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*Original Article*

# Factors affecting recurrent positive RT-PCR results in clinically cured COVID-19 patients: a multicenter study

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**Abstract:** The aim of this study was to evaluate factors affecting the recurrence of positive RT-PCR results. By performing a retrospective analysis, we evaluated the clinical data of recurrent positive coronavirus disease 2019 (COVID-19) patients in multiple medical institutions in Wuhan. We recruited COVID-19 patients who were hospitalized from January 1 to March 10, 2020, in three tertiary hospitals in Wuhan, met the discharge criteria and received at least one additional nucleic acid test before leaving the hospital. According to the RT-PCR results, patients were split into a recurrent positive group (RPos group) and a nonrecurrent positive group (non-RPos group). Clinical characteristics, therapeutic schedules and antibody titers were compared between the two groups. AI-assisted chest high-resolution computed tomography (HRCT) technology was applied to investigate pulmonary inflammatory exudation and compare the extent of lung areas with different densities. This study involved 122 COVID-19 patients. There were no significant differences in age, sex, preexisting diseases, clinical symptoms, clinical classification, course of disease, therapeutic schedules or serum-specific antibodies between the two groups. A higher proportion of patients who showed pulmonary inflammatory exudation on HRCT scans were recurrent positive at the time of discharge than other patients (81.6% vs 13.7%, $P < 0.01$). In addition, the degree of pulmonary fibrosis was higher in the RPos group than in the non-RPos group ($P < 0.05$). Subpleural exudation at the peripheral edge of the lung and extensive pulmonary fibrosis at the time of discharge represent risk factors for the recurrence of COVID-19.

**Keywords:** CT, AI-assisted, COVID-19, recurrent positive

## Introduction

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) causes coronavirus disease 2019 (COVID-19), which is characterized by a complex transmission route, strong infectivity, general susceptibility, diverse clinical symptoms, and a long course of recovery [1-3]. Since the first report in January 2020, COVID-19 has affected more than 200 countries around the world, with nearly 42,894,221 confirmed cases of COVID-19 [4] (https://covid19.who.int/table). As experience with COVID-19 accumulated, COVID-19 patients who had recurrent positive RT-PCR test results within 2 weeks of discharge from the hospital (with or without clinical symptoms) were increasingly identified. Research by Lan et al. revealed that the RT-PCR test results of 4 patients who recovered from COVID-19 were positive again 5-13 days after hospital discharge [5]. According to Lu et al., 87 (14.1%) of 619 discharged patients in Guangdong Province had recurrent positive RT-PCR results, even when they adhere to social isolation policies [6], and Kang et al. reported that 292 (3.3%) of 8,922 recovered patients in Korea had recurrent positive RT-PCR test results after hospital discharge [7]. The Korea

Centers for Disease Control and Prevention (KCDC) collected 285 patients with recurrent RT-PCR positivity, and 126 (44.7%) of 284 asymptomatic patients also had recurrent positive results (https://www.cdc.go.kr/board/board.es?mid=a30402000000&bid=0030&act=view&list_no=367267&nPage=8). Our previous study showed recurrent positive RT-PCR test results in 53 (20.6%) of 257 COVID-19 patients before hospital discharge. These findings indicated that at least some patients who meet the current discharge criteria may still be virus carriers, and it may be a sensible precaution to isolate patients who have recovered from COVID-19 for 14 days after leaving the hospital [8]. However, large-scale and multicenter studies have not yet been performed to determine the causes of recurrent positivity on RT-PCR, whether patients with recurrent positivity can transmit the virus, and how to avoid the recurrence of positive RT-PCR results after hospital discharge.

High-resolution CT (HRCT) of the chest is important for the diagnosis and management of patients with suspected cases of COVID-19 [9]. The newly applied artificial intelligence (AI)-assisted pneumonia diagnosis system has been described as an objective tool that can qualitatively and quantitatively assess the progression of pulmonary inflammation [10]. The present retrospective cohort study included 122 COVID-19 inpatients in Renmin Hospital of Wuhan University, Tongren Hospital of Wuhan University, and Central Theater General Hospital of the Chinese People's Liberation Army. All research subjects received at least one more RT-PCR test after meeting the discharge criteria [8], and based on the results, the patients were classified into a recurrent positive group (RPos group) and a nonrecurrent positive group (non-RPos group). In addition, their clinical characteristics, therapeutic schedules, time of recurrence, and serum-specific IgM and IgG titers were analyzed. AI-assisted chest HRCT technology was applied to qualitatively and quantitatively assess differences in pulmonary inflammation, with the aim of identifying risk factors for the recurrence of positive RT-PCR results.

