Imaging features of evolving COVID-19 infection on computed tomography: Initial experience in Zhuhai, China.

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Research Article

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Abstract

Objectives To retrospectively analyze the most common imaging features on CT at baseline and as they evolve with time as the disease progresses or resolves in a cohort of patients affected with 2019 coronal virus disease (COVID-19) pneumonia in Zhuhai, China.

Methods We evaluated 38 patients with COVID-19 in the authors' institution from Jan 1 to Jan 31, 2020. Cases were confirmed by real-time RT-PCR and were analyzed for epidemiological, demographic, clinical, and radiological features. Outcomes were followed up until Feb 18, 2020.

Results 38 initial scans and 62 follow-up scans were obtained. 28 (74%) patients had the history of travel to or residence in Hubei Province of China in 14 days prior to the illness onset. Common findings included ground-glass opacification (GGO), sometimes mixed with consolidation, and interlobular septal and intralobular interstitial thickening. Follow-up imaging often demonstrated peripheral GGO and consolidations spreading to the remainder of the lungs and the increasing consolidative component reflecting the progression of the disease. 8 patients (21%) whose swabs or serum were positive for COVID-19 had no imaging findings on CT throughout the disease course. After treatment the serum and sputum tests became negative for COVID-19 in 32(84%) cases. 28(74%) patients were discharged and three (8%) of them were transferred to the Observation Ward, while seven (18%) patients were kept in Isolation Ward.

Conclusion The commonest pattern observed was GGO alone or GGO mixed with consolidation predominantly in lower and peripheral lungs. The follow-up CT scan is crucial for the diagnosis and evaluation of the disease process.

Key Words

coronavirus infections□Tomography□X-Ray Computed□ follow-up studies□

Key Points

- CT findings of COVID–19 may lag the development of clinical signs and symptoms by few days.
- The follow-up CT scan is crucial.
- We suggest these imaging negative patients should be isolated as these individuals could be carriers.

Abbreviations And Acronyms

2019 coronal virus disease, COVID–19;

ground-glass opacification, GGO;

severe acute respiratory syndrome coronavirus, SARS-CoV;

Middle East respiratory syndrome coronavirus, MERS-CoV;

real-time reverse-transcriptase–polymerase-chain-reaction, rRT-PCR;

Introduction

There have been more than 74,000 confirmed cases of 2019 coronal virus disease (COVID–19) infection reported in China alone since the beginning of the epidemic in mid-December till February 18th (China CDC, http://2019ncov.chinacdc.cn/2019-nCoV/). The infection has spread to several other countries including Vietnam, Thailand, Japan, South Korea, USA and Germany et al.[1–3] Besides the severe acute respiratory syndrome coronavirus (SARS-CoV) outbreak in 2002 and the Middle East respiratory syndrome coronavirus (MERS-CoV) outbreak in 2012, COVID–19 is the third significantly serious coronavirus in the human population in the past 20 years. Clinically it appears to be relatively mild compared to SARS and MERS[2,4]. COVID–19 infection demonstrates familial cluster characteristics indicating person-to-person transmission[2,5]. The infected humans who remain asymptomatic or are mildly symptomatic may not end up in the health care centers and continue to work or travel thus increasing the spread of infection at a larger scale[6]. It is therefore very important to institute aggressive preventative measures to halt or limit the spread of infection by early detection, education of public and limiting the human to human contact [6].

The symptoms of COVID–19 are nonspecific and include cough, fever, chest pain, fatigue, dyspnea and headache [7]. The primary means of diagnosis include accurate history of close contact, specimens from the respiratory tract for COVID–19 testing by real-time reverse-transcriptase–polymerase-chain-reaction (rRT-PCR) assay[8]. Imaging of the chest with general radiography and computed tomography provides vital corroborative information to confirm the diagnosis, although the imaging features are non-specific. However, so far there is scant data regarding the radiologic patterns and their correlation with clinical course as the disease presents and evolves with time. To our knowledge, the high-resolution CT features at presentation and on follow-up as the disease evolves has not been described so far in a larger case series of more than 22 cases.

The aim of our study is to:1. Describe the high-resolution CT findings of rRT-PCR positiveconfirmed COVID–19 pneumonia; 2. Demonstrate the evolution of imaging features as the clinical course progresses.

