Follow-up Chest CT findings from discharged patients with severe COVID-19: an 83-day observational study

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Research

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Abstract

Background: Chest computed tomography (CT) has been used to be a monitoring measure to assess the severity of lung abnormalities in corona virus disease 19 (COVID-19). Up to date, there has been no reports about follow-up chest CT findings from discharge patients with severe COVID-19. This study aims to describe the change pattern of radiological abnormalities from admission, to discharge, and to the last chest CT follow-up through an 83-day retrospective observation, and focuses on follow-up chest CT findings in discharged patients with severe COVID-19.

Methods: Twenty-nine discharged patients (17 males, 12 females; median age, 56 years, IQR, 47-67) confirmed with severe COVID-19 from 13 January to 15 February were enrolled in this study. A total of 80 chest CT scans was performed from admission to the last follow-up. Images were mainly evaluated for ground-glass opacity, consolidation, parenchymal bands, and crazy-paving pattern. A semi-quantitative CT scoring system was used for estimating lung abnormalities of each lobe.

Results: All patients received nasal cannula or/and high-flow mask oxygen therapy. Admission occurred 9 days (IQR, 5-13) after symptom onset. The median in-hospital period was 18 days (IQR, 11-26). The last follow-up chest CT was performed 66 days (IQR, 61-77) after symptom onset. Total CT scores in follow-up decreased significantly compared to that of performed in-hospital ([3, IQR, 0-5] to [13, IQR, 10-16], $P < 0.001$). Predominant patterns on follow-up chest CT performed 64 days after symptom onset were subpleural parenchymal bands (47%, 9/19) and complete radiological resolution (37%, 7/19). Consolidation absorbed earlier than ground-glass opacity did, and subpleural parenchymal bands were the longest-lasting feature during radiological resolution.

Conclusions: Radiological abnormalities in patients of severe COVID-19 could be completely absorbed with no residual lung injury in more than two months' follow-up. Serial chest CT scans could be used as a monitoring modality to help clinician better understand the disease course.

Introduction

Coronavirus Disease 2019 (COVID-19) has become a global pandemic with a soaring infected population reaching 2.8 million by 26 April 2020[1]. Real-time reverse transcription-polymerase chain reaction was considered to be the golden diagnostic criteria despite reported relatively low sensitivity[2, 3]. Instead, chest computed tomography (CT) was recommended for screening suspected patients and monitoring temporal changes of COVID-19 with higher sensitivity of 97%[4, 5].

Previous studies reported a typical change revealed by chest CT, featuring from subpleural ground-glass opacity (GGO) to extensive consolidation to lesion absorption within 3-4 weeks[5-7]. Wang Y et al mentioned in their study that severe patients could reveal longer illness duration and radiological abnormalities[5]. However, the follow-up radiological findings from discharged patients with severe COVID-19 has not been reported. This study aims to describe temporal radiological change pattern on

chest CT from discharged patients with severe COVID-19, and focus on the last follow-up chest CT findings in these patients.

Materials And Methods

The retrospective study was conducted according to the Declaration of Helsinki. Informed consent of patient permission form for this retrospective study was waived by Ethics of Committees of Union Hospital, Tongji Medical College, Huazhong University of Science and Technology. Only the anonymous data was collected and analyzed to facilitate better clinical decisions and treatment.

Patients

Patients in hospital with confirmed COVID-19 were reviewed retrospectively from 13 January to 7 April in two medical centers (Western Campus, Wuhan Union Hospital and Wuhan Jinyintan Hospital). Severe patients with at least one time of chest CT scan after discharge were included in this study, categorizing and evaluating by national criteria[8]. Discharge criterion matched the following conditions: 1. no fever for more than 3 days; 2. relief of dyspnea; 3. improvement in radiological abnormalities on chest CT; and 4. two consecutive negative COVID-19 nucleic acid detection at least 24 hours apart[8]. A total of 29 discharged patients with severe COVID-19 and 80 serial chest CT scans were included.

Chest CT scan protocol

Chest CT scans were performed by using a multi-detector CT. Images were acquired during a single breath-hold, with fixed tube voltage of 120 kV and automatic tube current. Reconstructed section thickness was 1.5 mm and increment were 1.5 mm, with a matrix size of 512 × 512 in transverse slice. All patients underwent a median of 3 (IQR, 2-3) serial chest CT scans with a median interval of 35 days (IQR, 13-44).

