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Clinical and CT features of mild-to-moderate COVID-19 cases after two sequential negative nucleic acid testing results: a retrospective analysis

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Abstract

Background Numerous studies have been focused on the clinical and imaging features among COVID-19 patients positive for SARS-CoV-2, but the data after negative is limited. We aims to describe these features after negative respiratory nucleic acid testing results.

Methods From January 31 to February 28, 2020, 51 mild-to-moderate COVID-19 cases (median: 34.0 years and 47.1% male) were retrospectively enrolled. Demographic, clinical, laboratory, and CT imaging data were collected before and after two sequential negative results for respiratory SARS-CoV-2 .

Results After negative for respiratory SARS-CoV-2, the clinical symptoms continued to recover and the abnormal imaging were observed for all of the moderate cases. 77.4% of the moderate patients had multi-lobar involvement and lesions were more frequent in the lower lobes. The most common CT imaging manifestations were ground glass opacity (51.6%) and fibrous stripes (54.8%%). Among 12 out of 31 moderate patients with repeated chest CT scan after negative for SARS-CoV-2, 7 patients (58.3%) with ground-glass absorption reduced over 60% within one week, but there were still 4 cases (13.8%) with absorption less than 5%.

Conclusions The clinical symptoms and abnormal imaging persisted but continued to recover after negative for respiratory SARS-CoV-2.

1. Introduction

On December 2019, cases of pneumonia of unknown cause were reported in Wuhan City, China. This disease is caused by a novel coronavirus named “2019 novel coronavirus (SARS-CoV-2)”, first isolated on 7 January 2020 [1]. COVID-19 is an emerging outbreak and the World Health Organization (WHO)'s International Health Regulations Emergency Committee has declared COVID-19 as a Public Health Emergency of International Concern (PHEIC) on 30 January 2020 [2]. According to the latest statistics in April 18, 2020, a total of 2,078,605 COVID-19 cases and 139,515 deaths have been confirmed by 213 countries, areas or territories globally [2]. At present, how to treatment and control of COVID-19 is the major public health issues, also largely unknown [3].

Several large studies and meta-analyses had widely described and summarized the clinical and imaging features of patients with COVID-19 in order to recognize the COVID-19 at early stage and assess its evolution [4–12]. However, scare evidence has focused on the data for COVID-19 patients after negative test results for SARS-CoV-2, which is important for guidance for discharge and ending isolation in the context of widespread community transmission. Considering the factors such as the existing healthcare capacity, laboratory diagnostic resources, and the current epidemiological situation, the discharge criteria varied among countries and regions [13]. In China, patients with afebrile for > 3 days, improved respiratory symptoms, pulmonary imaging shows obvious absorption of inflammation, and PCR negative for respiratory tract twice consecutively, at ≥ 24 hours interval could be discharged from hospital [14]. However, Wu et al. [15]. reported that patients with negative respiratory tract sample results could still had

positive fecal samples, and the evolution of disease after discharge remains unclear. Base on the current evidence, no practical measures has developed targeting those patients. Thus, there is a need to describe the clinical characteristics of patients after negative nucleic acid testing results to add evidence in dealing with this group of patients.

This study aimed to describe the clinical and imaging characteristics of patients with COVID-19 after two sequential negative nucleic acids testing results with a retrospective study conducted in Shenzhen, China. Our results might provide more evidence on the treatment and prevention of transmission for COVID-19 patients in recovery stage.

2. Methods

2.1 Study Design and Participants

This single-center case series was retrospectively conducted using data from all consecutive patients with confirmed COVID-19 transferred to Hezheng ward of Shenzhen Hospital, Southern Medical University, from January 31 to February 28, 2020. In Shenzhen, China, confirmed COVID-19 patients had to accept nucleic acid testing every day until two sequential negative results were obtained, then base on the condition of COVID-19 patients may discharge or transfer to other government assigned hospital for further treatment. The Hezheng ward is responsible for the further treatments for COVID-19 patients who had obtained two sequential negative results for SARS-CoV-2. All COVID-19 cases were diagnosed in other government assigned hospitals in Shenzhen according to the Chinese programme for the diagnosis and treatment of COVID-19 [16]. The clinical characteristics and outcomes were monitored up to March 7, 2020, the discharge date of follow-up.

This study was approved by the institutional ethics board of the Shenzhen Hospital. Requirement for individual patient consent was waived because no identifiable information is collected.

