Original Article

Evolution of chest CT manifestations of COVID-19: a longitudinal study

Min Kong[1#], Hai Yang[2#], Xiaodong Li[3], Jianfei Shen[3], Xinjian Xu[4], Dongqing Lv[5]

[1]Department of Thoracic Surgery, Taizhou Enze Medical center (Group) Enze Hospital, Taizhou, Zhejiang Province, China; [2]Department of Radiology, Taizhou Enze Medical Center (Group) Enze Hospital, Taizhou, China; [3]Department of Cardiothoracic Surgery, Taizhou Hospital of Zhejiang Province, Linhai, China; [4]Department of Interventional Radiology, Jiangyin People Hospital, Jiangyin, China; [5]Department of Respiratory and Critical Diseases, Taizhou Enze Medical Center (Group) Enze Hospital, Taizhou, China

Contributions: (I) Conception and design: M Kong, X Xu; (II) Administrative support: D Lv; (III) Provision of study materials or patients: H Yang; (IV) Collection and assembly of data: X Li, J Shen; (V) Data analysis and interpretation: X Xu, M Kong; (VI) Manuscript writing: All authors; (VII) Final approval of manuscript: All authors.

[#]These authors contributed equally to this work.

Correspondence to: Xinjian Xu. Department of Interventional Radiology, Jiangyin People Hospital, Jiangyin, China. Email: qiezinb@126.com; Dongqing Lv. Department of Respiratory and Critical Diseases, Taizhou Enze Medical Center (Group) Enze Hospital, Taizhou, China. Email: lvdq855@126.com.

Background: The aim of this study was to investigate the chest CT manifestations of COVID-19 and its CT evolving process to explore its inherent outcomes.

Methods: Inpatients diagnosed with COVID-19 at the Enze Hospital from January 17, 2020 to February 15, 2020 were included. The evolving characteristics of CT manifestations and treatment outcomes were analyzed.

Results: Twenty-two patients with COVID-19 were included in the study. Clinical symptoms at the time of onset included fever (n=19) and cough (n=8). The first CT findings mainly included ground-glass opacities (GGOs) (n=18), lung consolidation (n=7), interlobular septal thickening (n=5), and fibrosis-like stripes (n=4). Dynamic CT showed GGOs, lung consolidation, and fibrosis-like stripes, all of which demonstrated a trend that initially increased in number, and then gradually decreased in number or disappeared. According to the characteristics of CT evolution. COVID-19 could be divided into early stage, progressing stage, recovery stage, and dissipation stage. The median times of the respective stages were: early stage—3 days (1–8 days) after disease onset, progressing stage—7 days (4–17 days) after onset, recovery stage—10 days (8–14 days) after onset, and dissipation stage—19.5 days (11–25 days) after onset.

Conclusions: COVID-19 has an acute onset, with main imaging manifestations of different types of GGO with or without lung consolidation in the subpleural regions of the bilateral lungs. The CT manifestations of lung lesions change rapidly. The lung lesions of mild and ordinary types of COVID-19 may improve significantly or disappear in a short period after active treatment, with good prognosis. Moreover, fibrosis-like stripes may be a sign of atelectasis of sub-segment lung tissue of COVID-19 and may be a specific sign for the diagnosis of COVID-19.

Keywords: Coronavirus disease 2019 (COVID-19); pneumonia; CT; evolution; longitudinal study

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Introduction

As of March 11,2020, the coronavirus disease 2019 (COVID-19) pneumonia, which initially emerged in Wuhan city, China, has led to 118,000 infections and 4,291 fatalities in 114 countries (1-4). It poses a great threaten to the global public health and human life.

In confronting the tremendous threat of COVID-19, many important scientific issues need to be resolved immediately. Among these, imaging examinations (chest X-ray and CT) are important methods for diagnosing COVID-19. However, current imaging studies on COVID-19 are mainly cross-sectional studies (5-11). Systematic imaging studies regarding the evolving patterns of COVID-19 are still insufficient. Therefore, it is necessary to conduct studies on the image evolution of COVID-19 to explore its evolving patterns from the perspective of radiology.

In this study, we aim to investigate the evolution of chest CT features and outcome patterns of COVID-19 by analyzing the imaging and clinical data of 22 COVID-19 patients treated in our hospital. Such analysis will provide a basis for clinical diagnosis and treatment. We present the following article in accordance with the STROBE reporting checklist (available at http://dx.doi.org/10.21037/jtd-20-1363).

Methods

Study design and participants

This was a retrospective, single-center, observational study. A total of 76 patients with COVID-19 confirmed by RT-PCR tests of sputum, throat swabs, and lower respiratory tract secretion specimens at Taizhou Enze Hospital from January 17, 2020 to February 15, 2020 were selected. The inclusion criteria were: (I) the patient's first visit was to our hospital, and subsequent clinical treatments and examinations were all conducted at our institution; (II) the clinical treatment plan and laboratory examination data were complete; (III) the patient received at least two chest CT examinations. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). This study was approved by the Medical Ethics Committee of Taizhou Enze Hospital. Because of the retrospective nature of the study, patient consent for inclusion was waived.

Clinical information collection

The collected data included epidemiological history (history of Wuhan residence or exposure), clinical data (demographic data, clinical symptoms, physical signs, laboratory test indicators, complications, and clinical outcomes) and image data (dynamic evolving characteristics of chest CT).

Statistical analysis

Continuous data conforming to the normal distribution were expressed as the mean ± standard deviation (mean ± SD), otherwise expressed using the median; categorical variables were represented by frequency. All statistical analyses were performed using SPSS 26.0 software.

Results

General clinical information

A total of 22 COVID-19 patients (13 males and 9 females) were included in this study, all of whom were diagnosed with mild or ordinary type COVID-19 (12). Age of onset was 20 to 74 years old, with a median age of 45 years. All patients had a history of Wuhan residence or exposure in Wuhan. The median time from onset of the disease to admission was 1 day (0–7 days), and the median time from onset to diagnosis was 3 days (0–9 days). Among the patients, 19 patients had a fever at the time of onset; 8 patients had a cough, of whom 6 had a dry cough and 2 had sputum; other symptoms included diarrhea (n=3), pharyngalgia (n=2), runny nose (n=1), fatigue (n=1), and dyspnea (n=1) (*Table 1*).

Laboratory information

Eleven patients had lymphopenia, 4 patients had thrombopenia, and 3 patients had leukopenia and neutropenia. Besides, 8 patients had hypoalbuminemia, and 8 patients had myoglobinemia. In addition, 12 patients had CRP values higher than normal, and 7 patients had an ESR higher than normal (*Table 2*).

Imaging results

General information on imaging examination

All 22 COVID-19 patients underwent two chest CT examinations during hospitalization, 20 patients underwent three chest CT examinations, and 11 patients underwent four chest CT examinations. The median interval time was 3 days (2–10 days) between the first

Table 1 Demographics and baseline characteristics of COVID-19 patients

Characteristics	All patients (n=22)
Age (years)	45 [20–74]
Sex	
Male	13 (59.1)
Female	9 (40.9)
Height (cm)	166.20±7.75
Weight (kg)	65.23±18.98
Body surface area (m^2)	1.81±0.26
Exposure to Wuhan city	22 (100.0)
Smoking history	1 (4.5)
Accompanying disease	
Klebsiella pneumonia	1 (4.5)
Cerebral aneurysm underwent interventional therapy	1 (4.5)
Left breast cancer underwent surgery	1 (4.5)
Splenectomy	1 (4.5)
Gallstone	1 (4.5)
COVID-19 confirmed by real-time RT-PCR	
Sputum	7 (31.8)
Throat swab	15 (68.2)
Days from illness onset to admission	1 [0–7]
Days from illness onset to confirmed disease	3 [0–9]
Signs and symptoms at admission	
Fever	19 (86.4)
Cough	6 (27.3)
Sputum production	2 (9.1)
Diarrhoea	3 (13.6)
Pharyngalgia	2 (9.1)
Fatigue	1 (4.5)
Running nose	1 (4.5)
Dyspnea	1 (4.5)
Temperature (℃)	
<37.3	0
37.3–38.0	10 (45.5)
38.1–39.0	9 (40.9)
>39.0	0
Oxyhemoglobin saturation (%)	97 [91–100]
Systolic pressure, mmHg	128 [110–155]

Data are mean or median [IQR], mean ± SD, or n (%). COVID-19, coronavirus disease 2019.

and second CT examinations, 5 days (3–18 days) between the second and third CT examinations, and 9 days (4–16 days) between the third and fourth CT examinations (http://cdn.amegroups.cn/static/application/f60ac1df948fd97212228bd6cf343dbe.docx).