Image interpretation

Major CT demonstrations were described according to Fleischner Society and peer-reviewed literatures, including GGO, consolidation, parenchymal bands, and crazy-paving pattern[5, 9-12]. A semi-quantitative scoring system was used to assess pulmonary involvement of abnormalities[7, 13]. This scoring system was performed by two radiologists with more than ten-year experiences on thoracic diagnostic radiology. Decisions about scoring were reached in consensus. Each lung lobe scoring from 0 to 5: 0, no involvement; 1, < 5% involvement; 2, 5% - 25% involvement; 3, 26% - 49% involvement; 4, 50% - 75% involvement; 5, > 75% involvement. The total CT score ranged from 0 to 25.

Statistical analysis

Statistical analyses were performed with IBM SPSS Statistics Software (version 24; IBM, New York, USA). Quantitative data were presented as median with inter-quartile range (IQR), and frequency data were presented as percentage of total. Mann-Whitney U test was used for comparing non-paired quantitative

data, and Chi-square test was used for comparing frequency data. A *p*-value of < 0.05 was defined as having statistical significance.

Results

1. Patient characteristics

Details of patients' clinical information were summarized in **Table 1**. A total of 29 patients (17 males and 12 females) were included in this study. The median age of patients was 56 years (IQR, 47-67).

Admission occurred 9 days (IQR, 5-13) after symptom onset. Discharge occurred 27 days (IQR, 21-35) days after symptom onset, and the median in-hospital period was 18 days (IQR, 11-26).

The most common symptoms at illness onset were moderate to high degree of fever (15 moderate fever, 52%; 9 high fever, 31%), dyspnea (20/29, 69%) and dry cough (16/29, 55%). Ten patients (10/29, 35%) had at least one medical comorbidities, and the most common comorbidities were hypertension (7/29, 24%) and hepatitis B infection (5/29, 24%). The median value of blood oxygen saturation on admission was 87% (IQR, 85%-91%). All patients received nasal cannula or/and high-flow mask oxygen therapy.

Laboratory investigations were generally performed once a week in-hospital. Details of laboratory results were summarized in **Table 2**. The most common abnormalities during hospitalized period were lymphopenia (26/29, 90%), elevated ferritin (26/29, 90%), elevated lactate dehydrogenase (25/29, 86%), and decreased albumin (25/29, 86%).

2. Radiological abnormalities on chest CT

Intervals from symptom onset were divided into four stages by interquartile range: stage-1, ≤ 15 days; stage-2, 16-29 days; stage-3, 30-63 days; stage-4, ≥ 64 days. Dynamic patterns of lung abnormalities were analyzed based on the four stages.

Twenty-one patients (21/29, 72%) underwent chest CT scan at stage-1 (≤ 15 days after symptom onset). The median chest CT score was 12 (IQR, 8-15), and predominant patterns in patients were GGO (12/29, 57%), consolidation (6/29, 29%) and crazy-paving (3/29, 14%). Nineteen patients (19/29, 66%) underwent chest CT scan at stage-2 (16-29 days after symptom onset), and lesion progression peaked during this period with a median chest CT score of 13 (IQR, 10-15). Predominant patterns of lung abnormalities were consolidation (11/19, 58%) and GGO (8/19, 42%) (**Figure 1**).

Follow-up chest CT scans included in stage-3 (30-63 days after symptom onset) mainly described lung abnormalities at a period around one month after discharge, and included 21 patients (21/29, 72%). The median chest CT score decreased to 6 (IQR, 3-11). Four patients (4/21, 19%) in this period revealed complete radiological resolution. Predominant pattern of consolidation (1/21, 5%) decreased, while subpleural parenchymal bands emerged in 6 patients (6/21, 29%). The last follow-up chest CT was performed 66 days (IQR, 61-77) after symptom onset and were mostly included in stage-4 (≥ 64 days

after symptom onset). Nineteen patients (19/29, 66%) underwent chest CT scan during this period. Chest CT score continued decreasing to a median of 2 (IQR, 0-3). The most common pattern at last follow-up chest CT were subpleural parenchymal bands (9/19, 47%) and complete radiological resolution (7/19, 37%).