2.2 Data Collection

The clinical characteristics and outcomes of enrolled COVID-19 patients were drawn with structured data collection forms from electronic medical records at first admission due to COVID-19 and data after transferring to Hezheng ward after two sequential negative real-time RT-PCR results. All data were reviewed by a trained team of physicians. Information recorded included demographic data, epidemiological history, underlying comorbidities (ie, bronchial or lung diseases, other comorbidities), symptoms, signs, laboratory parameters (i.e., white blood cell count, percentage of neutrophils, lymphocyte count, percentage of lymphocytes, C-reactive protein [CRP], D-dimer, erythrocyte sedimentation rate [ESR], lactate dehydrogenase [LDH], alanine aminotransferase [ALT], aspartate aminotransferase [AST]), chest computed tomographic (CT) scans, if available. Treatment and outcomes data were also extracted.

2.3 Diagnosis of COVID-19 and clinical classification

COVID-19 cases were diagnosed following the criteria for the diagnosis and treatment of COVID-19 published by General Office of National Health Committee of China [16].

The suspected case was defined as patient with epidemiological history and had any 2 of the clinical features or patients without epidemiological history but had all the clinical features. Clinical features including: 1) fever and/or respiratory symptoms; 2) imaging features of COVID-19; 3) normal or reduced total white blood cell count and/or normal or reduced lymphocyte count in the early stages of the disease onset. Epidemiological history including: 1) travel to or residence in Wuhan or other cities with continuous transmission of local cases in the last 14 days before symptom onset; 2) contact with patients with SARS-CoV-2 infection in the last 14 days before symptom onset; 3) contact with patients with fever or respiratory symptoms from Wuhan or other cities with continuous transmission of local cases in the last 14 days before symptom onset; 4) clustered onsets.

The confirmed case was defined as suspected case with one of the following pathogenic evidence, 1) positive for the SARS-CoV-2 by the real-time PCR test for nucleic acid, 2) viral gene sequencing shows highly homogeneity to the known SARS-CoV-2, 3) positive for serum SARS-CoV-2 specific IgM antibody and IgG antibody; SARS-CoV-2 specific IgG antibody turns negative into positive or its serum levels in recovery phase 4 times higher than that in acute phase.

In the present study, COVID-19 patients with two sequential negative nucleic acid testing results were classified as mild or moderate according to the baseline severity. Mild cases were those with mild clinical features and no imaging features of pneumonia. Moderate cases were those with fever or respiratory symptoms, and had imaging features of pneumonia [16].

2.4 CT imaging manifestation of COVID-19

Because mild cases had no imaging features of pneumonia, chest CT scan re-examination was performed only in moderate COVID-19 cases. To determine the changes in imaging manifestation that appeared during COVID-19 recovery, the chest CT scan were tracked for 2 weeks at 5–7 days intervals. Typical CT imaging manifestation including, ground-glass density shadow only, interlobular septal thickening combined with ground-glass change, intralobular interstitial thickening combined with ground-glass change, consolidation combined with ground-glass change, strip-like density shadow, solid nodules, and other features such as pleural effusion. All of the CT images were reviewed by the same professional (Wang J).

2.5 Statistical Analysis

Baseline characteristics of COVID-19 patients were presented for all cases, and further grouped by severity of the disease (mild or moderate). Data are presented as frequency rates and percentages for categorical data or median with inter-quartile range (IQR) for continuous data. Comparisons of proportions for categorical variables were performed using the χ^2 test, and the Fisher exact test was used when the data were limited. Comparisons median were performed using the Mann-Whitney test between two independent groups or Wilcoxon test between two paired groups. All statistical analyses were

conducted using SPSS (Statistical Package for the Social Sciences) version 21.0 software (SPSS Inc). A 2-sided α of < 0.05 was considered statistically significant.

3. Results

3.1 Characteristics of included participants

A total of 51 confirmed COVID-19 patients with two sequential negative nucleic acid testing results were transferred to our hospital for the further treatments and were included in this study. The median age was 34.0 years (range: 7 months to 67 years; IQR 20-44 years), 24 (47.1%) were men, and 36 (70.6%) ever went to Hubei (**Table 1**). The median (IQR) incubation time and time to negative nucleic acid testing were 7.5 (1.0, 11.75) days and 3 (2, 7) days.

The time course of symptoms, throat swab positive, hospital admission, and discharge of patients infected with SARS-CoV-2 for each patient was present in **Figure 1**. For the symptoms firstly admitted into hospital, 34/51 (66.7%) patients had fever and the duration for fever was 5.0 (IQR: 2.0, 7.0) days, followed by cough (31/51, 60.8%). In addition, the proportions of symptoms such as expectoration, sore throat, headache, fatigure, stuffy and runny nose, gastrointestinal reaction and chest tightness and dyspnea ranged from 3.9% to 13.7%. Generally, the proportions of symptoms were generally higher in moderate cases than mild cases (fever: 74.2% vs. 55.0%; cough: 71.0% vs. 45.0%), but the differences were not statistically significant. After entering into Hezheng Ward with two sequential negative real-time RT-PCR results, no patients reported fever and the proportion of cough (17/51, 33.3%) were also significantly reduced (both P <0.05). The proportions of other symptoms were generally the same.