Methods

Patients Selection

Following the WHO COVID–19 Interim Guidance[8], the enrolled patients should:

1) Have early recognition of severe acute respiratory infection (SARI) associated with COVID–19;

2) Have positive rRT-PCR test for the COVID–19 nucleic acid;

3) Undergo CT scanning.

This study includes a total of 38 cases who were admitted for COVID–19 infection at The Fifth Affiliated Hospital of Sun Yat-sen University from Jan 1 to Jan 31, 2020.

CT scan

All patients were scanned on uMI 760 CT and uMI780 PET-CT machines using High resolution CT technique with X-ray tube voltage of 100–120 kV and tube current of 210–250 mA. The images were reconstructed using high spatial resolution algorithm and at 1 mm slice thickness with 0·7 mm intervals. The entire thorax was scanned in supine position during full suspended inspiration. Scans were interpreted on the dedicated PACS workstations using lung windows (window width, 1200–1500 H; level, –1000 H) and mediastinal windows (window width, 400 H; level,40 H).

High-resolution CT scans were assessed for the presence and zonal distribution of ground-glass opacifications, consolidation, interlobular and intralobular interstitial septal thickening and bronchiectasis. The CT findings in the outer one third of the lung were defined as peripheral, and findings in the inner two thirds of the lung were defined as central. Consolidation was defined as an area of opacification that obscured the underlying vessels, ground glass opacity (GGO) was defined as a hazy increase in pulmonary parenchymal attenuation with no obscuration of underlying vessels. The presence of additional findings such as pleural effusions, lung fibrosis and emphysema were also evaluated.

The CT scans were reviewed by two radiologists with professional training in thoracic radiology who evaluated the pattern and distribution of the findings by consensus. The images were also evaluated for response to therapy on follow-up scans at different stages of infection. The initial CT scans were obtained at ±2 days of admission. The follow-up scans were obtained at 3–8 days after admission (intermediate scan) and 9–20 days after admission (late scan).

Statistical analyses were performed using IBM SPSS Statistics Software (version 25; IBM, New York, USA) and python(version: 3.7). The comparisons of CT imaging features of the 3 time-course were evaluated using the Student's t test and ANOVA analysis, the correlations between three stages were showed by correlation matrix. A p-value of <0.05 was defined as statistically significant.

Results

By Jan 30, 2020, a total of 38 admitted patients were included in this study, of which there were 19 female and 19 male patients. The age range was from 11 months to 75 years (mean, 45·7 years; median,

44 years). 17(45%) were 50–70 years old, 20 (53%) were 18–49 years old, one patient was 11 months old. Seven familial clusters (17 patients) were included in our cohort. No health-workers were included. The demographics and baseline clinical features are listed in Table 1. According to the WHO COVID–19 Interim Guidance[8] and the Fifth Edition Guideline of 2019-nCoV published by National Health Commission of China[9], patients were divided into four groups: mild, severe, critical and an additional group called 'imaging negative group'. In this group we included the patients whose CT imaging had no positive findings but the swabs or serum were tested positive for COVID–19. There was a total of nine patients in the 'imaging negative group'. There were two patients in the severe and two cases in the critical group. The remainder of 25 cases were categorized as mild. The average age of four patients in sever and critical groups was 69 years. It was noted that these four patients had preexisting underlying disease. Out of these four, three were discharged to home care, their average length of stay was 18.3 days.

In all the 38 patients, sputum was positive for the COVID–19 nucleic acid. 28 patients had been to several cities in Hubei Province such as Wuhan (n = 25)，Ezhou，n = 1，，Xiaogan，n = 1，and Huanggang，n = 1， while another 8 patients had close contact with the COVID–19 positive patients. All patients denied the history of visiting the Huanan Seafood Wholesale Market in Wuhan in January. Some patients had history of preexisting conditions such as diabetes (n = 5), hypertension (n = 2), lung cancer after surgery and radio-chemo therapy (n = 1) and chronic obstructive pulmonary disease (n = 1).

After treatment the serum and sputum testing became negative for COVID–19 in 32(84%) cases. 28(74%) patients were discharged and three (8%) of them were transferred to the Observation Ward, seven (18%) patients were kept in Isolation Ward. There were no deaths among these patients.

