Pulmonary Function and Chest CT in Patients Recovering From COVID-19 Pneumonia

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Pulmonary function and chest CT in patients recovering from COVID-19 pneumonia

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Abstract

Background

COVID-19 is a new and highly contagious disease caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). However, there is a paucity of data regarding long-term CT findings and pulmonary function in COVID-19 survivors. The aim of this study was to investigate the influence of COVID-19 pneumonia on pulmonary function and chest high-resolution computed tomography (CT) in convalescent patients.

Methods

A retrospective study of COVID-19 pneumonia patients in the Beijing Youan Hospital, Capital Medical University, was conducted. Serial assessments, including pulmonary volumes (TLC), spirometry (VC, FVC, FEV1), pulmonary diffusing capacity for carbon monoxide (DLCO, DLCO/VA), and chest high-resolution CT were collected 3 months after discharge.

Results

Forty-six patients completed the serial assessments. There were 38 non-severe and 8 severe cases. Abnormalities were detected in pulmonary function tests in 17 patients (37.8%). One (2.2%), 2 (4.3%), and 17 (37.8%) patients had FEV1/FVC ratio, TLC, and DLCO values less than 80% of predicted values, respectively. Twenty-eight patients (60.9%) had abnormal CT findings. Compared with patients with non-severe disease, those with severe disease had higher chest CT scores but a similar incidence of DLCO impairment. Similarly, patients who

received glucocorticoids had higher chest CT scores but a similar incidence of DLCO impairment than those in the nonglucocorticoid group.

Conclusions

Three months after discharge from the hospital, impaired diffusing capacity and CT abnormalities were detected in more than one third of COVID-19 patients. Compared with patients with non-severe disease, those with severe illness had a higher incidence of lung imaging abnormalities and similar lung function impairment.

Keywords: COVID-19; SARS-CoV-2; pulmonary function; chest computed tomography.

Background

The coronavirus disease 2019(COVID-19) caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) has caused a worldwide pandemic, which poses a serious threat to human health [1,2]. Pneumonia caused by SARS-CoV-2 is one of the main clinical manifestations, and the severity of pneumonia directly affects the prognosis. Chest high-resolution computed tomography (CT) can show abnormal conditions in the lung and depict the patterns and extent of the abnormalities. Previous scholars who maked scientific researches on imaging features of COVID-19 patients found that bilateral, multifocal ground-glass opacity (GGO) and consolidation, predominantly in the subpleural and peri-bronchovascular regions, were the typical characteristics [3,4].

COVID-19 leads to impaired lung diffusing capacity in about 52.6% of survivors 1 month after discharge [5]. However, there is a paucity of data regarding long-term CT findings and pulmonary function in COVID-19 survivors. The aim of this study was to assess changes in lung CT and lung function in 46 patients 3 months after discharge from our hospital. We also compared the outcomes of patients with severe disease to those with non-severe illness.

Materials and methods

Patient selection

From January 21, 2020 to April 3, 2020, 108 COVID-19 patients were admitted to the Beijing Youan Hospital of Capital Medical University. The diagnosis and clinical classification of COVID-19 were based on the New Coronavirus Pneumonia Prevention and Control

Protocol for COVID-19 (seventh edition), released by the National Health Commission of China [6]. All patients had laboratory-confirmed SARS-CoV-2 infection determined by real-time reverse-transcription polymerase chain reaction (RT-PCR). They all reached uniform hospital discharge standards issued by the National Health Commission of China.

Three months after discharge, patients were eligible to participate in the study if they were 18 years or older. Patients with a history of severe respiratory diseases or mental illness were excluded. We obtained written informed consent before pulmonary function testing. All experiments were performed in compliance with approved guidelines and regulations and in accordance with the ethical standards of the Declaration of Helsinki. The study was approved by the Beijing Youan Hospital Research Ethics Committee (No. 2020-031).

We retrospectively analyzed medical records, classifying patients as having non-severe or severe disease, according to their condition at hospital admission. Illnesses were classified as having severe COVID-19 if they met any of the following criteria: shortness of breath (respiratory rate ≥30 times/minute; blood oxygen saturation ≤93% at rest; partial arterial oxygen pressure (PaO_2)/fraction of inspiration O_2 (FiO_2) ≤300mm Hg; or if they required mechanical ventilation or developed shock or other organ failure requiring intensive care unit (ICU) monitoring and treatment[6].

Pulmonary function tests

Lung function was determined using MasterScreen (CareFusion Germany 234GmbH). Total lung volume (TLC), forced vital capacity (FVC), residual volume (RV), forced expiratory volume in the first second (FEV1), FEV1 / FVC ratio, maximum expiratory flow rate at 25/50/75% vital capacity (MMEF25/50/75%) ,diffusing capacity of the lung for carbon monoxide (DLCO), diffusing capacity divided by the alveolar volume (DLCO/VA) were determined. Predicted values for each patient based on sex, age, weight, and height were obtained from standard tables. Data were expressed as percentages of predicted values.

We used the same method as Nöbauer et al to quantify pulmonary function[7].Lung function was considered abnormal if lung volumes were less than 80% of predicted values. Obstruction was defined as FEV1/VC less than 80% of the predicted value, whereas restriction was defined as VC and TLC less than 80% of the predicted value. Reduced dispersion function was defined as less than 80% of the predicted value. An impulse oscillation system (IOS) was used to measure airway resistance. Total airway resistance was defined as an oscillation frequency of 5 Hz(R5), central airway resistance was an oscillation frequency of 20 Hz (R20), and peripheral elastic resistance was reactance of an oscillation frequency of 5 Hz(X5). Upper-airway resistance was an oscillation frequency of 35 Hz(R35).

Lung imaging acquisition and CT quantitative evaluation

All chest CT scans were performed with a 256-section scanner (Brilliance iCT, Philips Healthcare, Cleveland, OH, USA) without intravenous contrast. CT examination parameters were as follows: 120 kV; automatic tube current (100 mA-400 mA); iterative reconstruction technique; detector collimation, 128 × 0.625 mm; section thickness, 5 mm; rotation time,

0.4 s; pitch, 0.914; matrix, 512 × 512. Images were assessed by 2 radiologists, both of whom were blinded to clinical information and lung function[8].