19.6% (10/51) patients complicated with bronchial or lung diseases or other coexisting conditions such as glioma, nephrectomy, and hyperlipidemia, and all these complications were occurred among moderate cases. 34.7% of cases were treated with western medicine only, 30.6% with Chinese medicine, and 34.8% with both treatments.

3.2 Laboratory Parameters

The laboratory results of the included COVID-19 patients after two sequential negative nucleic acid testing were presented in **Table 2**. Compared with baseline characteristics, no statistically significant difference was observed in repeated-measures after 3 to 5 days (**Table 3**). For longer repeated-measure interval (over 1 week; **Table 4**), the laboratory results reduced steadily, but without significantly difference.

3.3 CT Imaging Manifestations

By the time of transfer to Hezheng Ward, all patients with moderate COVID-19 had performed chest CT scan. Among these patients (**Table 5 and figure 2)**, 7 (22.6%) had only one lobe affected and 24 (77.4%)

had two or more lobes affected. Left lower lobe was the most common location of lesions (71.0%, 22/31), followed by right lower lobe (61.3%, 19/31), left upper lobe (48.4%, 15/29) and right middle robe (38.7%, 12/29). For right upper and lower and left lower lobes, the distribution was generally even for single or multiple affected lobes. However, for right middle lobe, 83.3% (10/12) patients had single lobe involved, whereas for left upper lobe, 66.7% (10/15) patients had multiple lobes involved.

The most common CT imaging manifestations were ground glass opacity (51.6%, 16/31) and fibrous stripes (54.8%, 17/31) (**Table 6 and Supplementary tabe 1)**. Among 12 out of 31 patients with repeated chest CT scan after negative for SARS-CoV-2, 7 patients (58.3%) with CT ground-glass absorption reduced over 60%. However, there were still 4 cases with absorption less than 5%. For case 17, the ground-glass with absorption <5% lasted for almost one month. In addition, we found occasionally that, for 12 cases (case no. 38-47, 49, 50) with throat swab negative, the fecal tests were positive with repeated tests (**Supplementary tabe 2)**.

4. Discussion

This is a descriptive case series of 51 COVID-19 patients after obtained two sequential negative nucleic acid testing results. It presents the clinical and CT imaging features when COVID-19 cases turn to negative in nucleic acid detection tests. The clinical data continue return to normal, and nearly half of the moderate patients with CT ground-glass absorption reduced less than 60% within one week, which might need further attention. In addition, fecal positive for SARS-CoV-2 is common among this group of cases.

Since December 2019, COVID-19 first occurred in Wuhan [17, 18]. China, this disease had rapidly spread from Wuhan to other areas and worldwide. The rapid escalation in the number of COVID-19 cases has resulted in an insufficiency of health-care resources [19]. To improve the availability and accessibility of health-care resource in China, the Chinese government had issued policies and criteria for the diagnosis and treatment of COVID-19. In Shenzhen, China, all suspected and confirmed cases were sent to the government assigned hospital for diagnosis and initial treatment, and patients that reached discharge criteria but still had clinical symptoms would be transferred to other hospital for further treatment, which helped to improve quality of medical services and make a better use of medical resources. However, the effectiveness and the usefulness of this further treatment for COVID-19 remain unclear.

In our study, the most common symptoms by the time of diagnosis were fever and cough, which was similar with previous studies [12]. In a meta-analysis with a total of 61 studies (59,254 patients) [12], the most common disease-related symptoms were fever (82%, 95% confidence interval (CI) 56%-99%) and cough (61%, 95% CI 39%-81%). Compared with mild cases, moderate cases had higher proportion of comorbidities. After negative in nucleic acid detection tests, no cases suffered fever and the proportion of cough also decreased significantly (60.8% vs. 33.3%), indicating that the initial symptomatic treatments were effective. However, the proportions of other symptoms such as sore throat, nasal congestion and runny nose, and dyspnea were generally the same, but the non-specific symptoms were observed.

In our study, left lower lobe was most commonly affected, and right lower lobe was second common location of lesions. This finding is consistent with the previous radiological studies of patients with COVID-19 infection [20, 21]. Generally, lower lobes are commonly affected due to the anatomical structure of the trachea and bronchi: the right bronchus is short and straight. By the time patients transferred to our hospital, the most common CT imaging manifestations were ground-glass density shadow only and strip-like density shadow. Serial CT imaging of patients helped to continuously monitor disease changes.