CT imaging Features

All of the 38 patients had the initial scan as the baseline. The initial high-resolution CT scan was performed 0·5±0·9 days after admission to the hospital.

Majority (n = 23) of patients had bilateral lung involvement while two patients had unilateral right lung infection and one had unilateral left lung infection. The lesions were predominantly peripheral in 62% of patients and both peripheral and central in 38%. Majority of patients (22 out of 25) had multiple lobe involvement while only three patients had single lobe lesion (one upper lobe involvement and two lower lobe involvement).

The details of the CT findings are summarized in Table 2. Ground-glass opacity was the earliest and most common CT finding 45% (n = 13) in the initial scan(0·5±0·9 days) after admission followed by GGO mixed with consolidation (n = 12; 41%) cases, interlobular septal thickening (n = 10; 34%), intralobular septal thickening(n = 9; 31%), bronchiectasis(n = 4; 14%),consolidation (n = 1; 3%), pleural effusion (n = 1; 3%) (Fig1–2).The lesion most often showed GGO alone or mixed with GGO and consolidation in 86% (25/29) cases. Consolidation without GGO was seen in only one case in the initial scan. The lung cancer survivor had small amount of bilateral pleural effusion in the 19 days after admission.

The most common pattern was GGO alone or GGO mixed with consolidation in 24 of the 25 patients. Consolidation without GGO was seen in only one case on the initial scan.

Out of a total of 38 patients, nine patients with clinical symptoms of COVID–19 were categorized as imaging negative with the CT scan showing no pulmonary parenchymal abnormalities. three of these nine patients had stable pre-existing lung abnormalities including one patient (a 23-year-old woman) had a 6*4mm stable GGO in the right upper lobe for nine days. Another patient, a 38-year-old woman had scarring in the lingula, a 59-year-old manhad the lung cancer surgery and radio-chemo therapy change, one patient (a 60-year-old woman) had scarring in the right middle lobe and in lingula from previous infections. The remaining five out of nine patients had normal CT findings including four males aged 25ys, 29ys, 44ys, 55ys and a 11 months old female infant. These nine patients had no findings related to COVID–19 infection on the baseline CT scan.

Bronchiectasis in the peripheral lungs in the region of parenchymal opacities was seen in four cases (Fig3). Ten cases had thickening of interlobular septa (n = 10) and intralobular septa (n = 9) compatible with crazy-paving pattern (Fig 4). Small right sided pleural effusion was seen in a 75 years old female who was admitted in the ICU for ten days with septic shock.

Among the mild group, there were four cases showing no lesion on the initial scan but on the subsequent follow-up scans GGO or GGO mixed with consolidation developed rapidly.

Follow-up CT scan were evaluated according the time of admission: intermediate stage (3–8 days after admission) and late stage (9–20 days after admission). 30 patients had the follow-up scan after 3–8 days (5·5±1·4 days), and 32 cases had the follow-up scan after 13·3±2·7 days of admission. On the follow-up CT scan, the number of GGO lesions decreased from 13 to five and the number of mixed GGO and consolidation case increased from 12 to 16 (Fig1–3). Consolidation without GGO was uncommon through the entire period (n = 1 to 2). In the late stage, five patients developed scars in the peripheral area especially in the lower lobes (Fig 3). One 21-year-old male patient improved significantly after 15 days' treatment and the GGO in his left lower lobe resolved completely. One patient (a 59-year-old man) with prior lung cancer surgery and post chemo-radiation therapy changes. The initial scan and the intermediate chest CT scan showed no imaging change connected with the COVID–19, but in 19 days after admission small amount of bilateral pleural effusion was observed. Now this patient is still in patient. 31/32 of the patients still had the lesion partially resolved when their PCR had become negative. The comparisons of 9 CT imaging features (including GGO, mixed GGO and consolidation, consolidation, interlobular septal thickening, intralobular septal thickening, Scar, Bronchiectasis, Plural effusion, Atelectasis) in different time-course were analyzed and the p value between the intermediate stage and late stage is 0.05.(Table3 and Supplementary Materials).