We used the same method as Li et al to quantify pulmonary inflammation severity [9]. To quantify lung parenchymal changes, we divided the lung parenchyma into 12 compartments on each side. Horizontal lines along the eminence and lower pulmonary vein divided the lungs into 3 parts: upper, middle, and lower. Each part included 4 subparts: central, peripheral, ventral, and dorsal. If the lung parenchymal lesion in each region did not cover more than one-third of the total surface area of the region, it was defined as a focal lesion.

In this study, pulmonary parenchymal lesions were classified into 3 types [9]. Mild pulmonary parenchymal changes mainly included changes in the line shadow. Each compartment was assigned a score based on the following: 0 (no involvement), 1 (focal lesion), 2 (widespread lesions). Moderate changes included GGO-like changes, bronchiectasis, grid-like fibrosis, and pulmonary hyperinflation symptoms, and severe changes mainly included honeycombing lesions or solid-shadow changes accompanied by traction bronchiectasis. CT scores of lung involvement were also obtained after discharge. All CT scores were independently performed by 2 radiologists, and agreement was reached by consensus.

Statistical methods

Statistical analysis was performed using Statistical Package for Social Science (SPSS) Version 22.0. Normal variables were expressed as mean ± standard deviation (x±s) and

analyzed by the independent or paired sample t-test. Nonnormal variables were expressed as medians (Q1, Q3) and analyzed by the Mann-Whitney U test. Categorical variables were described as percentages and compared using χ^2 or Fisher's exact test between groups. All statistical tests were 2-tailed. Statistical significance was defined as $P<0.05$. GraphPad Prism 8.0 was used to produce charts.

Results

1. Characteristics of the enrolled COVID-19 patients

This study evaluated a total of 108 patients. Seven patients were excluded because they were younger than 18 years. Twenty-five patients were excluded because it had been less than 3 months since discharge, 3 were excluded because they had a history of severe respiratory diseases or mental illness, and 7 were lost to follow-up. Forty-six patients completed the serial assessments in the study (Fig. 1). The 20 men and 26 women had a mean age of 46.74 ± 12.12 years (range, 28 to 73 years) and a mean body mass index (BMI) of 24.78 ± 2.93 kg/m^2. Three of the 46 patients (6.5%) had a history of smoking, while 38 (76.1%) had cough, nasal congestion, pharyngeal pain, shortness of breath, and other respiratory symptoms. The three most common underlying illnesses were hypertension (6 patients [13.0%]), diabetes (5 [10.9%],) and cardiovascular disease (4 [8.7%]). One patient had chronic respiratory diseases.

Of all patients, 8 (17.4%) had severe disease, and 38 (82.6%) had non-severe disease. Patients in the severe group were, on average, older than those in the non-severe group (58.50 ± 12.48 VS 44.26 ± 10.63, P=0.002). More patients with severe disease had hypertension and coronary heart disease than those with non-severe disease (P=0.005,

0.013). The use of methylprednisolone in patients with severe disease was more common in patients with severe disease than in those with non-severe disease (*P*=0.000), and those with severe illness had higher serum C-reactive protein (CRP) peaks and neutrophil counts than those with non-severe disease. However, there were no significant difference in levels of white blood cells, hemoglobin, platelets, alanine aminotransferase (ALT), aspartate aminotransferase (AST), creatine kinase (CK), PaO_2/FiO_2 ratio, or length of hospitalization (Table 1).

2. Pulmonary function tests and high-resolution chest CT

Three months after hospital discharge, 37.8% of COVID-19 patients still had diffusion dysfunction, and 60.9% of their chest CTs had not completely returned to normal (Table2-2). One (2.2%), 2 (4.3%), and 17 (37.8%) patients had FEV1/FVC ratios and TLC and DLCO values less than 80% of predicted values, respectively. There was no significant difference in recovery of pulmonary function between the severe and non-severe group (Table 2-1, Table 2-2). On the contrary, there was a significant difference in recovery observed on chest CTs between the severe and non-severe group, and that of the non-severe group was better than that of the non-severe group [2.0 vs 5.5, *P*=0.004] (Table 2-1). Chest CT was more sensitive than the lung function test in reflecting the difference in pulmonary lesions between the severe and non-severe groups (Table 2-1, Fig.2-1). In addition, CT scans showed significant improvement in both groups, compared with the worst CT in the early phase (*P*<0.001) (Fig.2-2, Fig.2-3).

3.Pulmonary function tests and CTs in glucocorticoid and nonglucocorticoid groups

Nine patients (39.1%), 2 men (4.3%) and 7 women (15.2%), with an average age of 47.74 ± 12.12 years (range, 39 to 69 years) were treated with glucocorticoids, and that of the nonglucocorticoid group was 44.59 ± 11.39 years (*P*=0.013). In the glucocorticoid group, 6 patients (13.0%) had severe illness, and 2 (4.3%) had non-severe disease (*P*=0.000). There were no significant differences in PaO2/FiO2 ratio or lymphocyte or hemoglobin levels.

Through analysis of pulmonary function in the recovery period, we found that the diffusion function in the glucocorticoid group was worse than that in the nonglucocorticoid group (DLCO 68.61 ± 26.22 vs 83.39 ±12.37, *P*=0.016). The comparison of chest CT scores showed that basic pulmonary lesions in the glucocorticoid group were more severe than those in the nonglucocorticoid group (43.44 ±10.43 vs 22.96 ±11.75, *P*=0.000). Three months after discharge, pulmonary lesions in the glucocorticoid group were still more severe than those in the nonglucocorticoid group (CT score 43.44 ± 10.43 vs 22.96 ± 11.75, *P*=0.000) (Table 3).

Discussion

Since COVID-19 spread worldwide over the last year, its mechanism, clinical characteristics, prognosis, and effective treatment have been gradually elucidated through much hard work. Consistent with previous studies, the clinical symptoms of COVID-19 patients in our research were similar to those of those with influenza or severe acute respiratory syndrome (SARS) [10-11]. We found that, compared with patients with nonsevere COVID-19, those with severe COVID-19 were older and more likely to have high BMIs and CRP levels, as well as hypertension and cardiovascular disease. Age was a strong

risk factor for severe illness, complications, and death [10,12,13]. The case-fatality rate was higher for patients with comorbidities, at 10.5% in those with cardiovascular disease. People with hypertension may be at increased risk for severe COVID-19 and should continue to take their medications as prescribed [14]. High CRP levels may be associated with more severe illness [15].