At the end of the first week, lesion range reduced over 50% than that of the baseline among 7/12 patients. However, there were still half of the patients with abnormal imaging, and 4 cases with absorption were less than 5% within one week. The phenomenon suggested that, even after the negative for throat swab nuclear acids test, the virus might be still existed in the human body, but under the detection threshold level of throat swab test [22]. Study has showed that chest CT was more sensitive than RT-PCR [23]. Further repeated tests for this group of patients, even with negative for throat swab, positive results for fecal tests were observed in same of the patients, which mean that the virus might be not completely eliminated and still be a risk of transmission. Though the clinical features of the participants continued return to normal after negative throat swab nuclear acids test with treatment, the imaging features still abnormal and further isolation and treatment for patients after the negative for throat swab nuclear acids test is necessary. Studies has indicated that if patients had clinical symptoms, epidemiological characteristics, and chest CT imaging characteristics of viral pneumonia that were compatible with COVID-19 infection, careful consideration of the isolation and treatment of these patients is still needed even if the RT-PCR test is negative [24].

In one case (case 17), the ground-glass with absorption < 5% lasted for almost one month. Considering the asymptomatic persistently and negative for nuclear acids, we speculated that this abnormal imaging might cause by old lesions due to other respiratory diseases.

There were also several limitations in the present study. First, the COVID-19 cases were confirmed through nucleic acid tests using respiratory tract specimens. After these patients obtained two sequential negative respiratory tract sample results, part of they were transferred to our hospital for further treatment till the clinical symptoms were mostly improved. For some patients with fecal test were still positive. However, our study reported these patients' the clinical characteristics and its dynamic changes during hospitalization, which could be a supplement to the current evidence of 2019-nCoV. Second, given the small sample size, it is difficult to systematically explore the differences between mild case and moderate case, and the type I error should take into account. Moreover, the analyses have not been adjusted for multiple comparisons, the findings should be interpreted as exploratory and descriptive. Third, among the 51 cases, given the requirements of patients, the treatment including drug and traditional Chinese medicine, and this could be an important confounder for comparison. Finally, for retrospective study design, some of the data were not collected or measured. For example, only less than half of the patients with repeated clinical measurements.

5. Conclusions

In this retrospective cohort study of 51 COVID-19 patients with two sequential negative sample results, clinical features of the patients returned to normal. However, there still need further isolation and treatment of the abnormal imaging features to improve the prognosis and risk for further transmission. More researches are needed to explore the clinical and imaging feature, which is useful for decision-making for COVID-19.

Declarations

- **Ethics approval and consent to participate:** Not Applicable.
- **Consent for publication:** The authors agreed to publish.
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- **Authors' contributions:** Concept and design: Yan Rong. Acquisition, analysis, or interpretation of data: Jing Wang.Drafting of the manuscript: Jinfei Tian. Critical revision of the manuscript for important intellectual content: Xinhua Liang. Statistical analysis: Yang Zhou, Yi Shi. Obtained funding: Xiaoli Li, Huadong Zeng. Administrative, technical, or material support: Dandan Zhang, Jing Liu. Supervision: Yi Shi.
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Tables

Table 1 Clinical characteristics of the patients infected with mild-to-moderate SARS-CoV-2.

Variables	Total (n=51)	Moderate (n=31)	Mild (n=20)	p
Ever went to Hubei (n,%)				0.539
Yes	36 (70.6)	23 (74.2)	13 (65.0)	
No	15 (29.4)	8 (25.8)	7 (35.0)	
Age, years	34.0 (20.0, 44.0)	37.0 (25.0, 48.0)	31.0 (16.0, 37.5)	0.288
Gender (n,%)				0.813
Male	24 (47.1)	15 (48.4)	9 (45.0)	
Female	27 (52.9)	16 (51.6)	11 (55.0)	
Incubation time, days	7.5 (1.0, 11.75)	8.0 (1.75, 12.0)	6.5 (0.0, 9.0)	0.361
Time to negative nucleic acid testing, days	3 (2, 7)	2 (4, 8)	2.5 (1.25, 5.5)	0.291
Symptoms at admission				
Fever (n,%)	34 (66.7)	23 (74.2)	11 (55.0)	0.156
Duration of fever, days	5.0 (2.0, 7.0)	5.0 (2.0, 7.5)	4.0 (2.0, 6.0)	0.772
Cough (n,%)	31 (60.8)	22 (71.0)	9 (45.0)	0.083
Expectoration (n,%)	6 (11.8)	4 (12.9)	2 (10.0)	1.000
Sore throat (n,%)	6 (11.8)	3 (9.7)	3 (15.0)	0.668
Headache (n,%)	4 (7.8)	1 (3.2)	3 (15.0)	0.287
Fatigue (n,%)	2 (3.9)	2 (6.5)	0 (0.0)	0.514
Stuffy and runny nose (n,%)	4 (7.8)	1 (3.2)	3 (15.0)	0.287
Gastrointestinal reaction (n,%)	5 (9.8)	4 (12.9)	1 (5.0)	0.636
Chest tightness and dyspnea (n,%)	7 (13.7)	5 (16.1)	2 (10.0)	0.690
Symptoms after two sequential negative nucleic acid testing				
Fever (n,%)	0 (0)	0 (0)	0 (0)	-
Cough (n,%)	17 (33.3)	11 (35.5)	6 (30.0)	0.767
Expectoration (n,%)	7 (13.7)	5 (16.1)	2 (10.0)	0.690
Sore throat (n,%)	4 (7.8)	3 (9.7)	1 (5.0)	1.000
Headache (n,%)	2 (3.9)	0 (0.0)	2 (10.0)	0.149
Fatigue (n,%)	3 (5.9)	1 (3.2)	2 (10.0)	0.553
Stuffy and runny nose (n,%)	3 (5.9)	0 (0.0)	3 (15.0)	0.055
Gastrointestinal reaction (n,%)	3 (5.9)	2 (6.5)	1 (5.0)	1.000
Chest tightness and dyspnea (n,%)	3 (5.9)	1 (3.2)	2 (10.0)	0.553
Pulse oximeter O2 saturation, %	97.3±0.95	97.1±0.89	97.6±1.00	0.469
Heart rate, breaths/min	86.7±15.5	85.9±15.7	88.0±15.5	0.938
Disease history				
Bronchial or pulmonary disease (n,%)	4 (7.8)	4 (12.9)	0 (0.0)	0.094
Other diseases (n,%)*	6 (11.8)	6 (19.6)	0 (0.0)	**0.036**
Treatment (n,%)**				0.216
Western medicine	17 (34.7)	11 (35.5)	6 (33.3)	
Chinese medicine	15 (30.6)	7 (22.6)	8 (44.4)	
Both	17 (34.8)	13 (41.9)	4 (22.2)	