Discussion

In this study we reported a cohort of 38 patients with laboratory confirmed COVID–19 infection in Zhuhai city. We included seven family clusters 17 patients 44.7% in our study, which indicates human to human

transmission as reported by other authors[5,7]. 95% (36/38) of the cases in our cohort had the history of travel to or residence in Wuhan or other cities of Hubei Province or close contract history with confirmed patients. The imaging features of patients with COVID–19 infection are similar to the previously reported imaging characteristics of other significant coronal virus infection such as SARS and MERS[10,11]. These include GGO which is observed to be the earliest and most common CT finding, followed by GGO mixed with consolidation and crazy paving pattern. Moreover, the COVID–19 pneumonia lesions predominantly affected the lower lobes, and most lesions were peripherally located. In the two severe cases and two critical cases, the peripheral GGO and consolidations rapidly spread to remainder of the lungs and the consolidative component increased significantly reflecting the rapid progression of the disease and causing ARDS or acute lung injury type pattern.

In contrast to the cases reported from Wuhan Jinyintan Hospital[12], most of the patients in our cohort had milder abnormalities and the outcomes were much better compared to the patients in Wuhan[12]. This may be due to the fact that Zhuhai City is 1,000 km from Wuhan and the virus may be of less virulent type or the people travelling from Wuhan or other cities of Hubei Province to Zhuhai may have stronger immunity and therefore the infection was less severe. And the hospital in Zhuhai is well staffed compared to Wuhan where the outbreak of COVID–19 was initially detected which could have overwhelmed the medical staff. The medical workers in Wuhan have been facing enormous pressure, including a high risk of infection, overwork and inadequate protection from contamination et al. These factors may have contributed towards the spread of infection and relatively poorer initial outcomes. In our study, nine patients (24%) were included in a new group termed as 'imaging negative' group. In these patients, the initial and follow-up CT scans did not demonstrate abnormalities that were expected with COVID–19 infection. None of them had obvious symptom such as fever after admission and the symptoms were milder compared to the patients in other groups. Another study included 18 patients of our cohort monitored COVID–19 viral loads in upper respiratory specimen and the viral load that was detected in the asymptomatic patient was similar to that in the symptomatic patients, which suggested the transmission potential of asymptomatic or minimally symptomatic patients[13]. So we suggest the imaging negative patients should also be kept in Isolation Ward with treatment and close follow-up.The interval between CT imaging change in clinical picture in these intervals requires close attention as different patients may have different clinical course. The interval between imaging is driven by the clinical course of the disease and therefore it is not consistent across our patient group. The CT finding reflecting the pulmonary parenchymal damage lag the development of clinical signs and symptoms by few days. In our study, this pattern was seen in four patients whose initial scans were normal but several days later the GGO or the mixture of GGO and consolidation developed. We strongly recommend close follow-up with CT scan in the patient who have negative initial imaging but have positive swabs or serum for COVID–19. Furthermore, complete resolution of radiological abnormalities was seen a few days later than complete clinical recovery.

There are few limitations in our study. Firstly, this is a single center study with a small number of cases. It is important to note that the entire range of imaging features may not have been fully demonstrated

during the time course since the emergence of COVID–19 outbreak. Future studies should involve a large and multi-center patient population. Secondly, we do not have the histopathologic evidence to reflect the imaging change of the entire infection process.

In summary, the CT imaging features of COVID–19 are predominantly ground-glass opacities or ground-glass mixed with consolidation, predominantly in lower lobes and peripheral in distribution similar to SARS and MERS imaging features. Moreover, some patients whose nasopharyngeal and oropharyngeal swabs or serum positive for COVID–19 had no imaging findings on CT imaging during the disease course.

Declarations

This study has received funding by the National Natural Science Foundation of China (NSFC) under Grant 81801809 and by the Guangdong Province Key Laboratory of Computational Science Open Grant 2018009. The co-corresponding authors Yaqin Zhang and Hong Shan designed the work, wrote and revised the manuscript. Aamer Chughtai revised the paper, Pengfei Pang, Han Ma, Binghui Chen, Yingqin Li, Guanmin Jiang finished the acquisition, analysis, and interpretation of data, Zeyu Cai and Yujuan Qin serached and reviewed the literatures.