Preliminary studies on imaging features of patients with COVID-19 found that bilateral, multifocal GGO and consolidation, predominantly in the subpleural and peri-bronchovascular regions, were typical features. Recent research and our data showed that more than half of the discharged patients had residual abnormalities on chest CT [16-17]. Small GGO, fiber cord shadow, and subpleural lines were still more intense in patients with severe versus non-severe disease 3 months after discharge. Meo et al reported that SARS and COVID-19 have similar biological and clinical characteristics [11]. Lung fibrosis was found at 3 and 6 months in recovering SARS patients in previous studies [18-19] and could be a long-term sequela of SARS-CoV-2 infection as well [20].

More concerns have been focused on the assessment of the pulmonary injury in discharged persons of COVID-19 . This study showed that in convalescence, about one-third of COVID-19 patients had pulmonary function impairments, the most common of which was impaired diffusing capacity. Research results indicated COVID-19 pneumonia has a characteristic of impaired diffusion pathways in the intra-alveolar space. Various types of viral pneumonia usually self-limited have a feature of diffuse alveolar damage, and imaging abnormalities usually disappear within three weeks in immunocompetent patients [21].

Autopsies of COVID-19 decedents showed different degrees of destruction in the alveolar structure and pulmonary interstitial fibrosis [22-23]. Pathological changes in the lungs can explain the impaired DLCO to an extent. Surprisingly, many patients' DLCO normalized but with residual imaging abnormalities. We think that mild lung lesions in convalescence (eg, fibrous cord shadow, subpleural line, small ground glass shadow) may not cause severe pulmonary diffusion disorder and would not cause the significant difference in pulmonary function between patients with severe versus non-severe illness. We will continue to perform long-term follow-up on these patients to observe DLCO impairment trends.

In this study, glucocorticoids were used more often in patients with severe COVID-19 than in those with non-severe illness. The recovery seen on chest CT in patients who received glucocorticoids was not as advanced as that in patients not given the drugs. As for the small sample size, we did not compare CT expression in patients with severe disease who received or did not receive glucocorticoids. Use of glucocorticoids in COVID-19 patients has been controversial. Some experts have said that glucocorticoids may prolong the duration of illness. However, many studies have shown that proper use of glucocorticoids can reduce the mortality rate [24]. In a meta-analysis of 7 trials with 1703 critically ill COVID-19 patients, glucocorticoids reduced 28-day mortality compared with standard care or placebo (32% vs. 40%; odds ratio 0.66; 95% confidence interval, 0.53 to 0.82) and were not associated with increased risk of severe adverse events [25].

The US Centers for Disease Control and Prevention recommend dexamethasone for severely ill COVID-19 patients on supplemental oxygen or ventilatory support. In this study,

recovery observed on CT in the glucocorticoid group was poor, but glucocorticoids were clearly beneficial, which may be related to the poor status of basic CT in patients with severe disease [26]. Though the lung function parameters were not different between the non-severe and severe groups, DLCO values in the glucocorticoid group were lower than those in the nonglucocorticoid group. Furthermore, the use of glucocorticoids, total methylprednisolone dosage, and length of treatment were negatively correlated with DLCO (data not shown).

There are some limitations in our study. First, it was a prospective study with a small sample size, which provides only a short follow-up of 3 months. The heterogeneity of our research conclusions was not comprehensive. Second, only 46 of 108 COVID-19 patients (42%) completed the serial assessments; therefore, the results might not be representative of the entire population. Last, because our research object was not drawn by random sampling, the calculation of seroprevalence was restricted to potential sampling bias.

Conclusions

Three months after hospital discharge, impaired diffusing capacity and lung imaging abnormalities were detected in more than one third of COVID-19 patients. Compared with patients with non-severe disease, those with severe illness had more lung imaging abnormalities. Longer follow-up studies in COVID-19 patients should be performed to investigate clinical outcomes after recovery.

Declarations

Ethics approval and consent to participate:The study protocol was approved by the ethics committee of Beijing Youan Hospital Research Ethics Committee (No. 2020-031).

Consent for publication: Not applicable.

Availability of data and materials: Not applicable.

Competing interests: The authors declare that they have no competing interests.

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Authors' contributions: B.S. and F.K.M conceived the idea, designed, and supervised the study, drafted the manuscript, had full access to all of the data, and took responsibility for the integrity of the data. J.Y.Z,X.M.Y,L.J.G, collected data. J.Y.Z, L.J.G,and X.Z.W. analyzed data and performed statistical analysis. X.M.Y, did much lung function analysis. J.Y.Z, and L.J.G did lots of chest CT assessment. All of the authors reviewed and approved the final version of the manuscript.

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Availability of Data and Materials: The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.

Reference

[1] Chen N, Zhou M, Dong X, Qu J, Gong F, Han Y, Qiu Y, Wang J, Liu Y, Wei Y, et al. Epidemiological and clinical characteristics of 99 cases of 2019 novel coronavirus pneumonia in Wuhan, China: a descriptive study. Lancet. 2020; 395(1)507-13.

[2] Huang C, Wang Y, Li X, Ren L, Zhao J, Hu Y, Zhang L, Fan G, Xu J, Gu X, et al. Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. Lancet. 2020;395(10223):497-506.

[3] Song F, Shi N, Shan F, Zhang Z, Shen J, Lu H, et al. Emerging coronavirus 2019-nCoV pneumonia. Radiology 2020:200274. https://doi.org/10.1148/radiol.2020200274.

[4] Kanne JP. Chest CT findings in 2019 novel coronavirus (2019-nCoV) infections from Wuhan, China: key points for the radiologist. Radiology 2020:200241. https://doi.org/10.1148/radiol.2020200241.

[5] Huang Y , Tan C , Wu J , et al. Impact of coronavirus disease 2019 on pulmonary function in early convalescence phase[J]. Respiratory research, 2020, 21(1).

