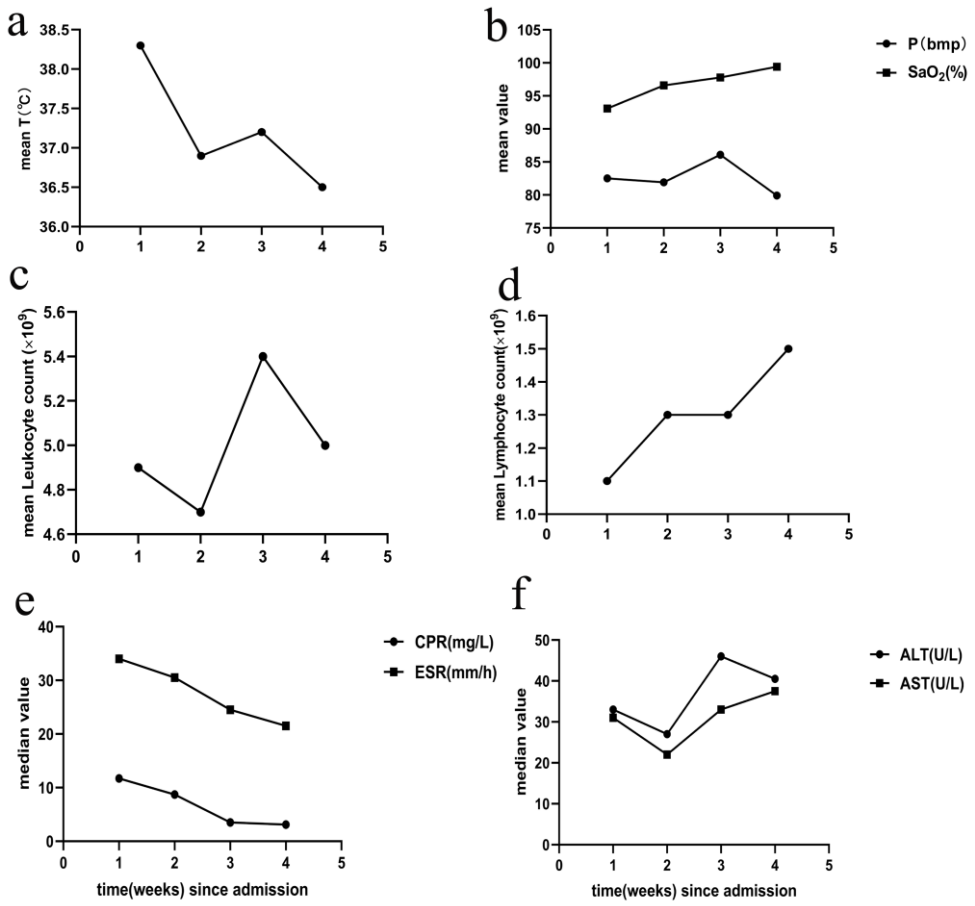
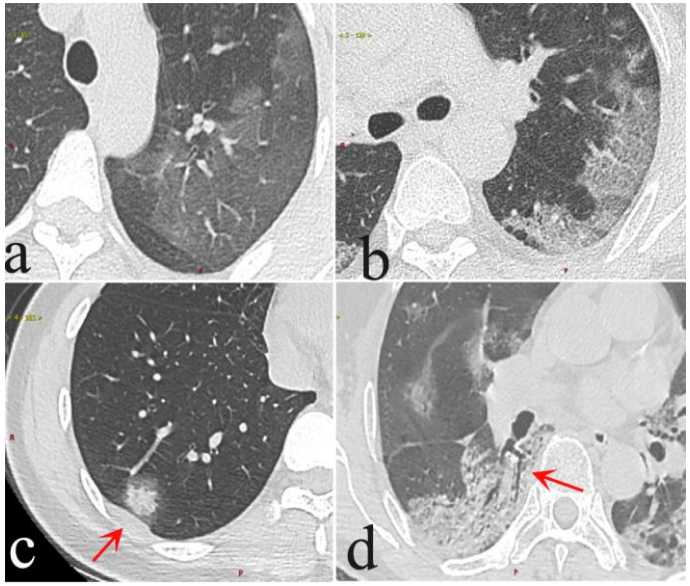