## Materials and methods

### *Subjects and group*

A total of 122 inpatients with confirmed cases of COVID-19 from January 1 to March 10, 2020, at Renmin Hospital of Wuhan University, Tongren Hospital of Wuhan University, and Central Theater General Hospital of the Chinese People's Liberation Army were included in this retrospective cohort study. All patients met the discharge criteria (including two consecutive negative RT-PCR test results) and received at least one more nucleic acid detection test before leaving the hospital. The patients were classified into a recurrent positive group (RPos group, 50 patients) and a nonrecurrent positive group (non-RPos group, 72 patients) based on the RT-PCR results. The clinical diagnosis, treatment, classification and discharge criteria for all patients were based on the *Diagnosis and Treatment of COVID-19 (trial version 7)* published by the National Health Commission of China (http://www.nhc.gov.cn/yzygj/s7653p/202003/46c9294a7dfe4cef80dc7f5912eb1989.shtml). The collection and use of relevant case data adequately protected patient privacy and met the ethics requirements. The experimental procedures used in this study were approved by the Ethics Committees of the Renmin Hospital of Wuhan University, Tongren Hospital of Wuhan University, and Central Theater General Hospital of the Chinese People's Liberation Army (WDRY2020-K110).

### *Data collection*

Practicing physicians screened the electronic records of patients with confirmed cases of COVID-19. We recorded information about their medical history, symptoms and signs, laboratory results, and main therapeutic strategies (antiviral therapy, corticosteroid treatment, antibiotic treatment, immunomodulatory therapy, or respiratory support).

### *RT-PCR tests*

RT-PCR tests were carried out with throat swab samples using SARS-CoV-2 test kits (Wondfo, China). This molecular technique principally examines the open reading frame lab (ORFlab) and nucleocapsid protein (N) regions of the SARS-CoV-2 genome, and the threshold cycle (Ct) value was evaluated based on the manufacturer's instructions. Questionable data were resampled and retested.

### *Serologic detection*

Levels of IgM and IgG antiviral antibodies in serum samples were tested by automatic che-

miluminescence immunoassay on the basis of the manufacturer's instructions, which provides results as relative light units (RLUs), whereby the amount of anti-SARS-CoV-2 IgM or IgG antibody is positively associated with the RLU value. The system automatically determined the IgM or IgG levels (AU/ml) based on the RLU and a built-in calibration curve. A result > 10.0 AU/ml is positive (+), and a result < 10.0 AU/ml is negative (-) [8].

*Chest HRCT examination*

In accordance with the COVID-19 Close Contacts Management Guidelines issued by the National Health Commission of China (http://www.nhc.gov.cn/yzygj/s7653p/202003/46c9294a7dfe4cef80dc7f5912eb1989.shtml), all patients underwent a chest HRCT examination in a designated room, in which the environment and equipment were completely sterilized. Moreover, the scanning technicians were all wearing primary personal protective equipment, and patients had to be masked. Patients were examined in a supine position and received breathing training prior to the scan. A Sino-vision 64-s spiral CT scan (SINO VISION, Beijing) was performed, covering the area from the apex pulmonis to the costophrenic angle. The scanning parameters were as follows: tube voltage 120 kV, application of intelligent milliampere second technology, scanning layer thickness and layer spacing 0.5-2 mm, spiral pitch 1.3, and scan direction in the pedal direction.