[6] http://www.nhc.gov.cn/yzygj/s7653p/202003/46c9294a7dfe4cef80dc7f5912eb1989.shtml

[7] Nöbauer-Huhmann IM, Eibenberger K , Schaefer-Prokop C , et al. Changes in lung parenchyma after acute respiratory distress syndrome (ARDS): assessment with high-resolution computed tomography[J]. European Radiology, 2001, 11(12):2436-2443.

[8]Li R , Liu G , Huang X , et al. Dynamic changes in clinical and CT characteristics of COVID-19 cases with different exposure histories: A retrospective study[J]. BMC Infectious Diseases, 2020, 20(1).

[9] Li X Y , Sun B , Wang C T , et al. A follow-up study on acute respiratory distress syndrome survivors after extracorporeal membrane oxygenation by pulmonary high-resolution CT[J]. Archives of Iranian Medicine, 2015, 18(1):6.

[10] Guan WJ, Ni ZY, Hu Y, et al. Clinical Characteristics of Coronavirus Disease 2019 in China. N Engl J Med

2020; 382:1708-20.6.

[11] Meo SA, Alhowikan AM, Al-Khlaiwi T, Meo IM, Halepoto DM, Iqbal M,Usmani AM, Hajjar W, Ahmed N. Novel coronavirus 2019-nCoV: prevalence,biological and clinical characteristics comparison with SARS-CoV and MERSCoV. Eur Rev Med Pharmaco. 2020;24(4):2012.

[12] Wang D, Hu B, Hu C, et al. Clinical Characteristics of 138 Hospitalized Patients With 2019 Novel Coronavirus-Infected Pneumonia in Wuhan, China. JAMA 2020.8.

[13] To KK, Tsang OT, Leung WS, et al. Temporal profiles of viral load in posterior oropharyngeal saliva samples and serum antibody responses during infection by SARS-CoV-2: an observational cohort study. Lancet Infect Dis 2020.

[14] https://www.cdc.gov/coronavirus/2019-ncov/hcp/clinical-guidance-management-patients.html

[15] Wu Z, McGoogan JM. Characteristics of and Important Lessons from the Coronavirus Disease 2019 (COVID-19) Outbreak in China: Summary of a Report of 72314 Cases From the Chinese Center for Disease Control and Prevention. JAMA 2020.

[16] Li K, Fang Y, Li W, Pan C, Qin P, Zhong Y, Liu X, Huang M, Liao Y, Li S. CT image visual quantitative evaluation and clinical classification of coronavirus disease (COVID-19). Eur Radiol. 2020.

[17] Huang Y, Tan C, Wu J, et al. Impact of coronavirus disease 2019 on pulmonary function in early convalescence phase[J]. Respiratory research, 2020, 21(1).

[18] Antonio GE, Wong KT, Hui DS, et al. Thin-section CT in patients with severe acute respiratory syndrome following hospital discharge: preliminary experience. Radiology. 2003; 228:810-15. [PubMed] [Google Scholar].

[19] Muller NL, Ooi GC, Khong PL, et al. High-resolution CT findings of severe acute respiratory syndrome at presentation and after admission. Am J Roentgenol. 2004; 182:39-44. [PubMed] [Google Scholar].

[20] Wu X , Dong D , Ma D . Thin-Section Computed Tomography Manifestations During Convalescence and Long-Term Follow-Up of Patients with Severe Acute Respiratory Syndrome (SARS)[J]. Med, Monit, 2016, 22(12):2793-2799.

[21] Fraser RS, Muller NL, Colman NC, Pare PD. Diagnosis of diseases of the chest. Philadelphia: WB Saunders; 1999. [Google Scholar]

[22] Yao X, Li T, He Z, Ping Y, Liu H, Yu S, Mou H, Wang L, Zhang H, F u W, et al.A pathological report of three COVID-19 cases by minimally invasiveautopsies. medRxiv, https://doi.org/10.3760/cma.j.cn112151-20200312-00193.

[23] Xu Z, Shi L, Wang Y, Zhang J, Huang L, Zhang C, Liu S, Zhao P, Liu H, Zhu L, et al. Pathological findings of COVID-19 associated with acute respiratory distress syndrome. Lancet Respir Med. 2020;8(4):420-2.

[24] Horby P, Lim W S, Emberson J, et al. Effect of Dexamethasone in Hospitalized Patients with COVID-19: Preliminary Report[J]. New England Journal of Medicine, 2020.

[25] Sterne J A C, Murthy S, Diaz J V, et al. Association Between Administration of Systemic Corticosteroids and Mortality Among Critically Ill Patients With COVID-19: A Meta-analysis[J]. JAMA The Journal of the American Medical Association, 2020.

[26] https://www.covid19treatmentguidelines.nih.gov/therapeutic-management

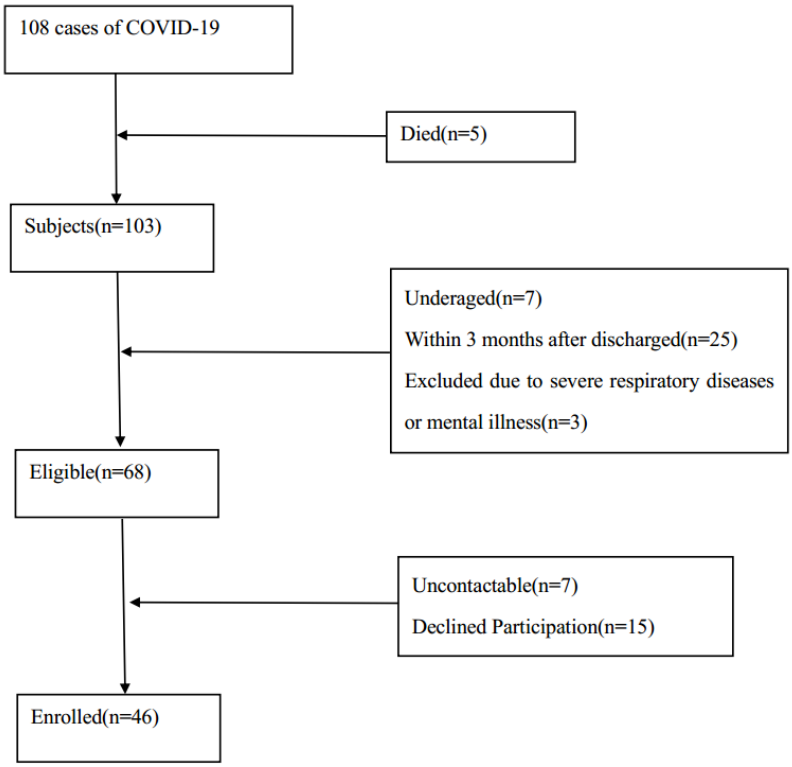

Fig.1 Enrollment of COVD-19 patients in convalescence

Table 1. General clinical characteristics of patients with COVID-19 at admission classified by disease severity.