*Other underlying diseases include glioma, nephrectomy, hyperlipidemia, gastric tumours, type 2 diabetes and thyroid cancer, etc.

**Western medicine: levofloxacin, moxifloxacin, ribavirin, abidol, lopinavir, ritonavir, interferon, thymoxin, chloroquine phosphate, interferon, oseltamivir, etc.

Chinese medicine: Jin Hua Qing Gan particles, antiviral particles, Xiang Sha Liu Jun pills, etc.

Table 2 Laboratory results of the included COVID-19 patients after two sequential negative nucleic acid testing

	N	Total	Moderate		Mild		*P*
			n	Median (IQR)	n	Median (IQR)	
WBC count, $\times 10^9$ /L	51	5.78 (4.38, 7.70)	31	5.90 (4.84, 8.39)	20	5.62 (3.99, 7.39)	0.298
Neutrophile granulocyte, %	49	55.2 (47.9, 63.3)	30	55.8 (46.9, 63.7)	19	52.4 (41.3, 60)	0.325
Lymphocyte count, $\times 10^9$ /L	46	2.01 (1.49, 2.53)	28	1.99 (1.41, 2.90)	18	2.07 (1.65, 2.34)	0.839
Lymphocyte, %	51	34.1 (27.9, 41.7)	31	32.3 (23.9, 37.9)	20	35.7 (29.4, 44.6)	0.162
C-reactive protein, mg/L	44	0.73 (0.34, 1.84)	26	0.86 (0.36, 2.04)	18	0.64 (0.21, 1.3)	0.481
D-dimer, μg/mL	20	0.27 (0.22, 0.42)	13	0.25 (0.22, 0.43)	7	0.28 (0.22, 0.39)	0.838
Erythrocyte sedimentation rate, mm/h	10	19 (3.75, 32)	7	19 (4, 24)	3	30 (2, 44)	0.568
Lactate dehydrogenase, U/L	37	362 (323.5, 424)	23	354 (322, 416)	14	369 (322, 448)	0.650
Alanine aminotransferase, U/L	43	21 (16, 36)	27	22 (18, 46)	16	20 (15, 34)	0.606
Aspartate aminotransferase, U/L	43	27 (22, 33)	27	27 (23, 32)	16	26 (20, 33)	0.763

Table 3 Laboratory results of the included COVID-19 patients after two sequential negative nucleic acid testing with repeated analyses after 3-5 days