Figure 2



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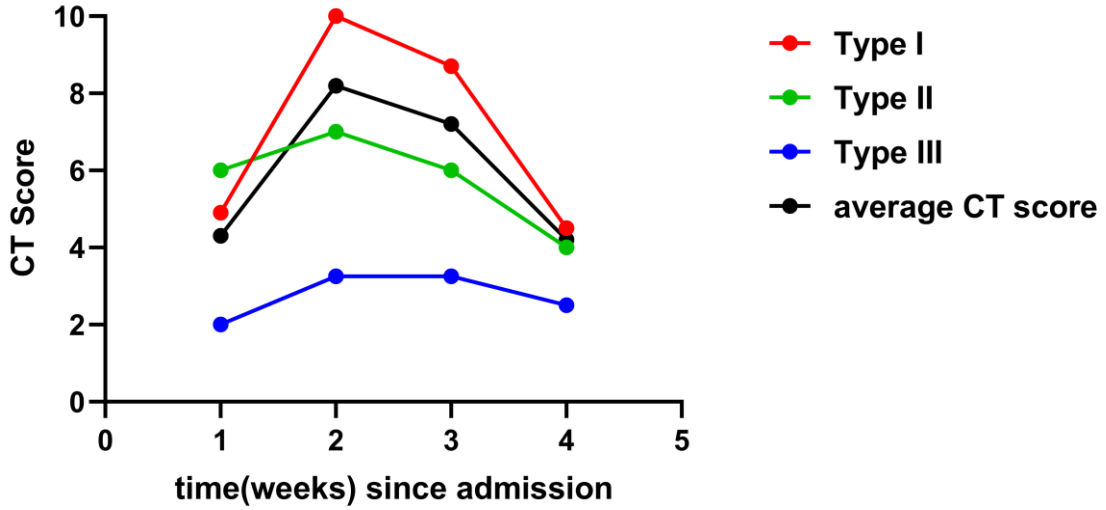

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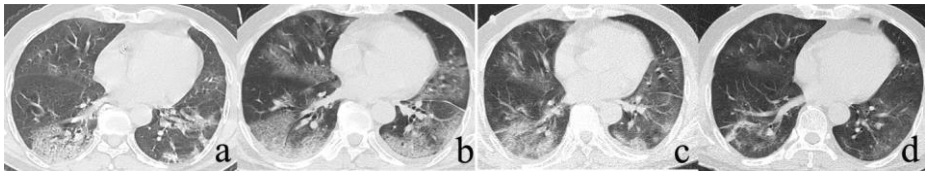

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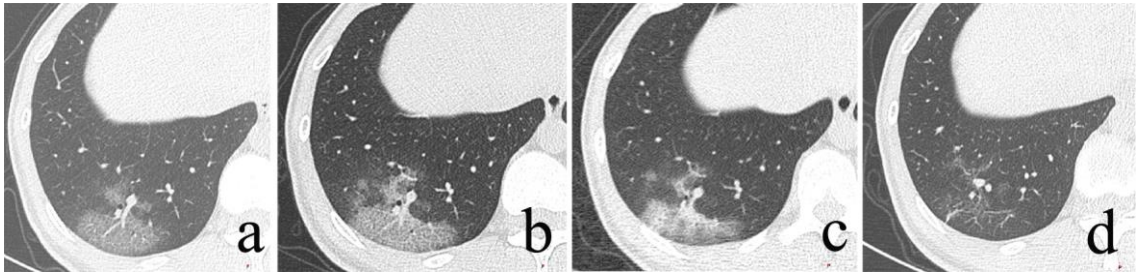

Figure 6

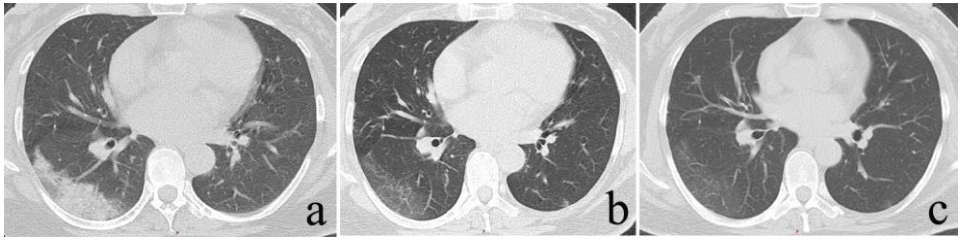

Figure 7