	All patients（n=46）	Disease severity		χ^2/Z	p value
		Non-severe(n=38)	Severe(n=8)		
Males (%)	20（43.5%）	18（39.15%）	2(4.3%)	1.346	0.251
Age (years)	46.74 ± 12.12	44.26 ± 10.63	58.50 ± 12.48		0.002**
BMI（kg/m^2）	24.78 ± 2.93	24.13 ± 2.66	27.86 ± 2.13		0.001***
Respiratory symptoms (%)	35（76.1%）	27(58.7%)	8（17.4%）	3.044	0.084
Cough (%)	34（73.9%）	26（56.5%）	8（17.4%）	3.418	0.067
Nasal congestion (%)	2(4.3%)	1（2.2%）	1（2.2%）	1.177	0.278
Pharyngeal pain (%)	11(23.9%)	9(19.6%)	2(4.3%)	0.006	0.937
Shortness of breath (%)	19(41.3%)	12(26.1%)	7(15.2%)	8.945	0.003**
Coexisting disorders (%)					
Chronic respiratory disease (%)	1(2.2%)	1(2.2%)	0(0%)	0.387	0.534
Cardiovascular disease (%)	4(8.7%)	1(2.2%)	3(6.5%)	10.120	0.013*
Hypertension (%)	6(13.0%)	2(4.3%)	4(8.7%)	11.661	0.005**
Diabetes (%)	5(10.9%)	4(8.7%)	1(2.2%)	0.026	0.873
Smoking history (%)	3(6.5%)	3(6.5%)	0(0%)	1.190	0.275
Glucocorticoids use (%)	9(19.6%)	3(6.5%)	6(13.0%)	18.910	0.000***

Total methyprednisolone dosage（mg）	290.61(229.68, 366.03)	440.0(280.0, 560.6)	350.0(235.0, 420.0)	-1.005	0.315
Antiviral therapy (%)	18(39.1%)	15(32.6%)	3(6.5%)	2.314	0.510
Lopinaviritonavir(%)	6(13.0%)	4(8.7%)	2(4.3%)		
Chloroquine (%)	9(19.6%)	8(17.4%)	1(2.2%)		
Arbidol(%)	3(6.5%)	3(6.5%)	0(0%)		
Chinese medicinal therapy (%)	41(89.1%)	34(73.9%)	7(15.2%)	0.026	0.873
LOS (days)	17.65±8.04	17.82±8.98	16.88±5.17		0.777
White blood cells (x10^9/L)	4.71±1.55	4.49±1.32	5.74±2.15		0.152
Neutrophils (x10^9/L)	2.42(2.03,3.45)	2.26(1.98,3.33)	3.85(2.50,5.43)	-2.108	0.035*
Lymphocytes (x10^9/L)	1.25±0.46	1.30±0.47	1.06±0.43		0.202
Hemoglobin（g/L）	135.64±15.86	137.30±14.02	128.00±22.14		0.134
Platelet (x10^9/L)	220.78±97.24	207.54±60.70	282.00±187.83		0.303
ALT(U/L)	30.0(19.25,45.75)	33.50(20.0,46.75)	23.0(17.0,44.0)	-0.930	0.352
AST(U/L)	28.0(19.5,40.0)	39.03±36.88	23.0(17.0,41.0)	-0.092	0.926
CK(U/L)	63．0（44.5,106.5）	63.0（45,113）	60.0(41.5,107.0）	-0.258	0.796
eGFR (ml/min/1.73m^2)	100.77±22.90	103.25±23.16	91.76±20.82		0.214
C-reactive Protein (mg/L)	27.32±33.97	22.19±29.38	50.40±45.03		0.032*

PaO2 to FiO2 ratio(mmHg)	290.61(229.68, 366.03)	299.33(243.0, 440.48)	257.67(191.90, 341.05)	-1.005	0.315

LOS:length of hospitalization;Data are expressed as mean ± standard deviation (x±s) , medians (Q1,Q3) or percentage; *Statistically significant.

Table 2-1 Results of pulmonary function tests and high-resolution chest CT tests among COVID-19 patients

Parameter	**All patients (n=46)**	**Disease severity**		**p value**
		Non-severe(n=38)	Severe(n=8)	
Pulmonary function				
VC (% of predicted)	104.92±9.56	104.39±9.79	107.44±8.48	0.418
FVC (% of predicted)	108.12±9.92	107.56±10.12	110.78±9.03	0.411
FEV1 (% of predicted)	103.87±9.39	102.85±9.61	108.73±6.74	0.108
FEV1/FVC (%)	96.32±6.74	96.03±6.91	97.69±6.12	0.510
TLC (% of predicted)	97.60±9.95	98.61±10.02	92.79±8.58	0.134
RV (% of predicted)	90.05±23.14	92.48±23.43	78.46±18.87	0.120
DLCO (% of predicted)	80.50±16.72	82.37±12.30	71.59±29.80	0.098
DLCO/VA	86.21±17.01	87.47±10.85	80.25±34.49	0.576
MFEF25%	70.66±25.72	69.26±25.31	77.33±28.39	0.426

MFEF75%	108.95±19.81	108.91±20.93	109.15±14.40	0.976
MFEF50%	92.48±22.79	90.07±21.68	103.93±25.96	0.119
R5(% of predicted)	87.60±23.87	86.87±20.69	91.09±37.21	0.764
R20(% of predicted)	93.16±22.33	94.61±21.50	86.29±26.40	0.344
R35(% of predicted)	143.65±39.01	146.55±37.41	129.86±46.08	0.276
Z5 (% of predicted)	91.70±24.59	90.93±21.09	95.35±38.96	0.763
X5 (% of predicted)	194.0(38.30,423.28)	221.40(-278.20, 680.10)	144.80(75.03, 220.55)	0.528 (Z=-0.985)
Chest CT				
The worst CT score	28.08±14.43	23.11±11.33	45.50±10.03	0.000***
Recovery CT score	2.0（0，3.0）	2.0（2.0，5.0）	5.50（2.25，10.0）	0.008** (Z=-2.646)

Values are shown as mean ± standard deviation (x±s) , medians (Q1,Q3) or percentage, severe vs non-severe with p values;

*Statistically significant.