Imaging manifestations of the patient's first CT examination

The lesions of 22 patients were located in the subpleural regions of the bilateral lungs, and those of 15 patients were located in the middle and lower lobes of the bilateral lungs. The first CT revealed the following signs: 18 patients showed single or multiple patchy or nodular ground-glass opacity (GGO) lesions, and 7 cases showed lung consolidation. Other accompanying signs included 5 cases of interlobular septal thickening inside the GGO lesions, 4 cases of fibrosis-like stripes, 2 cases of ground-glass nodules (GGNs) with reversed halo sign, 2 cases of air bronchogram sign, and 2 cases of vascular thickening. One patient showed no abnormalities in imaging (http://cdn.amegroups.cn/static/application/f60ac1df948fd97212228bd6cf343dbe.docx).

Evolution of main CT image manifestations

Over time, GGO in the lungs initially increased in number and density, or even progressed to consolidation, and later these GGO lesions gradually decreased in number and density or disappeared (*Table 3*, *Figures 1*,*2*,*3*). Besides, the lung consolidation demonstrated a trend of first increasing in number and then decreasing in number or disappearing over an extended time (*Table 3*, *Figure 4*). In addition, the signs of interlobular septal thickening within the GGO lesions demonstrated a trend of an increased size and density, and even the crazy-paving sign, followed by a decrease in size and reduced or disappeared density (*Table 3*, *Figure 5*). The fibrosis-like stripes also showed a trend of increasing in number first, and then decreasing in number or disappearing (*Table 3*, *Figures 6*,*7*,*8*,*9*).

Imaging staging

Based on the dynamic evolution and outcome characteristics of the CT images of this group of cases, this study divided the dynamic changes of COIVD-19 into four stages: early stage (lung lesions start to appear), progressing stage (lung lesions clearly increase in number or new lesions appear), recovery stage (lung lesions begin to decrease in number) and dissipation stage (lung lesions clearly decrease in number or disappear).

Table 2 Laboratory findings of COVID-19 patients on admission to hospital

Laboratory findings	Normal range	All patients (n=22)	All patients (n=22)		
			Level	Number	Count (%)
Haemoglobin (g/L)	130–175	149 [116–160]	Increased	0	0
			Decreased	2	9.1
White blood cell count ($\times10^9$/L)	3.5–9.5	4.35 [1.9–11.7]	Increased	1	4.5
			Decreased	3	13.6
Neutrophil count ($\times10^9$/L)	1.8–6.3	2.85 [0.8–7.7]	Increased	1	4.5
			Decreased	3	13.6
Lymphocyte count ($\times10^9$/L)	1.1–3.2	1.05 [0.3–2.7]	Increased	0	0
			Decreased	11	50
Platelet count ($\times10^9$/L)	125–350	196.5 [101–270]	Increased	0	0
			Decreased	4	18.2
Erythrocyte sedimentation rate (mm/h)	0–15	13 [2–47]	Increased	7	31.8
Procalcitonin (ug/L)	<0.5	0.03 [0.02–0.08]	Increased	0	0
C-reactive protein (mg/L)	<8.0	9.14 [1.11–47.15]	Increased	12	54.5
Prothrombin time (s)	11.0–14.5	12.15 [10.8–14.3]	Increased	0	0
			Decreased	2	9.1
D-dimer (mg/L)	0.0–0.5	0.24 [0.14–17.13]	Increased	3	13.6
Albumin (g/L)	40.0–55.0	40.85 [35.7–49.8]	Increased	0	0
			Decreased	8	36.4
Alanine aminotransferase (U/L)	9–50	21.50 [10–97]	Increased	3	13.6
			Decreased	0	0
Aspartate aminotransferase (U/L)	15–40	28.0 [19–77]	Increased	3	13.6
			Decreased	0	0
Total bilirubin (μmol/L)	3.4–20.5	9.75 [4–32.7]	Increased	1	4.5
			Decreased	0	0
Serum creatinine (μmol/L)	59–104	76.5 [53–110]	Increased	2	9.1
			Decreased	1	4.5
Urea nitrogen (mmol/L)	3.10–8.00	4.07 [2.37–8.57]	Increased	1	4.5
			Decreased	3	13.6
Lactate dehydrogenase (U/L)	80–285	192.5 [152–828]	Increased	3	13.6
			Decreased	0	0
Troponin-I (ng/mL)	<0.100	0.01 [0.01–0.02]	Increased	0	0
Myoglobin (ng/mL)	20–80	20 [12–92.1]	Increased	1	4.5
			Decreased	8	36.4

Data are median [IQR]. COVID-19, coronavirus disease 2019.

Table 3 The evolution tendency of first CT findings of COVID-19 patients

First CT findings	Number	Evolution tendency		
		Second CT findings	Third CT findings	Fourth CT findings
Ground-glass lesions	18			
Solitary focal GGO (case 6, 9, 16, 19, 20, 22)	6	GGO number increased (case 6, 9, 16, 19, 20, 22); GGO transformed into consolidation (case 6)	GGO number increased and partly became consolidation (case 16, 19); GGO transformed into consolidation (case 22); GGO significantly decreased (case 6, 9); consolidation disappeared (case 6)	GGO disappeared (case 16, 19); GGO number significantly decreased (case 22); consolidation significantly decreased (case 16, 19, 22)
Multiple GGNs (case 4, 8, 15, 21)	4	GGO number increased (case 4, 8, 15, 21); GGO density increased (case 4, 15)	GGO number significantly decreased (case 8, 15); GGO density decreased (case 4, 8); GGO number increased (case 21)	GGO number decreased (case 4, 21); GGO density decreased (case 4)
Solitary large GGO (case 1)	1	GGO disappeared (case 1)	NA	NA
Multiple patchy GGOs (case 3, 5, 7, 11, 12, 13, 17)	7	GGO number increased (case 3, 5, 11, 13); GGO density increased (case 5, 7, 17); GGO number increased and partly became consolidation (case 7, 17); GGO number decreased (case 12); GGO density decreased (case 13)	GGO number decreased (case 3, 5, 7, 11, 12, 17); GGO density decreased (case 5, 13); consolidation increased (case 7); consolidation disappeared (case 17); GGO number increased (case 13)	GGO number decreased (case 3, 5, 11, 13) GGO density decreased (case 5) Consolidation significantly decreased (case 7)
Lung consolidation	7			
Solitary patchy consolidation (case 1, 10, 14)	3	Consolidation increased (case 14); consolidation disappeared (case 1); consolidation transformed into GGO (case 10)	Consolidation decreased (case 14); GGO number significantly decreased (case 10)	Consolidation disappeared (case 14)
Multiple patchy consolidation (case 2, 3, 11, 12)	4	Consolidation increased (case 3, 11); consolidation decreased (case 2, 12)	Consolidation decreased (case 2, 3, 11); consolidation disappeared (case 12)	Consolidation significantly decreased (case 3, 11)
Interlobular septal thickening inside the GGO (case 5, 7, 13, 20, 22)	5	Enlarged (case 5, 20, 22); density increased (case 5, 20, 22); shrunken (case 7); disappeared (case 13)	Disappeared (case 7, 22); shrunken (case 5); density decreased (case 5)	Shrunken (case 5)
"Fibrosis-like" stripes (case 3,12,14,17)	4	Increased (case 3, 12, 14, 17)	Disappeared (case 12, 17); decreased (case 3); increased (case 14)	Disappeared (case 14); decreased (case 3)
GGN with "reversed halo sign" (case 15,21)	2	GGN transformed into patchy GGO (case 15, 21)	GGO decreased (case 15, 21)	GGO significantly decreased (case 15, 21)
Air bronchogram (case 5, 10)	2	Shrunken (case 5, 10)	Disappeared (case 5, 10)	NA
Vascular thickening (case 17)	1	Unchanged (case 17)	Unchanged (case 17)	NA
Normal CT findings (case 18)	1	Normal CT findings (case 18)	Normal CT findings (case 18)	NA