The authors of this manuscript declare no relationships with any companies, whose products or services may be related to the subject matter of the article.No complex statistical methods were necessary for this paper. Written informed consent was obtained from all subjects (patients) in this study. Institutional Review Board approval was obtained. This study subjects or cohorts have not been previously reported. This is a retrospective and observational study which was performed at one institution.

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Tables

Table1 Baseline clinical features of patients infected with COVID-19	
Features	**Patients(n=38)**
Age,years	
Average(SD)	45.7(16.9)
Range	1-75
≤29	7(18%)
30-39	8(21%)
40-49	6(16%)
50-59	8(21%)
60-69	7(18%)
≥70	2(5%)
Sex	
Female	19(50%)
Male	19(50%)
Epidemiological history	
Wuhan travel/residence history	25(66%)
Other cities in Hubei Province travel/residence history	4(11%)
Close contact with the COVID-19 patients	7(18%)
Underlying disease	
Cardiovascular disease	2(5%)
Digestive system disease	1(3%)
Endocrine system disease	2(5%)
Malignant tumor	1(3%)
Nervous system disease	1(3%)
Respiratory system disease	1(3%)
Admission to intensive care unit	4(11%)
Clinical Outcome	
Remained in hospital	28(74%)
Discharged	10(26%)
Died	0(0%)
Symptom	
Fever	29(76%)
Cough	17(45%)
Headache	2(5%)
Sore throat or throat discomfort	6(16%)
Palpitation	1(3%)
Chest distress	1(3%)
Haemoptysis	1(3%)
Chills	1(3%)
Dyspnoea	1(3%)
Fatigue	5(13%)
Shortness of breath	1(3%)
Muscle soreness	3(8%)

Table 2 CT imaging features of patients infected with COVID-19

	Baseline	Intermediate Stage	Late Stage
Average days after admission(days)	0.5±0.9	5.5±1.4	13.3±2.7
Virus pneumonia cases	29	29	29
Virus pneumonia cases with CT scan	29	25	24
Imaging negative cases	9	9	9
Imaging negative cases with CT scan	9	5	8
Whole cohort had CT scan	38	30	32
Whole cohort	38	38	38
Location			
Lobe			
Upper	1	1	1
Middle or Lingua	0	0	0
Lower	2	6	4
Upper and Lower	7	4	4
All	15	14	15
Area			
Central	0	0	0
Peripheral	16	14	12
both	10	11	12
Side			
Right	2	1	0
Left	1	1	0
Both	22	23	24
Features			
Ground Glass	13	8	5
Consolidation	1	2	2
Mixed GGO and consolidation	12	15	17
Scar	0	0	5
Interlobular septal	10	5	10
Intralobular septal	9	5	10
Bronchiectasis	4	3	4
Plural effusion	1	1	1
Atelectasis	0	0	1

Table 3 Temporal changes in CT imaging features (this table is an image - please see Figure 5)

Figures

Figure 1

Imaging changes on chest CT of a patient with COVID-19 pneumonia A 60-year-old male from Wuhan diagnosed with COVID-19 presented with a 5-day history of fever（100.4°F）and muscle soreness. The initial CT demonstrates multifocal ground glass opacities in both lower lobes (Fig 1). 4 days after admission he developed worsening fever (103.1°F), shortness of breath and cough productive of pink frothy sputum. A follow-up CT scan (Fig2) demonstrates worsening central and peripheral ground glass opacities mixed with consolidations and extensive interlobular septal thickening in the lower lungs. After treatment of 10 days of mechanical ventilation in ICU and 9 days in Isolation Ward, He recovered completely.