Table 2-2 The abnormal rate of pulmonary function parameters and chest CT imaging between severe cases and mild cases

Parameter	**All patients**	**Disease severity**		**χ^2 /Z**	**p value**
Pulmonary Function	**(n=46)**	**Non-severe (n=38)**	**Severe (n=8)**		
FEV1 < 80% of pred	0(0%)	0(0%)	0(0%)		
FEV1 ≥ 80% of pred	46(100%)	38(82.6%)	8(17.4%)		
FVC < 80% of pred	0(0%)	0(0%)	0(0%)		
FVC ≥ 80% of pred	46(100%)	38(82.6%)	8(17.4%)		
FEV1 / FVC < 80%	1(2.2%)	1(2.2%)	0(0%)	0.387	0.534
FEV1 / FVC ≥ 80%	45(97.8%)	37(80.4%)	8(17.4%)		
TLC < 80% of pred	2(4.3%)	1(2.2%)	1(2.2%)	1.177	0.278
TLC ≥ 80% of pred	44(95.7%)	37(80.4%)	7(15.2%)		
DLCO < 80% of pred	17(37.8%)	15(33.3%)	2(4.4%)	0.011	0.917
DLCO ≥ 80% of pred	28(62.2%)	23(51.1%)	5(11.1%)		
DLCO/VA< 80% of pred	14(31.1%)	13(28.9%)	1(2.2%)	1.233	0.267
DLCO/VA≥ 80% of pred	31(68.9%)	25(55.6%)	6(13.3%)		
Chest CT					

CT score=0	18（39.1%）	17（37.0%）	1（22.2%）	3.292	0.070
CT score>0	28（60.9%）	21（45.7%）	7（15.2%）		

pred predicted; *Statistically significant;

In pulmonary function test, the DLCO parameters of one case was not generated, which was missing data.

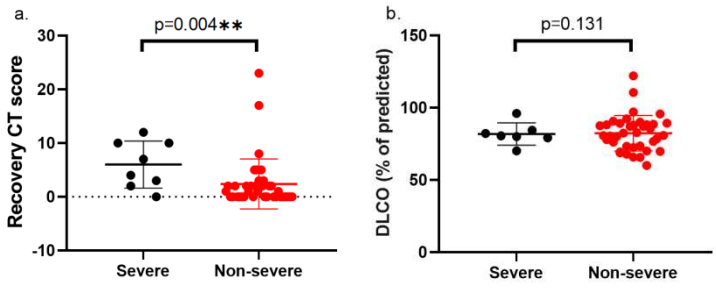

Fig.2-1 In convalescence phase of 3 months after discharge, 46 COVID-19 patients completed chest CT scan, including 8 patients in severe group and 38 patients in non-severe group (a). Among them, 45 patients completed pulmonary function DLCO examination, including 7 patients in severe group and 38 patients in non-severe group (b).

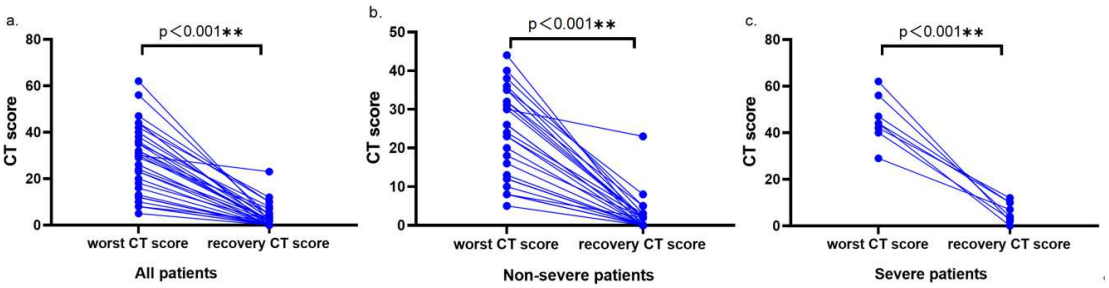

Fig.2-2 Dynamic changes in lung involvement CT scores in 46 COVID-19 patients between the worst CT imagine during hospitalization and the recovery CT imagine after 3 months after discharge (a), including 38 non-severe patients and 8 severe patients (b, c).

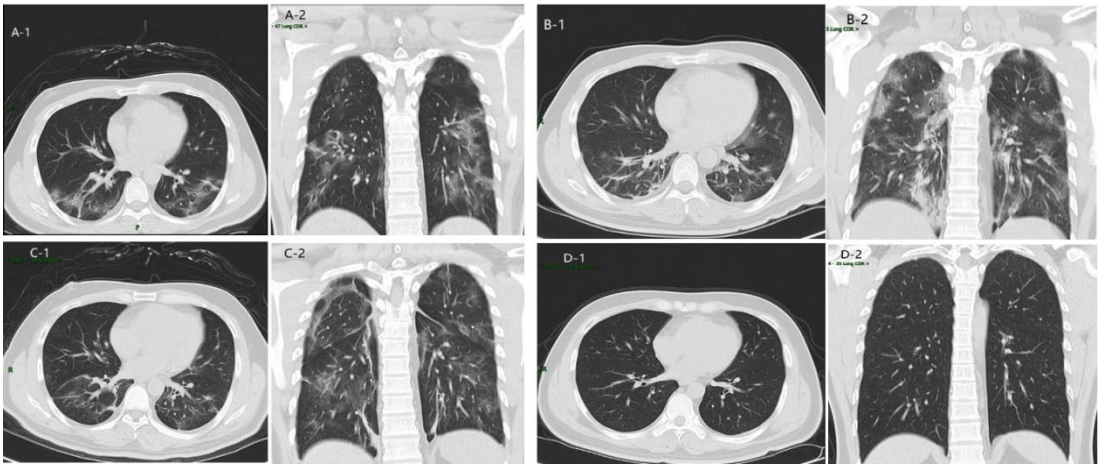

Fig. 2-3 A. HRCT scan of a 37-year-old man demonstrated bilateral peripheral ground-glass opacities (GGO) on admission. The CT score was 30. B. Worst CT scan of the same patient five days later showed diffuse GGO and consolidation. The CT score was 42.C. CT scan of the same patient nine days later showed less GGO on discharge. The CT score was 32. D. Follow-up CT of the same patient at three months after discharge from hospital showed that patchy GGO had obvious absorption. The CT score was 2.