COVID, coronavirus disease; NA, not available; GGO, ground-glass opacity; GGN, ground-glass nodule.

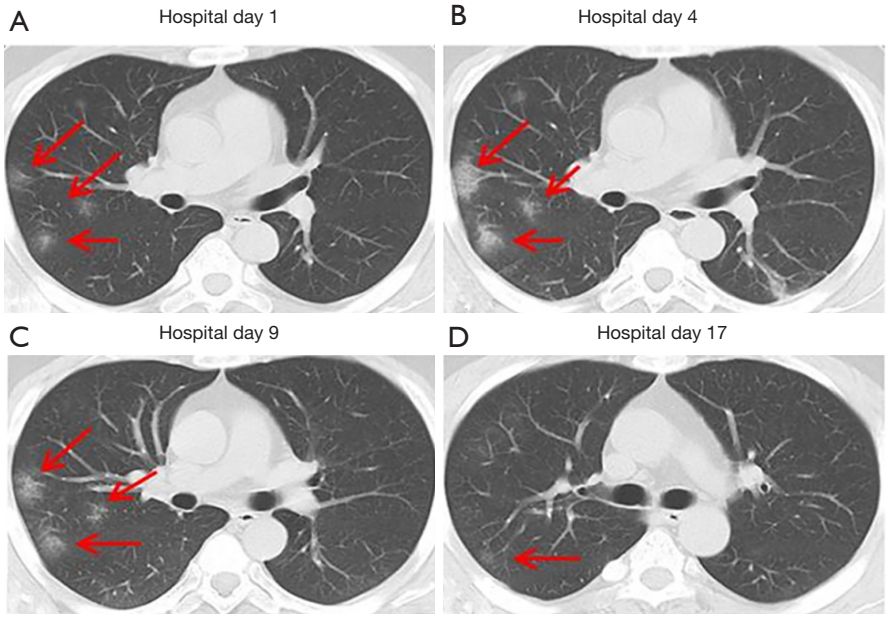

Figure 1 Images from case 4. (A) First CT performed on hospital day 1 shows multiple ground-glass nodules in subpleural region of right lung (red arrow); (B) second CT performed on hospital day 4 shows enlarged ground-glass opacities in subpleural region of right lung (red arrow); (C) third CT performed on hospital day 9 shows shrunken ground-glass opacities in subpleural region of right lung (red arrow); (D) fourth CT performed on hospital day 17 shows significantly decreased ground-glass opacities in subpleural region of right lung (red arrow).

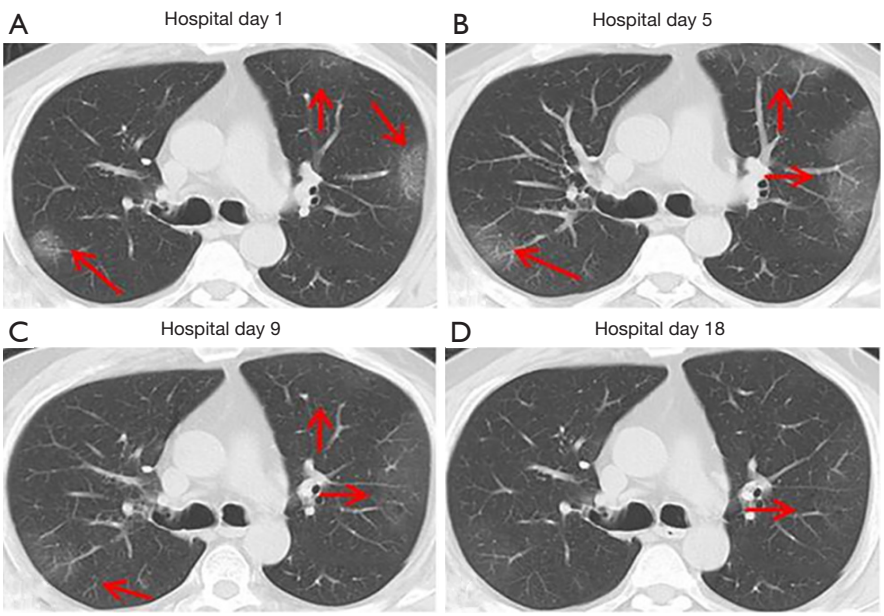

Figure 2 Images from case 13. (A) First CT performed on hospital day 1 shows multiple patchy ground-glass opacities combined with interlobular septal thickening in bilateral subpleural regions (red arrow); (B) second CT performed on hospital day 5 shows the size of ground-glass opacities increase but the density decrease (red arrow); (C) third CT performed on hospital day 9 shows the further decreased density of ground-glass opacities (red arrow); (D) fourth CT performed on hospital day 18 shows the ground-glass opacities become almost invisible (red arrow).

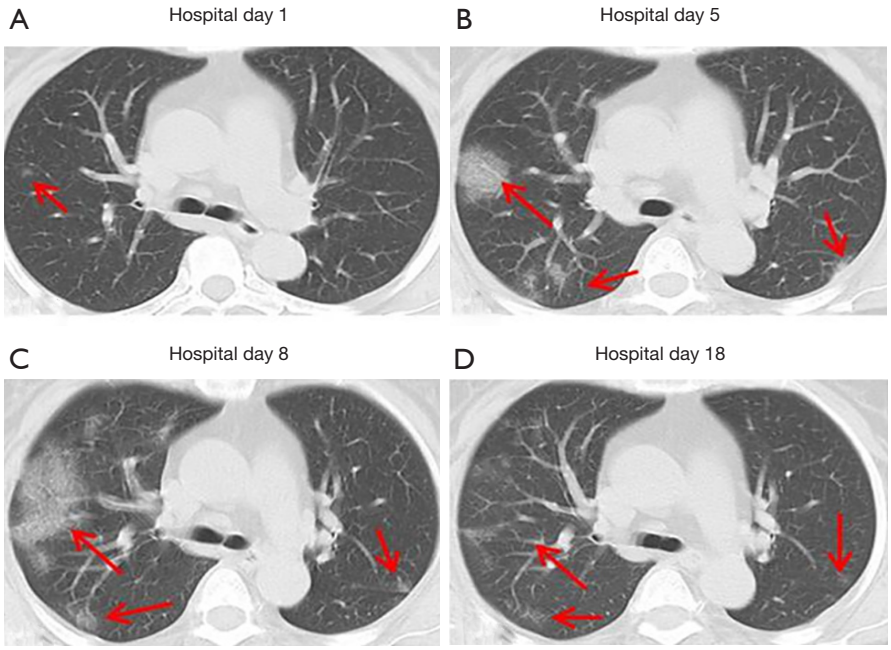

Figure 3 Images from case 21. (A) First CT performed on hospital day 1 shows ground-glass nodule in subpleural region of right lung (red arrow); (B) second CT performed on hospital day 5 shows increased patchy ground-glass opacities combined with interlobular septal thickening in bilateral subpleural regions (red arrow); (C) third CT performed on hospital day 8 shows further increased patchy ground-glass opacities combined with interlobular septal thickening in bilateral subpleural regions (red arrow); (D) fourth CT performed on hospital day 18 shows significantly decreased ground-glass opacities in bilateral subpleural regions (red arrow).