	Total				Moderate				Mild			
	N	After negative	3-5 days after negative	P	N	After negative	3-5 days after negative	P	N	After negative	3-5 days after negative	P
	20	7.7 (4.7, 10.2)	6.37 (5.1, 7.65)	0.080	13	7.7 (4.8, 10.2)	6.83 (5.04, 7.74)	0.126	7	7.7 (4.3, 10.4)	6.33 (5.05, 6.92)	0.310
, %	18	53.3 (50, 62.5)	52.7 (45.4, 57.6)	0.064	12	55.2 (49, 65.5)	53.3 (43.7, 60.7)	0.099	6	52.8 (45.9, 61.1)	50.2 (43.7, 54.2)	0.463
/L	15	2.11 (1.65, 2.82)	2.21 (1.66, 2.58)	0.609	10	1.99 (1.52, 2.86)	2.11 (1.51, 2.55)	0.721	5	2.11 (1.9, 4.21)	2.28 (1.76, 3.11)	0.893
, %	20	34.6 (29.6, 46.1)	34.9 (29.8, 44)	0.904	13	32.3 (26, 39.5)	34.4 (28.5, 42.5)	0.272	7	39.9 (30.5, 52)	35.4 (31.9, 45.1)	0.310
L	9	1.92 (1.02, 3.54)	0.87 (0.43, 2.13)	0.123	5	2.35 (1.15, 15.19)	1.24 (0.32, 3.73)	0.500	4	1.2 (0.97, 2.54)	0.75 (0.41, 0.91)	0.109

Table 4 Laboratory results of the included COVID-19 patients after two sequential negative nucleic acid testing with repeated analyses after over 1 week

	Total				moderate				Mild			
	N	After negative	1 week after negative	P	N	After negative	1 week after negative	P	N	After negative	1 week after negative	P
$\times 10^9$ /L	15	4.88 (4.16, 8.42)	6.69 (4.6, 7.33)	0.496	10	8.05 (4.84, 10.2)	7.20 (4.60, 7.97)	0.059	5	4.94 (4.07, 5.36)	4.78 (4.22, 6.75)	0.443
, %	14	60.1 (46.4, 65.6)	57.2 (49.2, 61.7)	0.802	10	61.3 (56.8, 69.5)	58.1 (51.6, 65.9)	0.114	4	50.2 (47.5, 58.8)	51.9 (47.1, 58.9)	0.844
count,	12	1.95 (1.42, 2.68)	1.91 (1.38, 2.5)	0.610	8	1.85 (1.42, 2.68)	2.18 (1.24, 2.71)	0.889	4	2.07 (1.43, 2.69)	1.68 (1.52, 2.15)	0.715
, %	15	30.8 (27.1, 43.4)	30.4 (24.1, 38)	0.363	10	30 (22.1, 32.1)	28.8 (21.8, 35.6)	0.721	5	45.6 (35.4, 50)	33.7 (28.2, 39.3)	0.080
rotein,	12	1.23 (0.21, 3.11)	0.43 (0.24, 1.39)	0.131	8	2.14 (0.72, 19.59)	0.86 (0.38, 2.55)	0.128	4	0.16 (0.04, 0.99)	0.28 (0.11, 0.47)	1.000

Table 5 Lung lobes involved of 31 moderate COVID-19 after two sequential negative nucleic acid testing

	Total	Single	Multiple
Number of lobes involved			
1	7 (22.6)	-	-
2	12 (38.7)	-	-
3	5 (16.1)	-	-
4	4 (12.9)	-	-
5	3 (9.7)	-	-
More than two lobes involved	24 (77.4)	-	-
Lobe of lesion distribution			
Right upper lobe	9 (31.0)	5 (55.6)	4 (44.4)
Right middle lobe	12 (41.4)	10 (83.3)	2 (16.7)
Right lower lobe	19 (65.5)	9 (47.3)	10 (52.6)
Left upper lobe	15 (51.7)	5 (33.3)	10 (66.7)
Left lower lobe	22 (75.9)	11 (50.0)	11 (50.0)

Table 6 CT imaging of 31 moderate COVID-19 after two sequential negative nucleic acid testing

	Moderate (n=31)
Density and inner features	
Ground glass opacity	16 (51.6)
Thickened intralobular septa	7 (22.6)
Thickened interlobular septa	3 (9.7)
Mixed ground glass opacity and consolidation	3 (9.7)
Fibrous stripes	17 (54.8)
Consolidation	8 (25.8)
Other features	
Pleural effusion	3 (9.7)

Table 7 Percentage change of CT ground-glass absorption of 12 cases after two sequential negative nucleic acid testing

	After 1 week	After 2 week	After 3 week	After 4 week
<5%	2	3	1	1
5~50%	1	0	0	0
51~70%	2	0	1	0
70~80%	3	0	0	0
>80%	2	4	1	1

Supplementary tabe 1 Percentage change of CT ground-glass absorption after two sequential negative nucleic acid testing