Table 3. Results of pulmonary function tests and chest CT among COVID-19 patients between the glucocorticoid group and the non-glucocorticoid group.

Parameter	All patients(n=46)	Glucocorticoid used		p value
		Glucocorticoid (n=9)	**Non-glucocorticoid (n=37)**	
Males	20(43.5%)	2(4.3%)	18(39.1)	0.289
Age (years)	47.74±12.12	55.56±11.57	44.59±11.39	0.013*
Severe patients	8（17.4%）	6（13.0%）	2（4.3%）	0.000***
PaO_2 to FiO_2 ratio(mmHg)	290.61(229.68, 366.03)	257.67（191.90，338.75）	299.33（243.0，440.48）	0.228 （Z=-1.206）
Lymphocytes (x10^9/L)	1.86±0.67	1.54±1.03	1.94±0.55	0.296
Hemoglobin（g/L）	134.54±39.04	111.22±63.98	140.22±28.75	0.218
Pulmonary Function				
VC (% of predicted)	104.92±9.56	105.53±8.48	104.77±9.90	0.833
FVC (% of predicted)	108.12±9.92	108.81±8.94	107.95±10.25	0.819
FEV1 (% of predicted)	103.87±9.39	107.23±5.47	103.05±10.00	0.235
FEV1/FVC(%)	96.32±6.74	98.84±7.13	95.70±6.60	0.214
TLC (% of predicted)	97.60±9.95	96.30±6.63	97.91±10.65	0.668
RV (% of predicted)	90.05±23.14	89.03±22.35	90.29±23.63	0.886

DLCO (% of predicted)	80.50±16.72	68.61±26.22	83.39±12.37	0.016*
DLCO/VA	86.21±17.01	76.21±30.39	88.65±11.20	0.260
MFEF25%	70.66±25.72	80.24±35.33	68.33±22.83	0.216
MFEF75%	108.95±19.81	110.21±17.55	108.65±20.54	0.835
MFEF50%	92.48±22.79	104.48±25.19	89.56±21.53	0.078
R5(% of predicted)	87.60±23.87	91.72±34.76	86.60±20.94	0.681
R20(% of predicted)	93.16±22.33	89.57±24.45	94.04±22.06	0.596
R35(% of predicted)	143.65±39.01	133.88±43.29	146.02±38.17	0.408
Z5 (% of predicted)	91.70±24.59	94.99±35.92	90.89±21.58	0.659
X5 (% of predicted)	194.0(38.3, 423.28)	128.10（88.10，204.70）	227.80（-280.50，711.70）	0.251（Z=-1.149）
Chest CT				
The worst CT score	28.08±14.43	43.44±10.43	22.96±11.75	0.000***
Recovery CT score	2.0（2.0,3.25）	5.0（2.50,11.0）	1.0（0,2.0）	0.003** 8（Z=-2.988）
CT score variation	25.06±13.41	36.33±15.26	21.30±10.56	0.002**

Values are shown as mean ± standard deviation (x±s) , medians (Q1,Q3) or percentage, severe vs non-severe with p values;