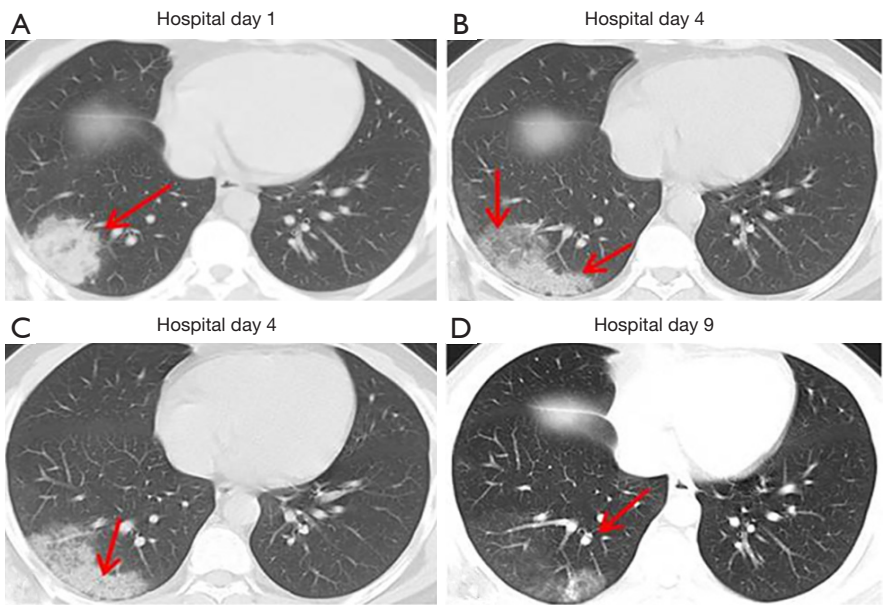

Figure 4 Images from case 10. (A) First CT performed on hospital day 1 shows solitary consolidation in subpleural region of right inferior lobe (red arrow); (B,C) second CT performed on hospital day 4 shows decreased consolidation as well as increased ground-glass opacities in subpleural region of right inferior lobe (red arrow); (D) third CT performed on hospital day 9 shows significantly decreased ground-glass opacities in subpleural region of right inferior lobe (red arrow).

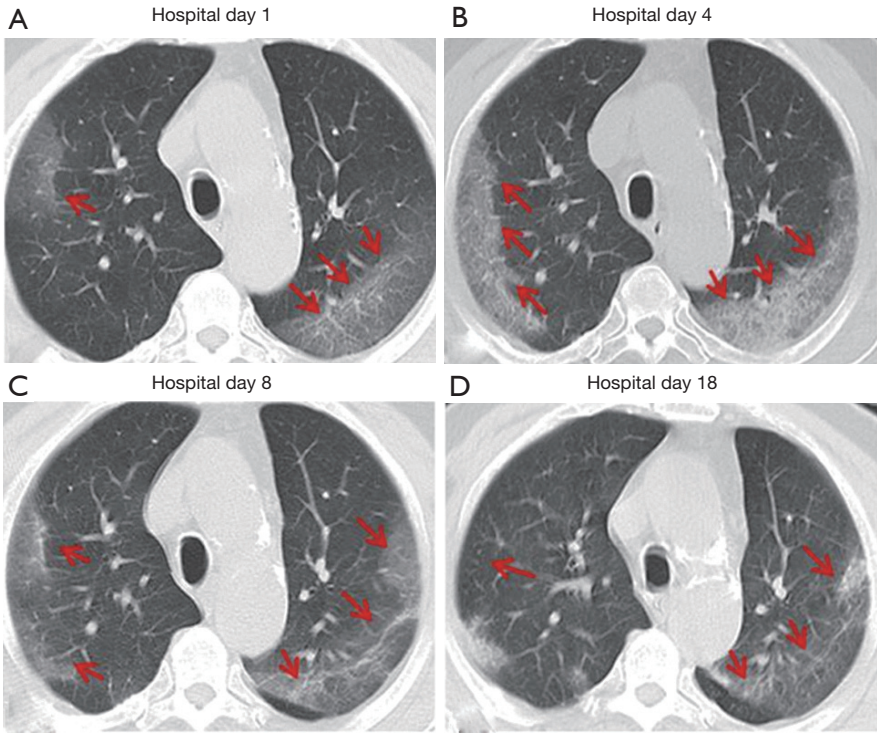

Figure 5 Images from case 5. (A) First CT performed on hospital day 1 shows patchy ground-glass opacities combined with interlobular septal thickening in bilateral subpleural regions (red arrow); (B) second CT performed on hospital day 4 shows enlarged patchy ground-glass opacities combined with "crazy-paving sign" in bilateral subpleural regions (red arrow); (C) third CT performed on hospital day 8 shows shrunken patchy ground-glass opacities in bilateral subpleural regions (red arrow); (D) fourth CT performed on hospital day 18 shows decreased ground-glass opacities in bilateral subpleural regions (red arrow).

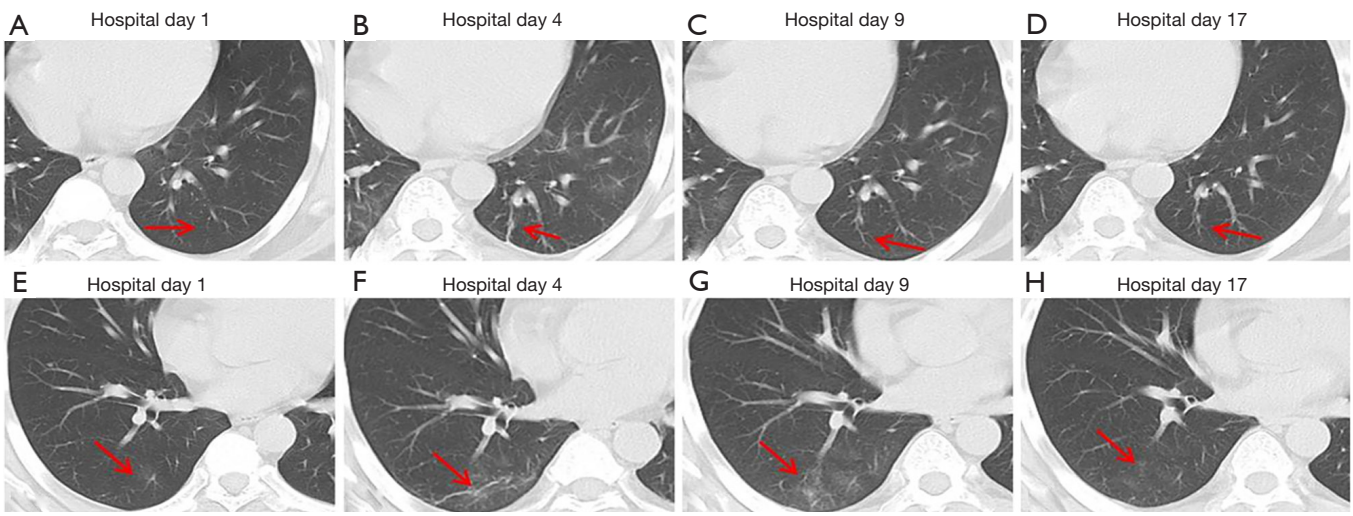

Figure 6 Images from case 4. (A,E) First CT performed on hospital day 1 shows no stripes in bilateral inferior lobes (red arrow); (B,F) Second CT performed on hospital day 4 shows "fibrosis-like" stripes in bilateral inferior lobes (red arrow); (C,G) Third CT performed on hospital day 9 shows "fibrosis-like" stripes in bilateral inferior lobes become almost invisible (red arrow); (D,H) fourth CT performed on hospital day 17 shows "fibrosis-like" stripes in bilateral inferior lobes disappear (red arrow).