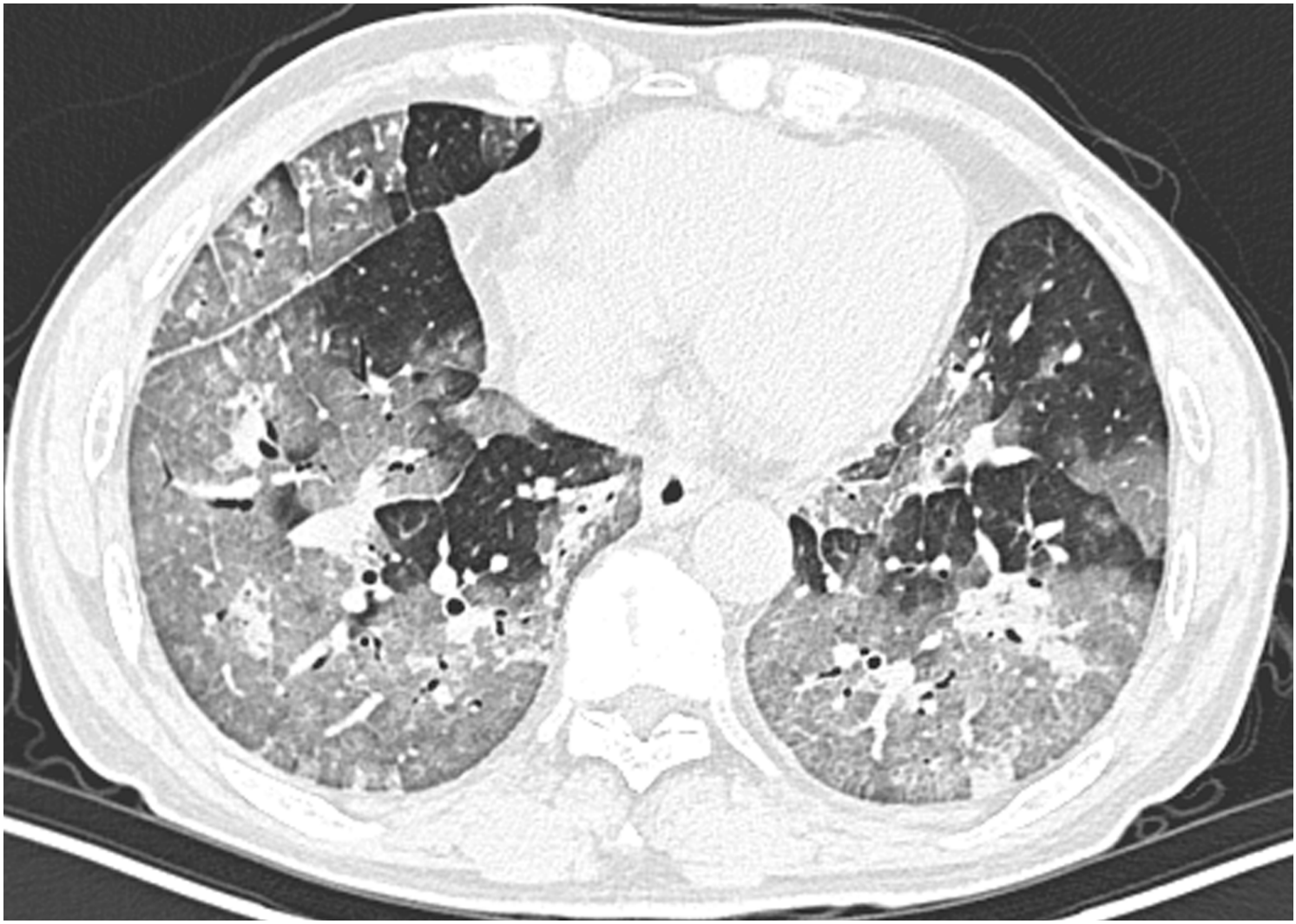

Figure 2

Imaging changes on chest CT of a patient with COVID-19 pneumonia A 60-year-old male from Wuhan diagnosed with COVID-19 presented with a 5-day history of fever（100.4°F）and muscle soreness. The initial CT demonstrates multifocal ground glass opacities in both lower lobes (Fig 1). 4 days after admission he developed worsening fever (103.1°F), shortness of breath and cough productive of pink frothy sputum. A follow-up CT scan (Fig2) demonstrates worsening central and peripheral ground glass opacities mixed with consolidations and extensive interlobular septal thickening in the lower lungs. After treatment of 10 days of mechanical ventilation in ICU and 9 days in Isolation Ward, He recovered completely.