Patients No.	Date of examination	Time lag after two sequential negative nucleic acid testing	Percentage change of CT ground-glass absorption
3	Feb. 5	0	Baseline
	Feb. 12	7	70%-80%
9	Feb. 3	0	Baseline
	Feb. 8	5	90-100%
	Feb. 14	11	100%
11	Feb. 8	0	Baseline
	Feb. 13	5	70-80%
	Feb. 20	12	80-90%
	Mar. 7	27	100%
13	Feb. 4	0	Baseline
	Feb. 13	9	↓5%
14	Feb. 13	0	Baseline
	Feb. 18	5	70%-80%
17	Feb. 14	0	Baseline
	Feb. 26	12	↓5%
	Mar. 5	19	↓5%
	Mar. 13	27	↓5%
19	Feb. 14	0	Baseline
	Feb. 20	6	↓5%
21	Feb. 16	0	Baseline
	Feb. 22	6	60-70%
	Feb. 28	12	80-90%
23	Feb. 16	0	Baseline
	Feb. 23	7	↓90%
27	Feb. 20	0	Baseline
	Feb. 28	8	60-70%
	Mar. 5	13	80-90%
29	Feb. 20	0	Baseline
	Feb. 28	8	↓5%
35	Feb. 1	0	Baseline
	Feb. 3	2	30-40%
	Feb. 25	24	60-70%
	Mar. 4	31	↓90%

Supplementary tabe 1 Patients with repeat focal positive tests

Patients No.	Date with focal test	Focal results	Throat swab results
38	Feb. 18	Positive	Negative
39	Feb. 18	Positive	Negative
40	Feb. 19	Positive	Negative
41	Feb. 21	Positive	Negative
42	Feb. 21	Positive	Negative
43	Feb. 21	Positive	Negative
44	Feb. 21	Positive	Negative
45	Feb. 21	Positive	Negative
46	Feb. 20	Positive	Negative
47	Feb. 22	Positive	Negative
49	Feb. 20	Positive	Negative
50	Feb. 18	Positive	Negative

Figures

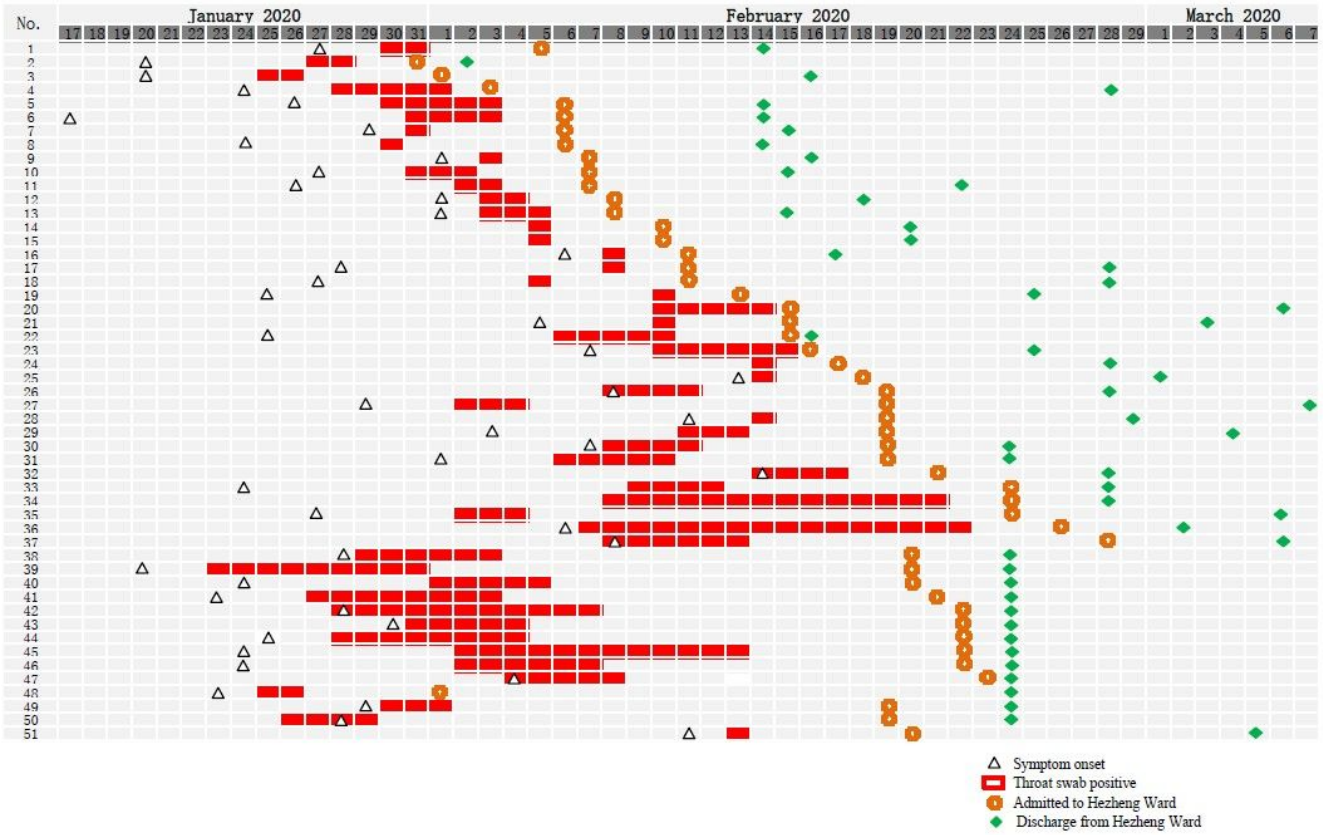

Figure 1

Time course of symptoms, hospital admission after RT-PCR negative, and discharge of patients infected with SARS-CoV-2