*AI-assisted HRCT analysis*

Image analysis was performed independently by 2 senior diagnostic radiologists in a double-blind fashion. When opinions differed, the chief physician of diagnostic chest imaging was asked to organize a discussion and obtain a final agreement. The AI parameters were calculated by the "Artificial Intelligence (AI)-assisted Pneumonia Diagnosis System" software developed by Hangzhou Etu Medical Technology Co. (https://www.yitutech.com). For each patient, the CT presentation was described according to the following parameters: (1) pulmonary manifestation-exudation and pleural effusion; (2) lesion distribution-mainly peripheral, center-oriented or diffuse distribution; and (3) lesion extent-the 3D lung model shows that the whole lung is divided into 5 lobes, with 3 lobes of the right lung and 2 lobes of the left lung, and the lesion extent ranges from a single lobe, 2-3 lobes to ≥ 4 lobes; (4) numbers of lesions - ≥ 3 or < 3; (5) lesion densit - ground-glass opacities, flaky consolidation shadow, linear opacities or reticulation; and (6) percentage of diseased lung (PIV/WLV)-pulmonary inflammation volume (PIV)/whole lung volume (WLV), which is defined as air if the CT value is -1000, water if the CT value is 0 and bone tissue if the CT value is 1000, and the density is higher with a higher CT value. AI software performs the quantitative calculations, combining convolutional neural networks with the threshold method for dissecting the left and right lungs and detecting the areas of inflammation and then calculating the percentage of diseased lung (PIV/WLV) under different CT densities.

*Statistical analysis*

Frequencies and percentages are used to describe categorical variables; means and medians are used to describe continuous variables. Comparisons between groups with measurement data conformed to a normal distribution were performed using t tests, and comparisons between groups with skewed distribution data were performed using Wilcoxon's test or the Mann-Whitney U test. The $\chi^2$ test and Fisher's exact test were used to analyze categorical data, and the Wilcoxon rank-sum test was used to analyze ranked data. Data analyses were performed with SPSS (version 20.0) software. Two-sided *P* values < 0.05 indicated statistically significant differences.

## Results

*Comparison of clinical characteristics*

The most common preexisting diseases in the 122 COVID-19 patients involved in the study were hypertension, diabetes and coronary heart disease. However, the RPos group and the non-RPos group did not differ in the prevalence of these preexisting diseases *(P* > 0.05).

The patients in the RPos group had an average age of 62.14 years, ranging from 26 years to 89 years; among them, 23 patients (46.0%) were male and 23 (54.0%) were female. The patients in the non-RPos group had an average age of 59.76 years, ranging from 28 years to 87 years; 42 (58.3%) were male, and 30

**Table 1.** The comparison of clinical characteristics in RPos group and non-RPos group

| | RPos group (n=50) | Non-RPos group (n=72) | $t/\chi^2$ Value | *P Value* |
|---|---|---|---|---|
| Age (year) | | | | |
| Mean | 62.14 | 59.76 | 0.893 | 0.374 |
| Range | 26-89 | 28-87 | | |
| Gender | | | | |
| male, No. (%) | 23 (46.0) | 42 (58.3) | 1.803 | 0.179 |
| female, No. (%) | 27 (54.0) | 30 (41.7) | | |
| Past medical histiory | | | | |
| hypertension, No. (%) | 15 (57.7) | 18 (25.0) | 0.374 | 0.541 |
| diabetes, No. (%) | 8 (16.0) | 15 (20.8) | 0.451 | 0.502 |
| Coronary heart disease, No. (%) | 4 (8.0) | 4 (5.6) | 0.288 | 0.592 |
| Other disease of respiratory system, No. (%) | 0 (0.0) | 3 (4.2) | - | 0.268 |
| Cerebrovascular disease, No. (%) | 2 (4.0) | 1 (1.4) | - | 0.567 |
| cancer, No. (%) | 0 (0.0) | 2 (2.8) | - | 0.512 |
| Total basic disease, No. (%) | 24 (48.0) | 40 (55.6) | 0.675 | 0.411 |
| Symptoms on admission | | | | |
| fever, No. (%) | 42 (80.4) | 60 (83.3) | 0.01 | 0.922 |
| fatigue, No. (%) | 8 (16.0) | 4 (5.6) | 3.63 | 0.057 |
| cough, No. (%) | 22 (44.0) | 27 (37.5) | 0.519 | 0.471 |
| myalgia, No. (%) | 0 (0.0) | 0 (0.0) | - | - |
| anorexia, No. (%) | 1 (2.0) | 0 (0.0) | - | 0.410 |
| dyspnea, No. (%) | 10 (20.0) | 11 (15.3) | 0.462 | 0.497 |
| Sore throat, No. (%) | 1 (2.0) | 0 (0.0) | - | 0.410 |
| diarrhea, No. (%) | 2 (4.0) | 0 (0.0) | - | 0.166 |
| nausea, No. (%) | 0 (0.0) | 0 (0.0) | - | - |
| dizzy, No. (%) | 0 (0.0) | 0 (0.0) | - | - |
| headache, No. (%) | 2 (4.0) | 1 (1.4) | 1.17 | 0.28 |
| vomit, No. (%) | 0 (0.0) | 0 (0.0) | - | - |
| stomachache, No. (%) | 0 (0.0) | 0 (0.0) | - | - |
| Clinical classification | | | | |
| mild, No. (%) | 0 (0.0) | 1 (1.4) | 1.454 | 0.146 |
| general, No. (%) | 34 (68.0) | 37 (51.4) | | |
| severe, No. (%) | 15 (30.0) | 34 (47.2) | | |
| critical, No. (%) | 1 (2.0) | 0 (0.0) | | |
| Duration from symptom onset to hospital admission, days | | | | |
| Mean | 25.74 | 24.76 | 0.668 | 0.506 |