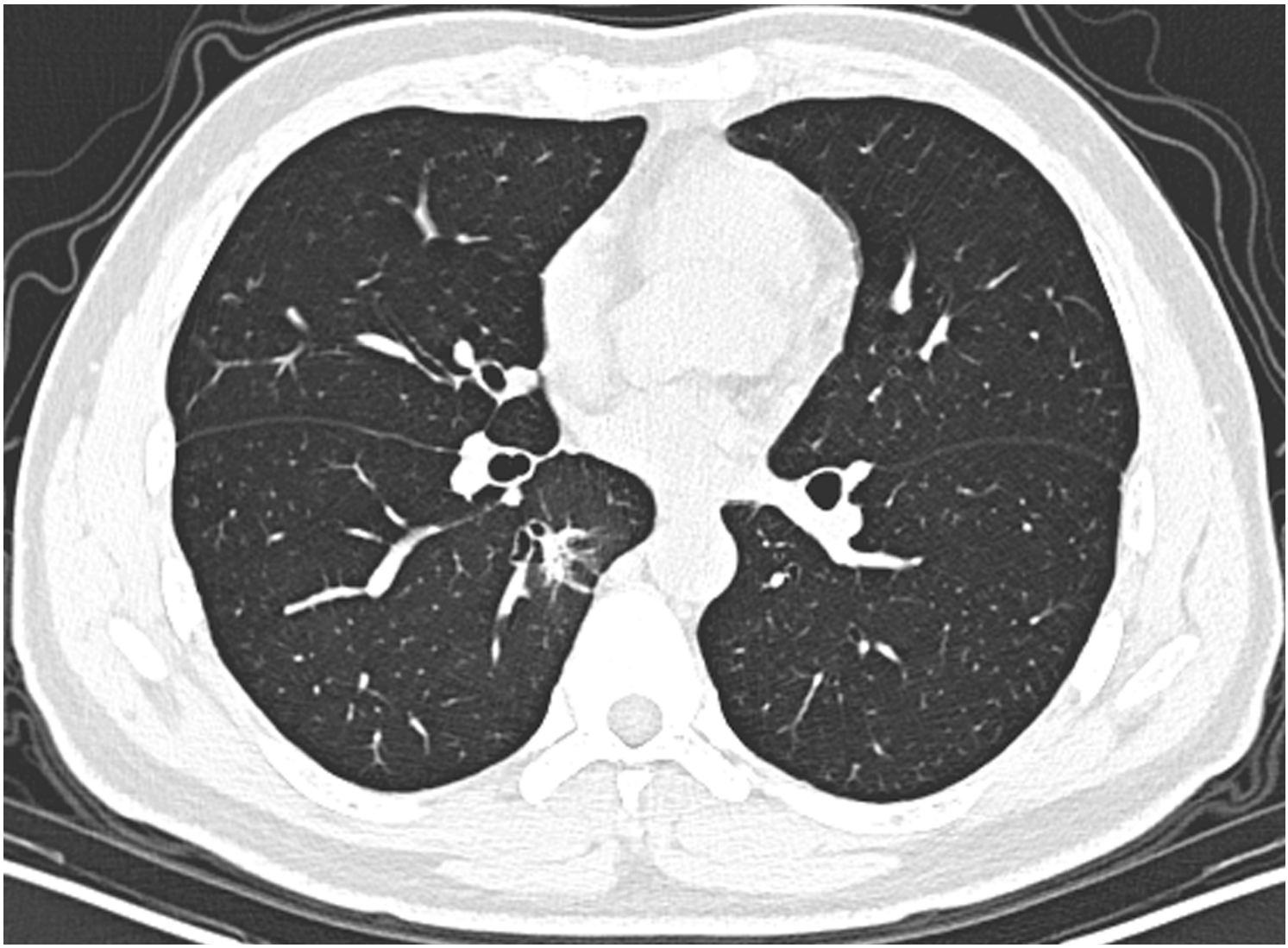

Figure 3

Chest image of a COVID-19 pneumonia patient with patchy consolidation and segmental bronchiectasis Axial contrast enhanced CT images of a 42-year-old male diagnosed with COVID-19 with recent travel history to Wuhan. He presented with a 1-day history of fever（100.04°F). The baseline CT demonstrates normal lung parenchyma. A follow-up CT scan 12 days after admission demonstrates patchy consolidation and segmental bronchiectasis in basal segments of right lower lobe.