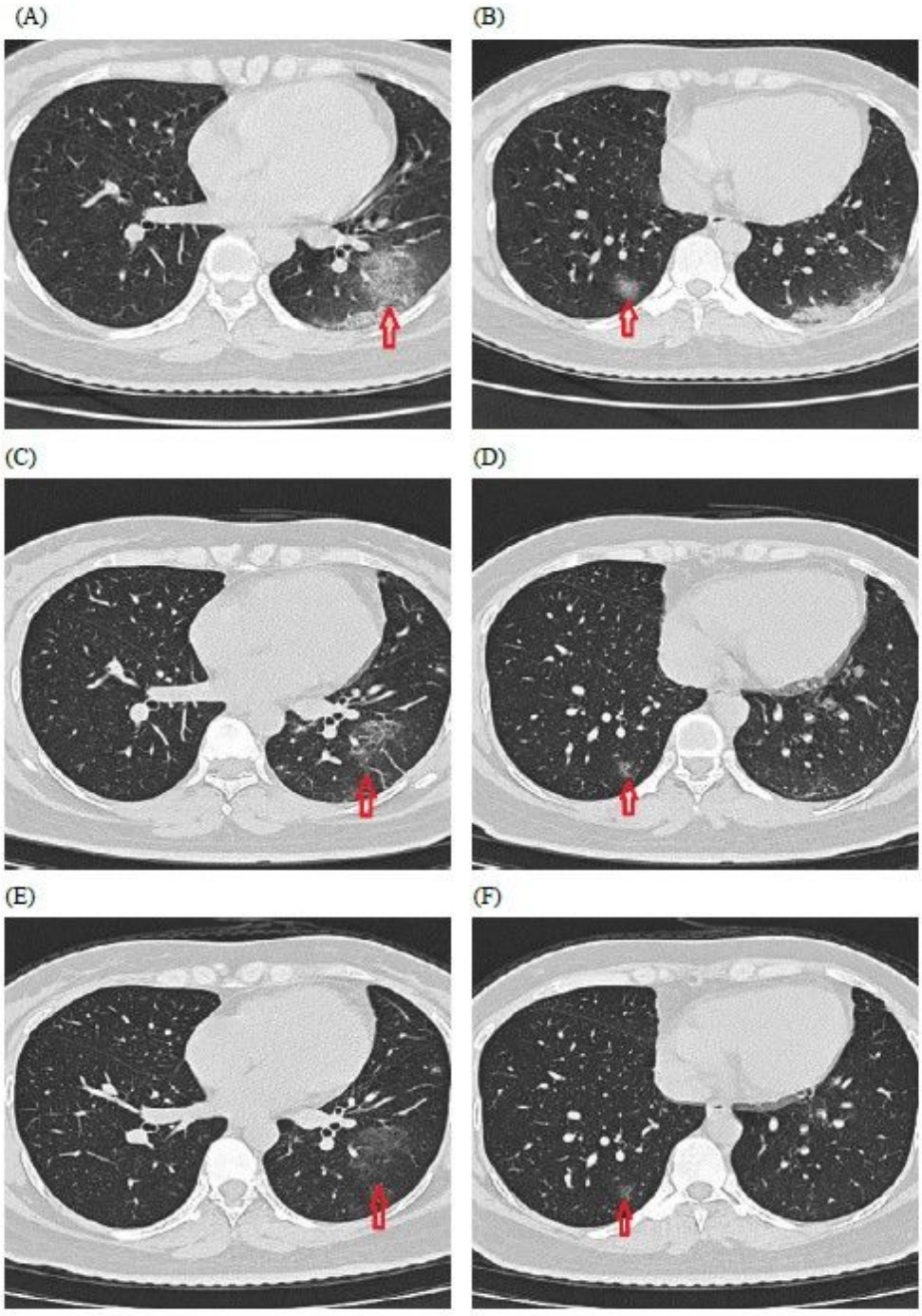

Figure 2

Transverse chest computed tomograms from a patient, showing ground glass opacity and consolidation of lower lobe of right and left lung on day 1 after negative for SARS-CoV-2 (A and B), on day 10 after negative for SARS-CoV-2 with absorption of 60%-70% (C and D), and on day 16 after negative for SARS-CoV-2 with absorption of 80%-90% (E and F).