(41.7%) were female. Age and sex did not significantly differ between the two groups *(P* > 0.05).

Fever (mostly 37.3-38°C), cough (mostly dry cough) and fatigue were the most common symptoms of COVID-19 on admission. Symptoms such as dyspnea, diarrhea, chest tightness, myalgia and headaches were rare. There were no marked differences in clinical manifestations between the two groups *(P* > 0.05). Additionally, the disease course in the RPos group (25.74 days) was not different from that in the non-RPos group (24.76 days) *(P* > 0.05) (**Table 1**).

*Comparison of main therapeutic schedules*

Most patients were given antiviral treatment [117 (95.9%)], antibiotic therapy [88 (72.1%)], corticosteroid treatment [44 (38.1%)], immunomodulatory therapy [69 (56.6%)], phlegm elimination therapy [59 (48.4%)], and oxygen

**Table 2.** The comparison of mainly therapeutic schedules in RPos group and non-RPos group

| Treatment methods | No. (%) | | | $\chi^2$ | *P* |
|---|---|---|---|---|---|
| | Total (n=122) | RPos group (n=50) | non-RPos group (n=72) | *Value* | *Value* |
| antiviral therapy | 117 (95.9) | 46 (92.0) | 71 (98.6) | - | 0.158 |
| antibiotic therapy | 88 (72.1) | 35 (70.0) | 53 (73.6) | 0.191 | 0.662 |
| corticosteroid treatment | 44 (36.1) | 21 (42.0) | 23 (31.9) | 1.294 | 0.255 |
| immunomodulatory therapy | 69 (56.6) | 24 (48.0) | 45 (62.5) | 2.525 | 0.112 |
| eliminating phlegm treatment | 59 (48.4) | 20 (40.0) | 39 (54.2) | 2.371 | 0.124 |
| oxygen therapy | 99 (81.1) | 37 (74.0) | 62 (86.1) | 2.829 | 0.093 |
| Noninvasive ventilation | 4 (3.3) | 2 (4.0) | 2 (2.8) | - | 1.000 |
| Invasive mechanical ventilation | 0 (0.0) | 0 (0.0) | 0 (0.0) | - | - |
| ECMO | 0 (0.0) | 0 (0.0) | 0 (0.0) | - | - |