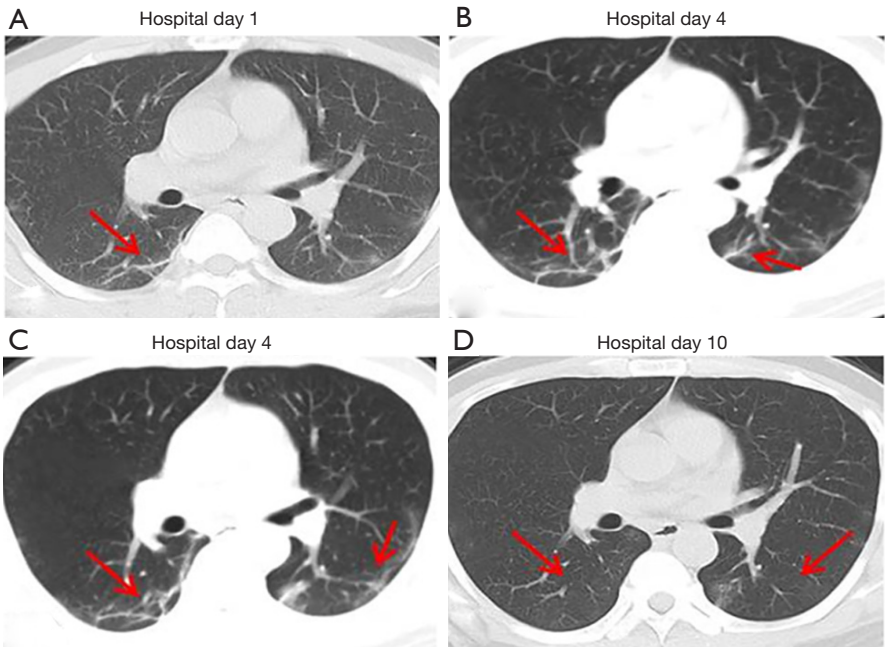

Figure 7 Images from case 12. (A) First CT performed on hospital day 1 shows "fibrosis-like" stripes in right inferior lobe (red arrow); (B,C) second CT performed on hospital day 4 shows increased "fibrosis-like" stripes in bilateral inferior lobes (red arrow); (D) third CT performed on hospital day 10 shows "fibrosis-like" stripes in bilateral inferior lobes disappear (red arrow).

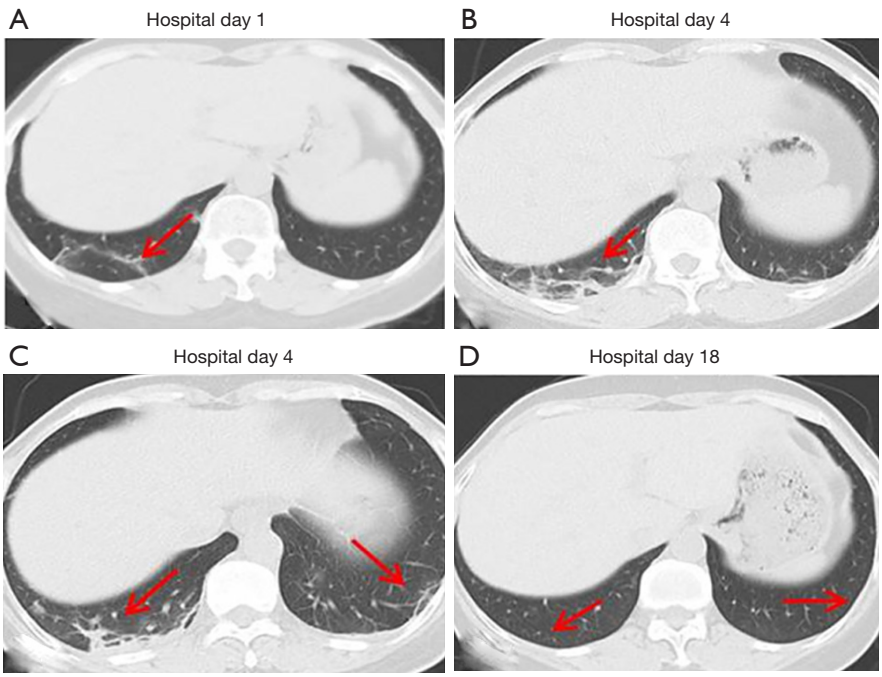

Figure 8 Images from case 17. (A) First CT performed on hospital day 1 shows "fibrosis-like" stripes in right inferior lobe (red arrow); (B,C) Second CT performed on hospital day 4 shows increased "fibrosis-like" stripes in bilateral inferior lobes (red arrow); (D) Third CT performed on hospital day 18 shows "fibrosis-like" stripes in bilateral inferior lobes disappear (red arrow).