* Statistically significant

Figures

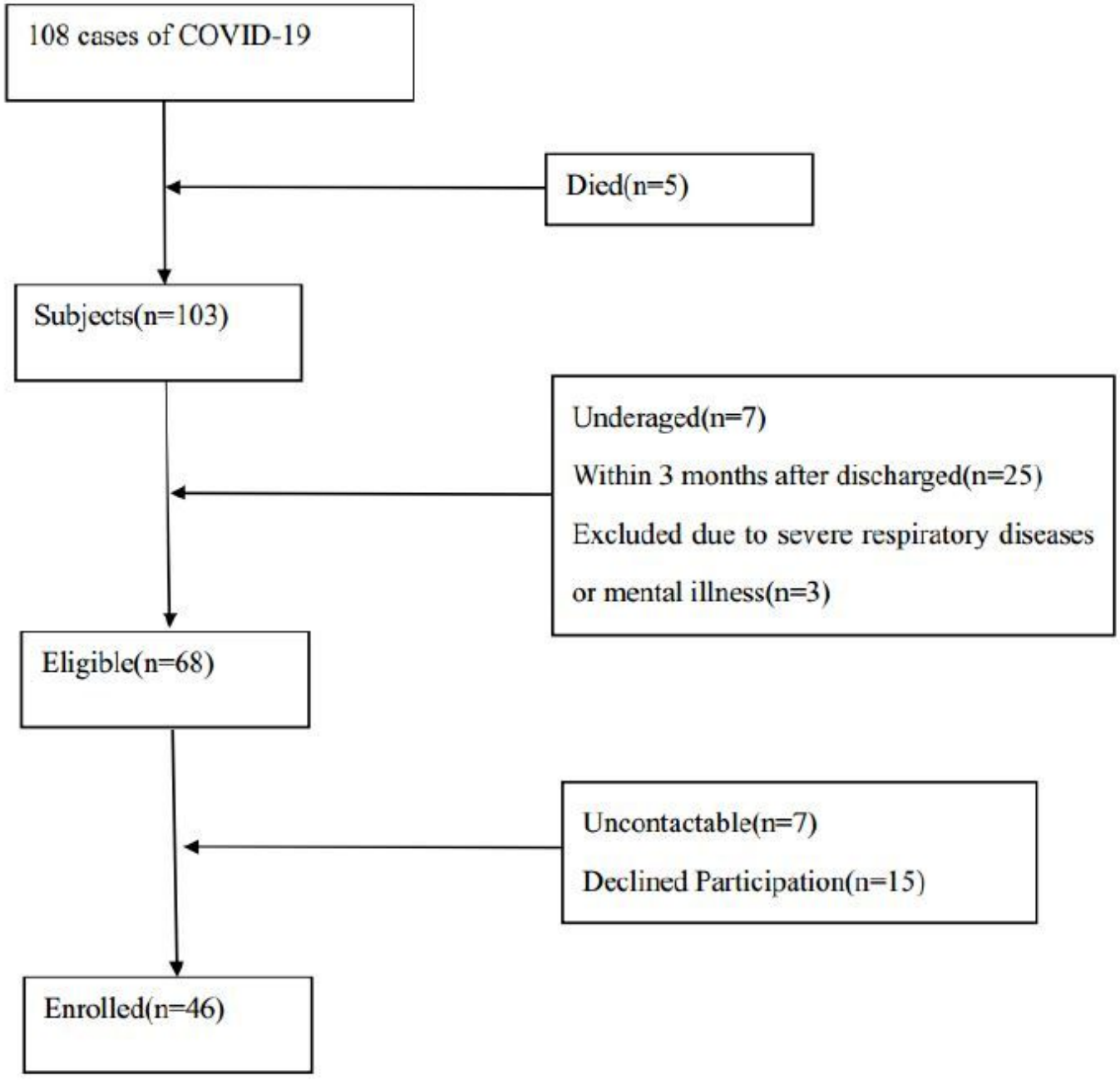

Figure 1

Enrollment of COVID-19 patients in convalescence

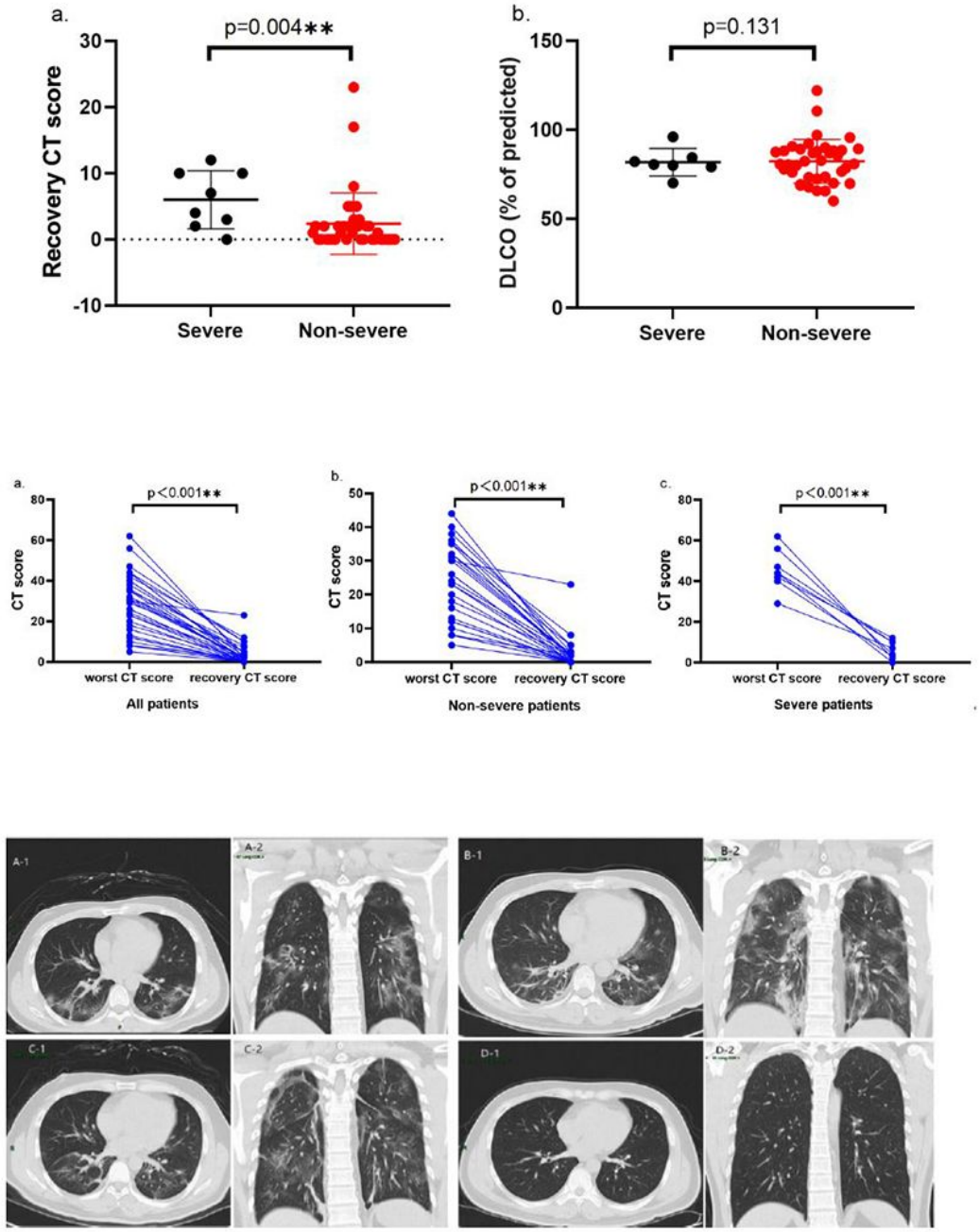

Figure 2

Fig.2-1 In convalescence phase of 3 months after discharge, 46 COVID-19 patients completed chest CT scan, including 8 patients in severe group and 38 patients in non-severe group (a). Among them, 45 patients completed pulmonary function DLCO examination, including 7 patients in severe group and 38 patients in non-severe group (b). Fig.2-2 Dynamic changes in lung involvement CT scores in 46 COVID-19 patients between the worst CT imagine during hospitalization and the recovery CT imagine after 3

months after discharge (a), including 38 non-severe patients and 8 severe patients (b, c). Fig. 2-3 A. HRCT scan of a 37-year-old man demonstrated bilateral peripheral ground-glass opacities (GGO) on admission. The CT score was 30. B. Worst CT scan of the same patient five days later showed diffuse GGO and consolidation. The CT score was 42.C. CT scan of the same patient nine days later showed less GGO on discharge. The CT score was 32. D. Follow-up CT of the same patient at three months after discharge from hospital showed that patchy GGO had obvious absorption. The CT score was 2.