**Table 3.** The comparison of serum specific IgG and IgM antibodies in RPos group and non-RPos group

| | RPos group (n=57) | Non-RPos group (n=20) | $\chi^2/Z$ *Value* | *P* *Value* |
|---|---|---|---|---|
| IgG | | | | |
| negative, No. (%) | 8 (14.0) | 1 (5.0) | 0.459 | 0.498 |
| positive, No. (%) | 49 (86.0) | 19 (95.0) | | |
| IgM | | | | |
| negative, No. (%) | 23 (40.4) | 8 (40.0) | 0.001 | 0.978 |
| positive, No. (%) | 34 (59.6) | 12 (60.0) | | |
| IgG & IgM | | | | |
| IgG (-) & IgM (-) | 8 | 1 | 0.299 | 0.765 |
| IgG (-) & IgM (+) | 0 | 0 | | |
| IgG (+) & IgM (-) | 15 | 7 | | |
| IgG (+) & IgM (+) | 34 | 12 | | |

therapy [99 (81.1%)]; 4 patients (3.3%) underwent noninvasive continuous positive airway pressure therapy. There were no significant differences in treatment between the two groups (all P > 0.05) (**Table 2**).

*Comparison of serum-specific antibodies*

Seventy-seven of 122 COVID-19 patients were tested for serum-specific IgG and IgM antibodies: 57 in the non-RPos group and 20 in the RPos group. Serum antibody IgG and IgM test results were described as negative (-) or positive (+). There were no significant differences in serum-specific IgG and IgM titers between the two groups (both P > 0.05) (**Table 3**).

*Qualitative and quantitative evaluations with AI-assisted diagnosis and treatment systems*

The recurrent positivity rate was markedly higher in patients who had pulmonary inflammatory exudation after meeting the discharge criteria (81.6%) than that in others (13.7%) *(P* < 0.01) (**Table 4**; **Figure 1**).

AI-assisted chest HRCT technology was used to analyze the proportion of different CT density values in the total lung volume, and there were no significant differences in the proportions of -1000~-700 HU, -700~-600 HU, -600~-500 HU, -500~-300 HU, -300~-200 HU, and -200~60 HU between the two groups *(P* > 0.05). The proportion of 60-1000 HU was significantly higher in the RPos group than that in the non-RPos group *(P* < 0.05) (**Table 5**). Since 60-1000 HU represents soft tissue lesions and the possibility of pulmonary malignancy was excluded in patients in this study, 60-1000 HU was considered pulmonary fibrosis. Pulmonary fibrosis occupied a larger proportion of the entire lung in the RPos group than that in the non-RPos group.

## Discussion

This study mainly examined the issue of recurrent RT-PCR positivity among COVID-19 patients who had met the current discharge criteria and explored possible risk factors. COVID-19 patients who met the current discharge criteria were included and received at least one additional RT-PCR test before discharge from the hospital; patients were divided into groups based on the result of that final RT-PCR test. Throat swab sample collection was performed by professional doctors to ensure accuracy. This study showed that there was no obvious difference in clinical characteristics between the RPos group and the non-RPos group, which

**Table 4.** Analysis of pulmonary inflammatory exudation in RPos group and non-RPos group

| | with pulmonary inflammatory exudation | without pulmonary inflammatory exudation | $\chi^2$ | *P* Value |
|---|---|---|---|---|
| RPos group (n=50) | 40 | 10 | 55.944 | 0.001 |
| non-RPos group (n=72) | 9 | 63 | | |
| total | 49 | 73 | | |

is consistent with the findings of He et al. [11]. Lan et al. reported that the RT-PCR test results of 4 patients who recovered from COVID-19 were positive again 5-13 days after hospital discharge. These findings showed recurrent positive RT-PCR results in some discharged patients, and the related factors are worthy of further exploration.

In this study, 81.6% of the patients who had subpleural exudation at the peripheral edge of the lung at the time of discharge were more likely to have recurrent positive RT-PCR results, whereas only 13.7% of the patients without subpleural inflammatory exudation had recurrent positive RT-PCR results. These results confirm that subpleural exudation at the peripheral edge of the lung is an important risk factor for recurrent positivity on RT-PCR. Using lung CT scans, Dou et al. found that lung inflammation was not completely controlled in patients with recurrent positive results [12]. The imaging features of COVID-19 patients are typical of viral pneumonia. Most of the lesions are subpleural and start from the peripheral edge of the lung, expanding around the trachea and bronchus and showing cotton-like, flake-like, strip-like or branch-like patchy shadows and lung interstitial alterations. For patients with mild or asymptomatic disease, CT imaging characteristics are mostly multiple atypical exudations in a small area. Therefore, under the current discharge criteria, pulmonary inflammatory exudation suggests that inflammation is still active. In general, exudation should be considered, regardless of the extent, and the rate of recurrence among these patients may be higher than that among others.