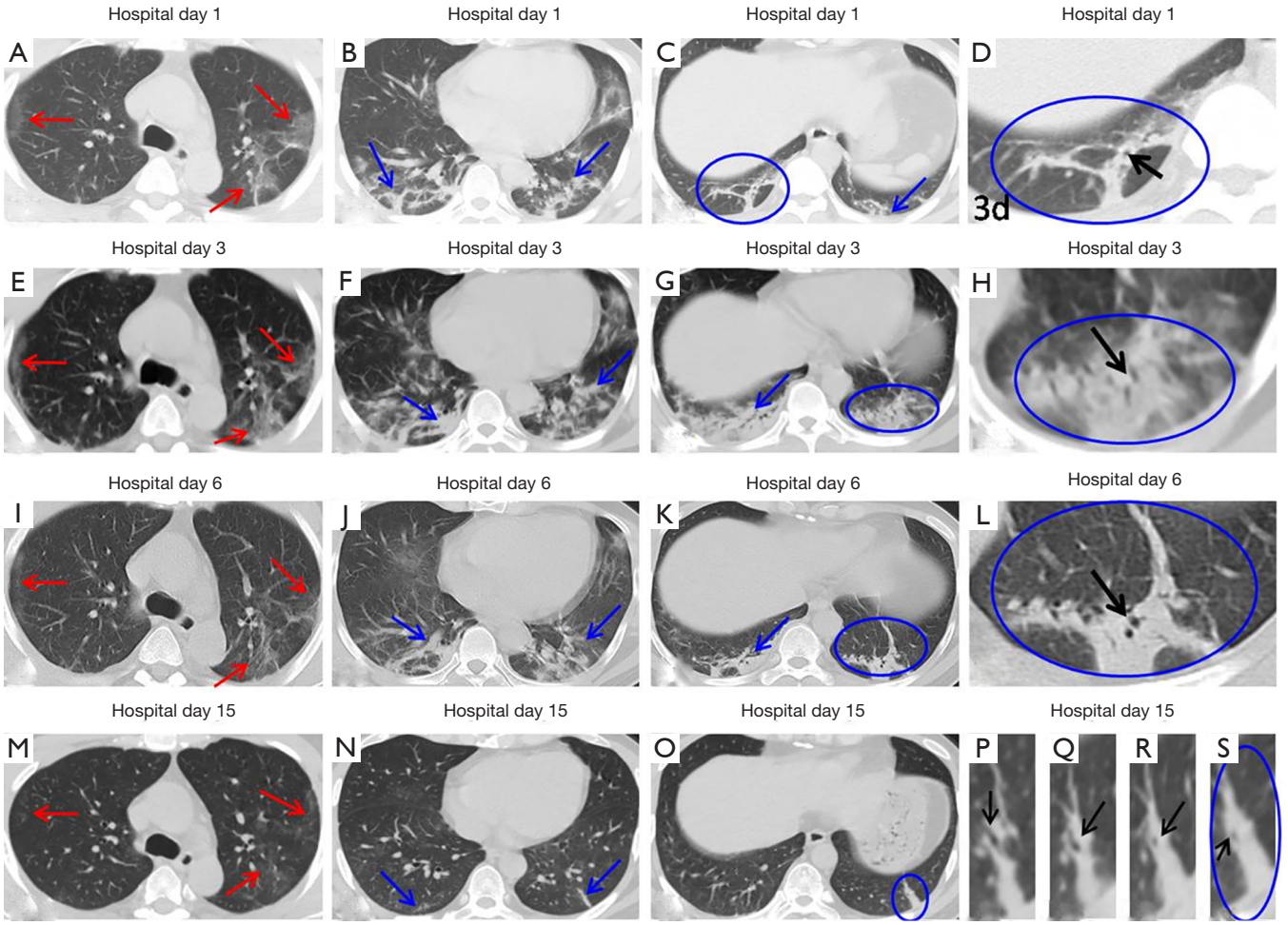

Figure 9 Images from case 3. Different slices on the same CT scans are horizontally arrayed; same slices on the different CT scans are vertically arrayed. (A,B,C,D) First CT performed on hospital day 1 shows multiple ground-glass opacities in bilateral subpleural regions (red arrow) and consolidation combined with "fibrosis-like" stripes in bilateral inferior lobes (blue arrow and circle); (E,F,G,H) second CT performed on hospital day 3 shows increased ground-glass opacities in bilateral subpleural regions (red arrow) and increased consolidation combined with "fibrosis-like" stripes in bilateral inferior lobes (blue arrow and circle); (I,J,K,L) third CT performed on hospital day 6 shows decreased ground-glass opacities in bilateral subpleural regions (red arrow) and decreased consolidation combined with "fibrosis-like" stripes in bilateral inferior lobes (blue arrow and circle); (M,N,O,P,Q,R,S) fourth CT performed on hospital day 15 shows decreased ground-glass opacities in bilateral subpleural regions (red arrow) and significantly decreased consolidation combined with "fibrosis-like" stripes in bilateral inferior lobes (blue arrow and circle); (D,H,L,P,Q,R,S) local enlarged images show bronchioles (black arrow) could be observed in consolidation (blue circle).

Evolution of time points of imaging staging

The hospitalization time points and the disease time points at the time of CT examinations of this group of patients were classified according to imaging stages, and the disease time points of each imaging stage in the course of disease evolution were obtained (*Table S1*). In this study, the median time for the appearance of early stage imaging manifestations was 3 days (1–8 days) after onset, the median time of the progressing stage was 7 days (4–17 days) after onset, the median time of the recovery stage was 10 days (8–14 days) after onset, and the median time of the dissipation period was 19.5 days (11–25 days) after onset.

Correlations between clinical and radiological findings

In the present study, the correlation between patients'

Table 4 Treatments and outcomes of COVID-19 patients

Treatments and outcomes	All patients (n=22)
Antiviral treatment	
A-interferon	22 (100%)
Lopinavir/ritonavir	22 (100%)
Arbidol hydrochloride	16 (72.7%)
Antibacterial treatment	14 (63.6%)
Levofloxacin	8 (36.4%)
Azithromycin	5 (22.7%)
Ceftriaxone	1 (4.5%)
Glucocorticoid treatment	8 (36.4%)
Immune globulin treatment	6 (27.3%)
Traditional Chinese medicine	19 (86.4%)
Oxygen therapy	11 (50%)
Prognosis	
Discharged	13 (59.1%)
In hospital	9 (40.9%)

clinical status (fever and cough) and the CT results was observed. However, the correlations between laboratory data and the CT results were not observed. For 19 patients with fever as the initial symptom, the median duration of fever was 4 days (2–19 days). Fourteen patients experienced the disappearance of their fever during the progressing stage (stage II), while 4 patients experienced such disappearance during the recovery stage (stage III), and 1 patient became fever free during the dissipation stage (stage IV). For 6 patients with a cough as the initial symptom, the median duration of the cough was 13.5 days (10–20 days). All 6 patients experienced the disappearance of the cough during the dissipation stage (stage IV).

Prognosis

After active treatment with oxygen therapy, antiviral and antibacterial drugs, and glucocorticoids, the patients in this study generally showed a good prognosis. In the present study, methylprednisolone sodium succinate (40 mg/qd) was used through an intravenous drip for three days. As of February 15, 2020, 13 patients had been discharged, 9 patients were still hospitalized, and no serious complications or deaths occurred (*Table 4*).

Discussion

COVID-19 is extremely contagious and spreads rapidly, making the population generally susceptible and posing a significant threat to public health security. Early diagnosis and isolated treatment are important ways of controlling the epidemic. However, it is difficult to make a clinical diagnosis of COVID-19 because some infected patients lack a clear history of epidemiological exposure and clinical features as well as specific laboratory indicators. Imaging examinations (chest X-ray and CT) are important means of early diagnosis. However, currently, systematic imaging studies on COVID-19 are rare, and most of them are cross-sectional studies. Thus, the imaging evolution of COVID-19 remains unclear. Therefore, this study focused on the chest CT manifestations of COVID-19 and its CT evolving process to explore its inherent outcomes.

We found that common CT manifestations in the early stage of COVID-19 were single or multiple localized GGOs or nodules (*Figure 1A*), single or multiple small patchy GGOs (*Figure 2A*), or large GGOs (*Figure 5*). Most GGOs had unclear edges, whereas some had clear edges. The lesions were mostly distributed in the middle and lower lobes, and were located mostly in the subpleural regions of the bilateral lungs (*Figures 1-11*). In addition, other common CT manifestation was single or multiple lung consolidation (*Figure 4A*). Some GGO lesions were accompanied by interlobular septal thickening within the lesions and an increase of the small blood vessel network, which is similar to fine grid-like shadows (*Figure 5A*) or a crazy-paving sign (*Figure 5B*). Other accompanying signs included fibrosis-like stripes (*Figures 7A,8A,9C*), GGNs with a reversed halo sign (*Figure 10A,11A*), air bronchogram sign (*Figure 4A*), and vascular thickening inside the GGO lesions. The above lesions could exist alone or coexist with other lesions. Over time, GGO in the lungs initially increased in number and density and even became consolidation. Later, these lesions gradually decreased or disappeared. The lung consolidation demonstrated a trend of first increasing in number and then decreasing in number or disappearing. Based on the evolution of these major CT signs, the dynamic imaging changes of COVID-19 can be divided into four stages: early stage (stage I), progressing stage (stage II), recovery stage (stage III), and dissipation stage (stage IV). In addition, the present study observed a correlation between patients' clinical status (fever and cough) and the CT stages. Fourteen of the 19 patients who presented with fever as the initial symptom, experienced