In addition, four patients (4/29, 14%) revealed mild traction bronchiectasis on follow-up chest CT, and 1 patient (1/29, 3%) revealed a small amount of pleural effusion in-hospital which was absorbed at follow-up. Nodules, cystic changes, and lymphadenopathy were rarely presented in this study.

3. Dynamic patterns of radiological abnormalities between in-hospital and follow-up chest CT

Comparing lung abnormalities between in-hospital and follow-up chest CT, chest CT scores decreased significantly after discharge from hospital ([13, IQR, 10-16] to [3, IQR, 0-5], $P < 0.001$). Lung abnormalities revealed by in-hospital chest CT scans were mainly GGO and consolidation. Crazy-paving pattern was presented on chest CT close to admission. Lesion progression occurred in-hospital was presented as increased consolidation from GGO or crazy-paving pattern. On follow-up chest CT scans, which were generally include in stage-3 and -4, patients with consolidation as predominant pattern decreased first and those with GGO in sequence. After discharge, subpleural parenchymal bands increasingly presented as predominant pattern in patients, and was the longest-lasting feature before complete radiological resolution.

Discussion

This study described dynamic patterns of radiological abnormalities of severe COVID-19 and focused on follow-up chest CT findings after discharge. The pulmonary involvement peaked at 3-4 weeks after symptom onset with consolidation and GGO as predominant pattern. There still existed abnormalities at chest CT when patients discharged, and pulmonary involvement continued decreasing at follow-up chest CT. Around 2 months after symptom onset, predominant abnormalities were subpleural parenchymal bands, and complete radiological resolution started in this period.

The most common predominant abnormalities at stage-1 was GGO, followed by increased consolidation at stage-2, which was consistent with previous literature[14]. Particularly, crazy-paving pattern only revealed at stage-1 and generally evolved into consolidation at stage-2. Pulmonary involvement assessed by semi-quantitative scoring system peaked at 3-4 weeks after symptom onset, which was occurred later than previous study that reported non-severe COVID[5-7]. The radiological abnormalities revealed by in-hospital chest CT demonstrated the transformation from GGO with or without crazy-paving pattern to increased consolidation, indicating progressive alveolar epithelial damage and more severe proteinaceous exudates in both alveolar and interstitial tissue[9, 12, 15, 16].

Serial follow-up chest CT scans lasted around two months from symptom onset, radiological findings during which has not reported yet. At follow-up chest CT after discharge, consolidation that presented as the most common predominant pattern in stage-2 started to absorb before GGO did, indicating the

absorption of alveolar edema and cellular infiltration[17]. The resolution of alveolar edema and cellular infiltration result in decreased attenuation of parenchyma and partial filling of airspaces, and explain that resolution of consolidation was prior to that of GGO. Subpleural parenchymal bands emerged and increased to be the most common predominant abnormalities during stage-3 and -4, without apparent distortion of lung architecture. It should be noted that parenchymal bands in most patients in this study could be completely absorbed without apparent injury, only 4 patients (4/29, 14%) revealed mild traction bronchiectasis.

In stage-4 (≥ 64 days after symptom onset) which generally covered the last follow-up chest CT (66 days, IQR, 61-77), the predominant pattern were parenchymal bands and complete resolution, indicating the disease improvement in terms of previous literature[18]. Similar to consolidation, subpleural parenchymal bands could be the manifestation of interstitial edema and cellular infiltration in collapsed alveoli[19]. The delayed resolution of parenchymal bands made it to be the longest-lasting feature during follow-up chest CT.

There are several limitations in this study. First, no follow-up laboratory investigation was obtained. Second, this study included a small sample because not all patients received serial chest CT scans until complete radiological resolution. Third, follow-up chest CT findings from patients with invasive mechanical ventilation and/or extracorporeal membrane oxygenation therapy remains further investigation.

In conclusion, subpleural parenchymal bands were the predominant radiological abnormalities after two months from symptom onset, and could be completely absorbed with no apparent residual lung injury. Serial chest CT scans could be used as a monitoring modality to help clinician better understand the disease course.