Moreover, we found that the proportion of the whole lung with 60-1000 HU was higher in the RPos group than that in the non-RPos group. Lung tissues in this density range are mainly pulmonary fibrotic nodules formed after recovery from lung inflammation. The main pathological features of pulmonary fibrosis are diffuse interstitial exudation, infiltration and fibrosis, most of which manifest as the coexistence of alveolitis and fibrosis. The higher proportion of the total lung volume with 60-1000 HU in patients with recurrent positive RT-PCR results indicates that a large extent of pulmonary fibrosis may be a risk factor, which may be explained by the persistence of SARS-CoV-2 in the fibrotic tissue.

The following diagnostic criteria were included in the New Coronavirus Pneumonia Prevention and Control Program (7th): initial positivity for serum SARS-CoV-2-specific IgM and IgG antibodies, the detection of serum SARS-CoV-2-specific IgG antibody positivity or a greater than 4-fold increase in the titer of SARS-CoV-2-specific IgG antibodies in the recovery stage. However, the serum titers of SARS-CoV-2-specific IgG and IgM antibodies were not included in the discharge criteria (http://www.nhc.gov.cn/yzygj/s7653p/202003/46c9294a7dfe4cef80dc7f5912eb1989.shtml). In this study, the results suggest that the recurrence of positive RT-PCR results in clinically cured COVID-19 patients is not associated with the serum titers of SARS-CoV-2-specific IgG and IgM antibodies. The serum titers of SARS-CoV-2-specific IgG and IgM antibodies have not been found to act as predictors of viral recurrence after hospital discharge, which suggests that the clinical utility of IgG and IgM for the prediction of recurrence is limited.

In this study, the close contacts of patients with recurrent positive RT-PCR results adopted strict protective measures, and no healthy people were infected due to contact with these patients. Therefore, the chance of infection associated with contact with people who have recurrent positive RT-PCR results is unclear. Lu et al. found that the viral genome in patients with recurrent positive RT-PCR results had been almost completely degraded, suggesting a greatly reduced risk of transmission (especially through the respiratory route). Kang also believed that the virus in these patients was not reactivated and therefore was not capable of infecting a healthy person [7]. Osman report-