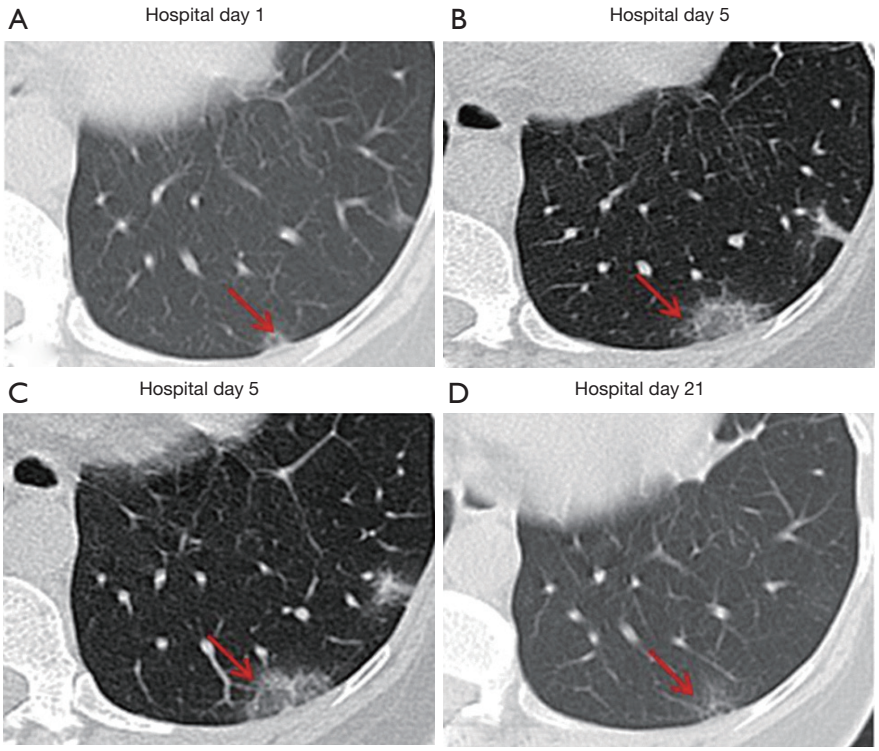

Figure 10 Images from case 15. (A) First CT performed on hospital day 1 shows ground-glass nodule combined with "reversed halo sign" in left inferior lobe (red arrow); (B,C) Second CT performed on hospital day 5 shows ground-glass nodule combined with "reversed halo sign" in left inferior lobe transformed into patchy ground-glass opacity (red arrow); (D) Third CT performed on hospital day 21 shows significantly decreased ground-glass opacity in left inferior lobe (red arrow).

the disappearance of fever during the progressing stage (stage II), 4 patients experienced the disappearance of fever during the recovery stage (stage III), and 1 patients became fever free during the dissipation stage (stage IV), which may indicate that image change has some lag compared to fever change. All 6 patients presenting with a cough as the initial symptom experienced a disappearance of their cough during the dissipation stage (stage IV). The longer duration of the cough may be associated with the stimulation of residual inflammation. These findings indicate that the imaging stages based on the CT results correlate with clinical status and may aid in assessing disease progression and in adjusting treatment strategies in a timely manner.

In a previous longitudinal study of CT images of SARS cases (13), the consolidation could transform into GGO or disappear, whereas GGO could persist or even progress to lobular septum thickening and fibrosis. This study found that in some COVID-19 patients, lesions in the bilateral lungs could also evolve into fibrosis-like stripes in a short period of time. However, the exact imaging pathological mechanism of this sign is currently unclear. Most radiologists in China believe it is a pulmonary interstitial stripe-shaped fibrotic lesion, and it may be a feature of the reversal of COVID-19 (14). Similar to COVID-19, SARS and MERS also often have pulmonary fibrosis. Some researchers have reported that the incidence of SARS-associated pulmonary fibrosis can be as high as 36.7–40% (15-17). Cao *et al.* autopsied patients who died of SARS and found that typical pulmonary fibrosis was detected 33 days after infection with SARS-CoV (18). A CT follow-up study by Zhang *et al.* also showed that pulmonary fibrosis in SARS patients first appeared at least 30 days after onset of the disease (19). Chen *et al.* and Lu *et al.* (20,21) found that stripe-shaped fibrosis lesions of varying degrees remained in SARS patients 1–12 months after the lesions were absorbed. Das *et al.* also found that 33% of patients with MERS still had stripe-shaped fibrosis lesions 1–7 months after recovery (22). A total of 8 cases of this group of patients had fibrosis-like stripes during the course of the disease. Four of these cases were identified at the first CT examination

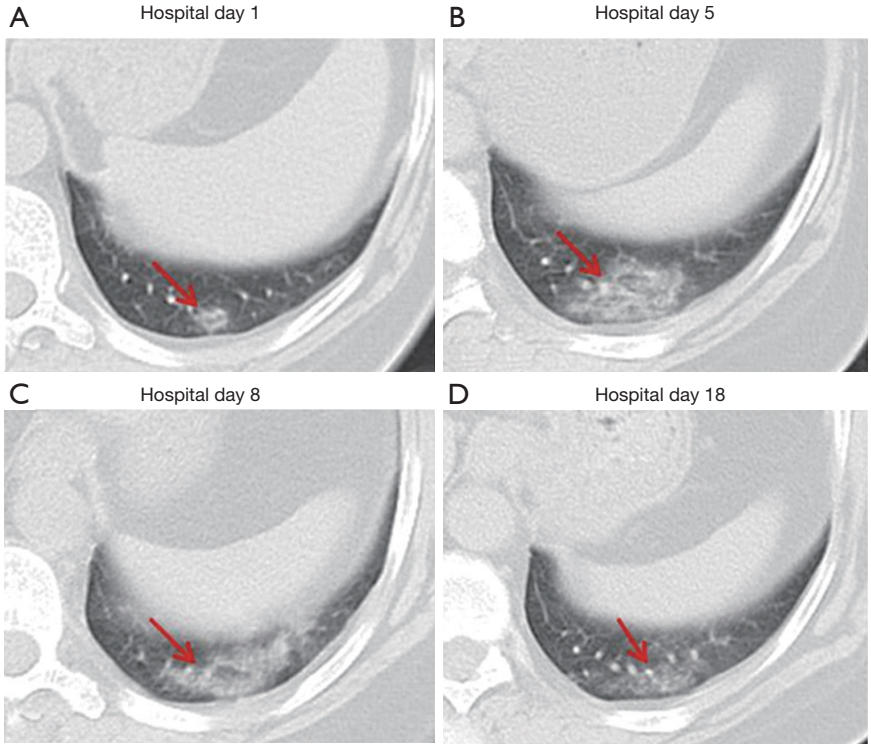

Figure 11 Images from case 21. (A) First CT performed on hospital day 1 shows ground-glass nodule combined with "reversed halo sign" in left inferior lobe (red arrow); (B) second CT performed on hospital day 5 shows ground-glass nodule combined with "reversed halo sign" in left inferior lobe transformed into patchy ground-glass opacity (red arrow); (C) third CT performed on hospital day 8 shows decreased ground-glass opacity in left inferior lobe (red arrow); (D) fourth CT performed on hospital day 18 shows significantly decreased ground-glass opacity in left inferior lobe (red arrow).