Figure 4

Chest image of a COVID-19 pneumonia patient with crazy-paving pattern A 33-year-old female diagnosed with COVID-19 had the close contract history with confirmed patients. High resolution CT scan demonstrated ground-glass opacification with thickening of interlobular and intralobular septa (crazy-paving pattern) in the subpleural lateral basal segment of left lower lobe.

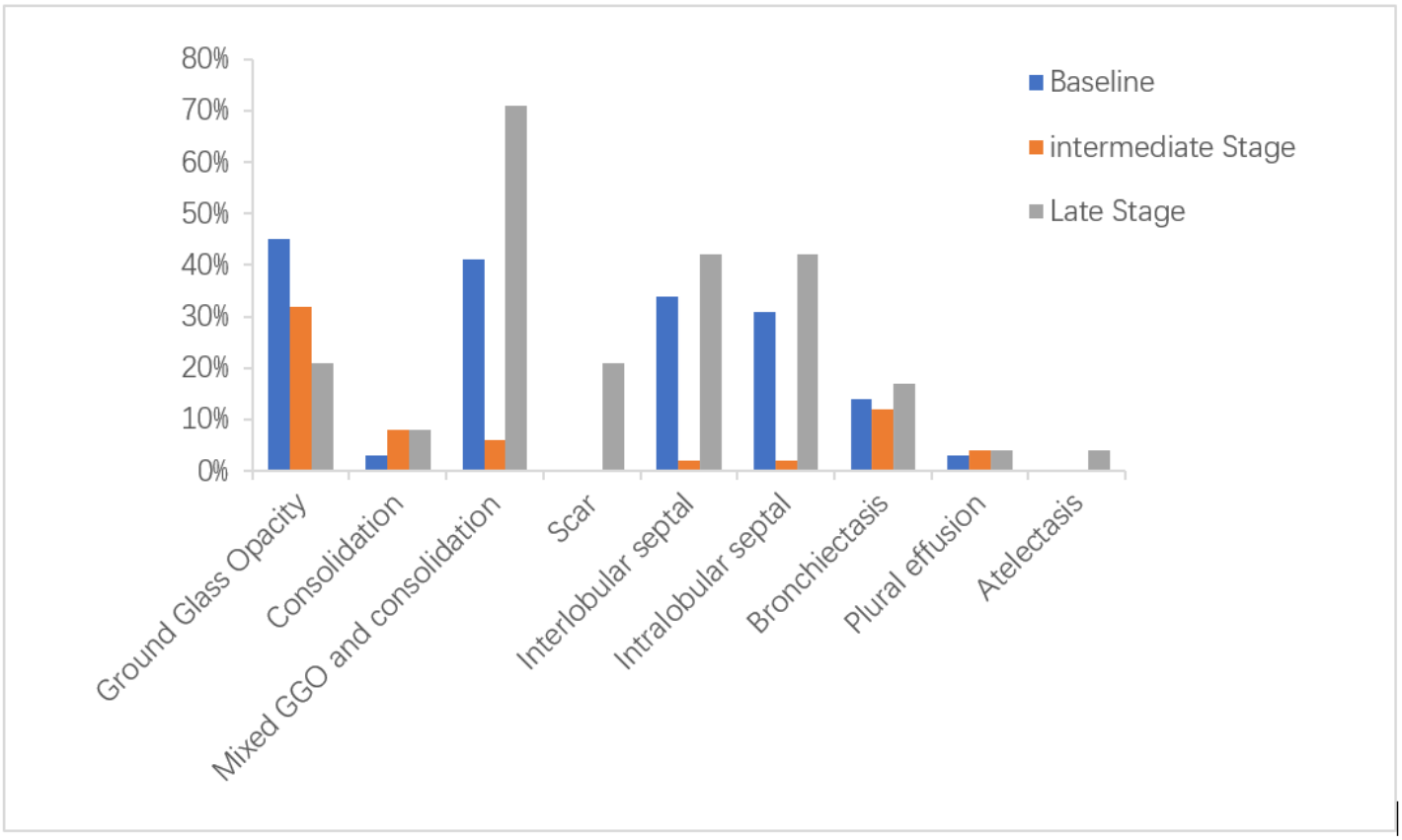

Figure 5

Table 3: Temporal changes in CT imaging features

Supplementary Files

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- SupplementaryMaterials.docx