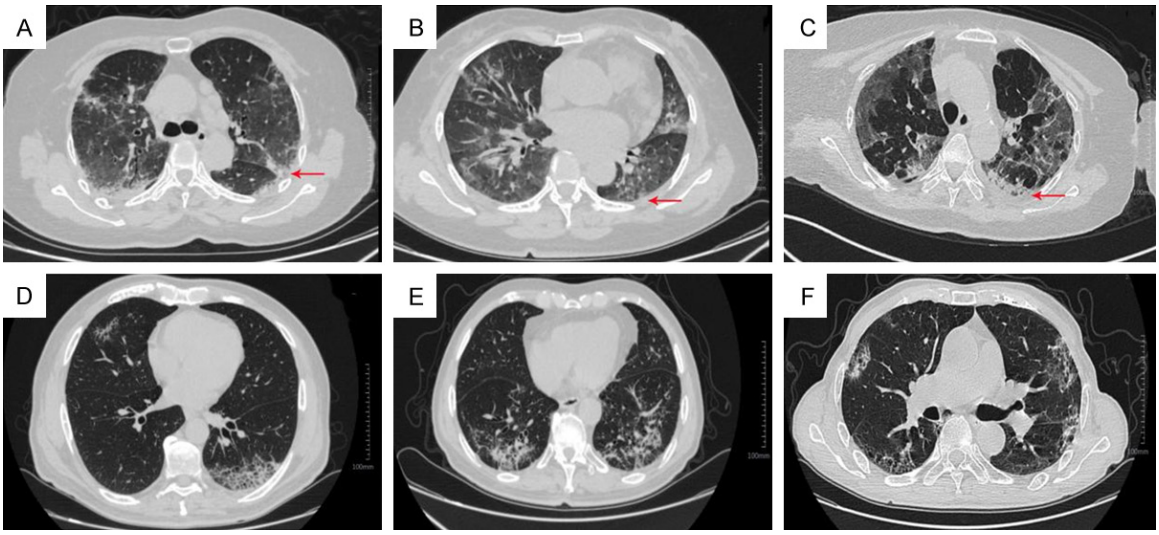


**Figure 1.** Representative chest HRCT at discharge in the RPos group and non-RPos group. A-C. Chest HRCT in the RPos group (the red arrows indicate acute exudation). D-F. Representative chest HRCT in the non-RPos group.

**Table 5.** The proportion of different CT density values in total lung volume in RPos group and non-RPos group

| | CT value (%) | | | | | | |
|---|---|---|---|---|---|---|---|
| | -1000~-700 | -700~-600 | -600~-500 | -500~-300 | -300~-200 | -200~60 | 60~1000 |
| RPos group (n=50) | 78.27 ± 2.19 | 6.03 ± 0.56 | 3.45 ± 0.42 | 4.05 ± 0.56 | 1.40 ± 0.20 | 3.82 ± 0.50 | 1.14 ± 0.13 |
| non-RPos group (n=72) | 77.43 ± 1.33 | 6.61 ± 0.41 | 3.75 ± 0.27 | 4.43 ± 0.34 | 1.51 ± 0.12 | 3.78 ± 0.32 | 0.55 ± 0.07 |
| T value | 0.346 | 0.861 | 0.627 | 0.621 | 0.516 | 0.079 | 4.154 |
| *P* value | 0.730 | 0.391 | 0.532 | 0.536 | 0.607 | 0.937 | < 0.001 |

ed that recurrent positive RT-PCR results may be due to false-negative RT-PCR results or prolonged shedding of SARS-CoV-2 rather than reinfection. Therefore, it is still necessary for patients who recover from COVID-19 to maintain social distancing measures and be isolated at home for at least 2 weeks [13]. In the absence of effective antiviral drugs and vaccines, active prevention and control measures are an effective way of preventing the human-to-human transmission of SARS-COV-2.

SARS-CoV-2 belongs to the genus β-coronavirus, and its genome has 85% homology with that of severe acute respiratory syndrome coronavirus (SARS-CoV) [2, 5]. SARS-CoV-2 is the largest positive-sense single-stranded RNA virus, with a high rate of RNA polymerase errors resulting in mutations. These mutations can lead to the development of new strains that can adapt to new hosts and microenvironments [14]. Thus, COVID-19 patients may receive false-negative RT-PCR test results or experience viral resurgence. Currently, several causes of recurrent positive RT-PCR results in COVID-19 patients during the recovery period have been described, including initial false-negative RT-PCR results, intermittent viral shedding, viral reactivation, infection with another SARS-CoV-2 strain, or exposure to a contaminated surface after discharge [15]. Based on the results of this study, we infer that the most likely reason for recurrent positive RT-PCR results before discharge is intermittent viral shedding associated with subpleural exudation along the peripheral edge of the lung and extensive pulmonary fibrosis.

As a retrospective study, this research has some limitations. For example, no prospective cohort study was performed to confirm our results. Moreover, as some patients received oral antiviral therapy during the period from hospital discharge to the time of recurrence or after recurrence, we cannot evaluate whether the recovery time of these patients would have

been prolonged without treatment or whether the patients' conditions would have worsened, leading to relapse.

In conclusion, this study provides evidence of the factors affecting recurrent positive RT-PCR results in COVID-19 patients who meet the discharge criteria. Subpleural exudation at the peripheral edge of the lung and extensive pulmonary fibrosis at the time of discharge are important risk factors for recurrent positive RT-PCR results. There is no obvious relationship between serum SARS-CoV-2-specific IgG and IgM antibodies and recurrence. These data will assist clinicians in setting more reasonable, evidence-based policies for COVID-19 diagnosis and treatment.

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## Disclosure of conflict of interest

None.

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