on admission, 3 cases were identified at the second CT examination, and 1 case was identified at the third CT examination. The fibrosis-like stripes were all located in the lower lobe (8/8, 100%), and mostly involved the bilateral lungs (7/8, 87.5%) (http://cdn.amegroups.cn/static/application/f60ac1df948fd97212228bd6cf343dbe.docx). The median time for the appearance of the fibrosis-like stripes was 4.5 days (1–8 days) after the onset of the disease, and in most cases (7/8, 87.5%) the stripes disappeared within a short period of time (median: 13 days, range: 9–20 days). Compared with the reported fibrosis lesions related to SARS (18-21) and MERS (22), the fibrosis-like stripes of the COVID-19 patients in this study have the characteristics of early appearance, rapid absorption, and rapid morphological changes. Therefore, we infer that the fibrosis-like stripes of COVID-19 may not be fibrosis lesions. Analysis of the CT signs of four consecutive chest CTs of case #3 (*Figure 2*) showed the following observations. The first CT showed consolidation of the lower lobe of the bilateral lungs and bronchial shadows (black arrow) in the consolidated lung tissue (*Figure 9C,D*), suggesting inflammation of the lower lobe of the bilateral lungs with local atelectasis. The second CT showed that the consolidation in the lower lobe of the bilateral lungs larger than before, with bronchial shadows (black arrow) in the consolidated lung tissue (*Figure 9G,H*). The third CT showed that the consolidation in the lower lobe of the bilateral lungs had reduced in size, but still had bronchial shadows (black arrow) in the consolidated lung tissue (*Figure 9K,L*), indicating that the inflammation was gradually absorbed, and the atelectasis of the lower lobe of bilateral lungs was gradually recovering. The fourth CT showed that only a few fibrosis-like stripes were left in the lower lobe of the bilateral lungs (*Figure 9O*). If dynamic CT examinations were not performed in this case, then it would be easy to mistake the small stripe-like shadows in

the left lower lobe as fibrosis lesions based on the fourth CT image. However, when the images of the continuous layers of this lesion (*Figure 9P,Q,R,S*) were magnified, it revealed that there were still small bronchial shadows (black arrow) within the lesion, which when combined with the history of the gradual reduction of the atelectasis on the previous three CT examinations, suggests that this type of fibrosis-like stripe is a sub-segmental atelectasis rather than a fibrosis lesion. Therefore, we speculate that this fibrosis-like stripe is a temporary CT manifestation during the evolution of atelectasis in COVID-19, which may also explain why this fibrosis-like stripe has the characteristics of early appearance, rapid morphological change, and fast absorption. In addition, recent pathological evidence also showed the appearance of mucous plug in the bronchus in COVID-19 (23). We speculate that the mucous plug in the bronchus may be one possible reason for the atelectasis.

Nonetheless, as the number of cases exhibiting this typical evolving process is still small and the evidence is not sufficient. Accordingly, this hypothesis awaits further confirmation by large sample studies and more pathological studies.

This study has several advantages: (I) currently, systematic longitudinal imaging studies are urgently needed. In this study, we systematically explored the evolving patterns of chest CT characteristics of COVID-19, and our results are conducive to guiding clinical diagnosis and prognosis prediction. (II) Based on the dynamic change characteristics of patients' chest CTs, we performed imaging staging of COVID-19 and conducted preliminary research on the disease's time points in each stage. The research results can help clinicians better judge disease progression and adjust treatment strategies. (III) In the present study, we propose a new hypothesis that fibrosis-like stripe is a sub-segmental atelectasis rather than a fibrosis lesion, and for the first time, we identify key imaging evidence to support the hypothesis. We think this finding may contribute to a better understanding of the pathogenesis of COVID-19. This study also has the following limitations: (I) this is a retrospective study, and potential selection bias and information bias are inevitable. However, as a real-world study, this study objectively reflects the changes of this disease and has clinical value. (II) This study is a single-center study based on data relating to COVID-19 patients in the Taizhou area. The included patients all had mild- or ordinary-type disease, lacking imaging data of severe and critically ill patients. Furthermore, the sample size (n=22) is relatively small, which may limit the generalization of the research results. (III) The timing of chest CT re-examination was decided mainly based on the empirical judgment of the clinicians on the severity of the disease and clinical efficacy. Therefore, consistency of the time interval of the CT re-examinations was difficult to achieve. Because of the rapid change in the condition of the diseased patients, some important signs might have been missed. (IV) Pathological evidence was lacking, so correlation analysis of imaging and pathology could not be performed.

Conclusions

COVID-19 has an acute onset, and the chest CT image manifestations are complicated with the main imaging manifestations of different types of GGO with or without lung consolidation in the subpleural region of the bilateral lungs. The CT features of lung lesions change rapidly. The lung lesions of mild and ordinary types of COVID-19 may significantly improve or disappear within a short period after active treatment, showing good overall prognosis. Moreover, fibrosis-like stripes may be a sign of atelectasis of sub-segment lung tissue of COVID-19 and may be a specific indicator of COVID-19.

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Footnote

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Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are

appropriately investigated and resolved. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). This study was approved by the Medical Ethics Committee of Taizhou Enze Hospital. Because of the retrospective nature of the study, patient consent for inclusion was waived.

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Supplementary

Table S1 The correlation between imaging staging and time of onset of illness

Patients	Early stage	Progressive stage	Recovery stage	Dissipating stage
1	Hospital day 1	–	–	Hospital day 11
	Illness day 2			Illness day 12
2	Hospital day 1	Hospital day 4	–	Hospital day 16
	Illness day 3	Illness day 6		Illness day 18
3	Hospital day 1	Hospital day 3	Hospital day 6	Hospital day 15
	Illness day 3	Illness day 5	Illness day 8	Illness day 17
4	Hospital day 1	Hospital day 4	Hospital day 9	Hospital day 17
	Illness day 2	Illness day 5	Illness day 10	Illness day 18
5	Hospital day 1	Hospital day 4, 8	–	Hospital day 18
	Illness day 6	Illness day 9, 13		Illness day 23
6	Hospital day 1	Hospital day 4	–	Hospital day 22
	Illness day 1	Illness day 4		Illness day 22
7	Hospital day 2	Hospital day 4, 9	–	Hospital day 25
	Illness day 2	Illness day 4,9		Illness day 25
8	Hospital day 1	Hospital day 4	–	Hospital day 17
	Illness day 4	Illness day 7		Illness day 20
9	Hospital day 1	Hospital day 4	–	Hospital day 11
	Illness day 2	Illness day 5		Illness day 12
10	Hospital day 1	Hospital day 4	–	Hospital day 9
	Illness day 3	Illness day 6		Illness day 11
11	Hospital day 1	Hospital day 5	Hospital day 10	Hospital day 18
	Illness day 5	Illness day 9	Illness day 14	Illness day 22
12	Hospital day 1	Hospital day 4	–	Hospital day 10
	Illness day 8	Illness day 11		Illness day 17
13	Hospital day 1	Hospital day 5	Hospital day 9	Hospital day 18
	Illness day 1	Illness day 5	Illness day 9	Illness day 18
14	Hospital day 1	Hospital day 3	Hospital day 8	Hospital day 14
	Illness day 6	Illness day 8	Illness day 13	Illness day 19
15	Hospital day 1	Hospital day 5	–	Hospital day 21
	Illness day 3	Illness day 7		Illness day 23
16	Hospital day 1	Hospital day 4, 16	–	Hospital day 20
	Illness day 2	Illness day 5, 17		Illness day 21
17	Hospital day 1	Hospital day 4	–	Hospital day 18
	Illness day 2	Illness day 5		Illness day 19
18	–	–	–	–
19	Hospital day 1	Hospital day 4, 7	–	Hospital day 20
	Illness day 2	Illness day 5, 8		Illness day 21
20	Hospital day 1	Hospital day 7	–	–
	Illness day 2	Illness day 8		
21	Hospital day 1	Hospital day 5, 8	–	Hospital day 18
	Illness day 4	Illness day 8, 11		Illness day 21
22	Hospital day 2	Hospital day 6, 11	–	Hospital day 19
	Illness day 3	Illness day 7, 12		Illness day 20