Abbreviations

COVID-19: corona virus disease 19

SARS-CoV-2: severe acute respiratory syndrome coronavirus 2

GGO: Ground-glass opacity

CT: computed tomography

Declarations

Ethics approval and consent to participate

The retrospective study was conducted according to the Declaration of Helsinki. Informed consent of patient permission form for this retrospective study was waived by Ethics of Committees of Union

Hospital, Tongji Medical College, Huazhong University of Science and Technology. Only the anonymous data was collected and analyzed to facilitate better clinical decisions and treatment.

Consent for publication

Not applicable.

Availability of data and materials

The datasets used during the current study are available from the corresponding author on reasonable request.

Competing interests

The authors declare that they have no competing interests.

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Authors' contributions

TY and YF contributed equally to this article. TY and YF: Conceptualization; writing original draft; review and editing; methodology. BX: Conceptualization; supervision. JL: data curation; investigation. CY and SH: resources; formal analysis.

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Tables

Table 1. Baseline characteristics

Variables	Values
Age (years)	56 (47-67)
Gender	17 males, 12 females
Hypertension	7 (24%)
Diabetes	2 (7%)
Cardiovascular disease	1 (3%)
Hepatitis B	5 (17%)
Uarthritis	1 (3%)
Fever	28 (97%)
Fatigue	5 (17.2%)
Sore throat	2 (7%)
Cough	16 (55%)
Diarrhea	3 (10%)
Dyspnea	20 (69%)
Headache	1 (3%)
Muscle or joint pain	2 (7%)

Table 2. Laboratory investigations in-hospital.

Laboratory investigations	1 week	2 weeks	3 weeks	4 weeks	5 weeks	≥ 5 weeks
White blood cell count (G/L)	4.2 (3.6-6.2)	6.48 (5.8-9.7)	7.2 (5.4-9.7)	6.8 (5.0-8.1)	5.1 (4.6-6.2)	6.5 (5.3-11.2)
Neutrophil count (G/L)	3.4 (2.2-6.0)	7.1 (5.0-10.6)	6.0 (3.8-9.0)	4.5 (3.2-9.7)	6.9 (6.8-7.0)	8.7 (2.7-10.3)
Lymphocyte count (G/L)	0.8 (0.7-1.3)	0.9 (0.6-1.0)	1.1 (0.7-1.3)	1.3 (0.7-1.6)	1.0 (0.8-1.3)	1.4 (1.0-2.1)
C-reative protein (mg/L)	63 (16-84)	35 (18-100)	36 (8-54)	4 (2-25)	35 (28-42)	62 (3-99)
Erythrocyte sedimentation rate (mm/h)	30 (8-58)	54 (40-75)	44 (17-64)	32 (8-58)	94 (69-119)	74 (37-111)
Alanine aminotransferase (U/L)	43 (24-54)	52 (36-87)	83 (50-115)	51 (34-103)	51 (20-66)	62 (45-105)
Aspartic aminotransferase (U/L)	44 (36-71)	44 (32-65)	37 (31-47)	40 (25-79)	33 (22-53)	44 (25-51)
Lactate dehydrogenase (U/L)	314 (295-415)	398 (306-451)	302 (285-335)	307 (236-308)	212 (188-296)	186
Albumin (g/L)	34 (32-37)	32 (28-34)	30 (28-32)	32 (29-34)	32 (32-33)	37 (36-42)
Ferritin (ng/ml)	593 (460-743)	635 (602-774)	648 (376-2000)	471 (314-1265)	582 (429-1652)	392 (382-401)
Interleukin-6 (pg/ml)	6.2 (4.5-7.8)	8.1 (6.7-10.0)	11.4 (9.0-16.1)	9.1 (8.2-13.3)	9.7 (6.2-13.3)	3.2 (2.5-4.6)
D-dimer (ug/mL)	0.3 (0.2-0.5)	1.5 (0.4-9.0)	2.3 (1.2-4.2)	4.8 (2.4-7.7)	4.1 (3.0-4.2)	1.6 (1.6-3.9)

Figures

Figure 1

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Figure 2

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Figure 3

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Figure 4

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