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Three-month outcomes of recovered COVID-19 patients: prospective observational study

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Abstract

Aims: A novel coronavirus SARS-CoV-2 has resulted in an ongoing global pandemic of Coronavirus disease 2019 (COVID-19). However, the outcomes of recovered patients have not been well defined.

Methods: This is a prospective observational follow-up study of survivors with COVID-19 from a designated tertiary center in Hefei, China. We examined chest computed tomography (CT) scanning, pulmonary function, 6-min walk distance (6MWD), and 36 item Short Form General Health Survey (SF-36).

Results: Among 81 enrolled patients, 62 (77%) patients and 61 (75%) patients, respectively, completed 1-month and 3-month follow-ups. Abnormal CT findings were still present in 73% of patients at 1 month and 54% at 3 months, whereas chest CT scan scores improved progressively at 1-month (5.0 ± 5.1) and 3-month follow up (3.0 ± 4.5) compared with that during hospitalization (11 ± 6.8). Mild restrictive pulmonary impairment was detected in 11% and 10% of patients at 1-month and 3-month follow up, respectively. The 6MWD was 523 ± 77 m in male patients and 484 ± 58 m in female patients, which was significantly lower than in healthy controls (606 ± 68 m, 568 ± 78 m, $p < 0.001$). SF-36 scores were significantly impaired in the domains of role physical (RP), role emotional (RE), and social functioning (SF) compared with the normal age-matched population. RP was improved at 3-month compared with 1-month follow up in the 41–64 years group ($p < 0.01$). Multivariable analysis showed that older age (over 40 years) and steroid administration during hospitalization were independently associated with worse chest CT scores at 3-month follow up.

Conclusions: At 3 months, chest CT abnormalities were present in one half of COVID-19 survivors and worse chest CT scores were independently associated with older age and steroid administration during hospitalization. Residual pulmonary function impairments were modest, whereas exercise capacity and SF-36 scores were significantly lower than the general population. Support program and further follow-up evaluations may be needed.

The reviews of this paper are available via the supplemental material section.

Keywords: Coronavirus disease 2019, functional capacity, lung function, SARS-CoV-2

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Introduction

In December 2019, an outbreak of an unknown pneumonia occurred in Wuhan and spread rapidly to other parts of China and the world. Later, it was named Coronavirus disease 2019 (COVID-19) and resulted in a global pandemic.[1,2] Typical clinical manifestations of this illness include fever, cough, dyspnea with rapid progression and ground-glass opacities (GGO) or consolidation on chest imaging.[3] Severe cases can present as acute respiratory distress syndrome (ARDS), and sudden death. As of 30 August 2020, COVID-19 has affected more than 25,000,000 patients globally, causing 840,000 deaths over a period of

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8 months since the initial recognition of this disease.[4]

Much of what has been learned about COVID-19, including its epidemiological, clinical features, and treatments, has been derived from studies focused on the acute phase of this illness. As the number of recovered patients gradually increases, there is a growing need to understand evolving aspects of clinical, radiological, and psychological outcomes of these survivors. Such post-illness outcome studies pertaining to another coronavirus-associated infection, Severe Acute Respiratory Syndrome (SARS), have demonstrated varying degrees of radiological, functional, and psychological abnormalities in the recovery phase.[5] A recent report showed most patients with COVID-19 pneumonia manifested residual abnormalities on chest computed tomography (CT) scans at the time of discharge, with ground-glass opacity as the most common abnormality. The occurrence of sequelae is unpredictable, and a careful assessment of clinical and radiological, pulmonary function, exercise capacity, and health-related quality of life (HRQoL) outcomes is therefore important for patients with COVID-19 after discharge. However, little information is available regarding recovered patients.[6–8]

In the current study, we conducted a prospective observational study to characterize the outcomes of patients with COVID-19 at 1 and 3 months after discharge from a tertiary designated hospital in Hefei, China. We evaluated clinical features, blood tests, chest CT, pulmonary function, exercise capacity, and the 36-item Short Form General Health Survey (SF-36).

Methods

Subjects

The initial study cohort comprised 84 patients discharged from The First Affiliated Hospital of University of Science and Technology of China between 22 January and 7 March 2020. Three patients were excluded due to age criteria including a 4-year-old child and two elderly men above 85 years of age.

The confirmed cases of COVID-19 were defined as patients who tested positive by real-time reverse-transcription polymerase chain reaction (RT-PCR) assay on pharyngeal or sputum specimens. According to the Chinese guidance,[9] disease severity was categorized as mild illness (mild symptoms without radiographic findings of pneumonia), pneumonia (presence of symptoms and radiographic evidence of pneumonia, with no requirement for supplemental oxygen), severe pneumonia (evidence of pneumonia with one of the following features: respiratory rate >30 breaths/min; severe respiratory distress; or $SpO2 \leqslant 93\%$ on room air at rest), and critical illness [e.g., respiratory failure requiring mechanical ventilation, septic shock, other organ failure, or admission into the intensive care unit (ICU)]. The criteria for discharge from the hospital included: (1) substantial improvement of respiratory symptoms (e.g., cough, chest discomfort and shortness of breath); (2) maintenance of normal body temperature for $\geqslant 3$ days without the use of steroids or antipyretics; (3) improvement in radiological abnormalities on chest CT or X-ray; (4) two consecutively negative RT-PCR test results separated by at least 24 h. Follow-up evaluations were performed on 62 patients at 1-month and 61 patients at 3-month follow up (number of studied patients at follow up was affected by their adherence and condition) (Figure 1). One patient who died had been on mechanical ventilation due to a severe stroke.

The Ethics Committee of The First Affiliation Hospital of University of Science and Technology (Anhui Provincial Hospital) approved the collection of clinical data from the included patients with COVID-19 infections [No.2020-XG (H)-007]. Written informed consent was obtained from all patients.

Assessment

All patients underwent blood examination, SARS-CoV-2 RT-PCR test, chest CT, and pulmonary function tests (PFTs) on follow up visits. We also performed 6-min walk test (6MWT) according to the American Thoracic Society (ATS) guideline.[10] Data were obtained from electronic medical records using standardized data collection forms shared by the International Severe Acute Respiratory and Emerging Infection Consortium. Extracted information included demographic data, medical history, underlying comorbidities, symptoms, laboratory findings, chest CT scanning, and treatment measures (i.e., antiviral therapy, steroid therapy, respiratory support). The data from chest CT scans, coronavirus nucleic acid results, and pulmonary function tests at 1 month and 3 months after discharge were collected. A special follow-up team including physicians (XH, JC, and XC) and several experienced nurses conducted multiple telephone interviews with each patient.

Chest CT scoring. Chest CT findings were assessed using a scoring method similar to the one previously described.[11] In general, each lung was divided into three zones (upper, middle, and lower); each zone was evaluated for percentage of lung involvement on a scale of 0–4. Overall CT score was the summation of scores from all six lung zones. All CT scores were assessed blindly by a chest radiologist with 20 years' experience (WW) according to the published method.[11] The radiologist was blinded to the clinical information.

PFT and 6MWT. PFTs and 6MWTs were performed according to the ATS guidelines and supervised by a designated physician. All PFTs were performed by the same physician at our follow-up clinic. The forced vital capacity (FVC), forced expiratory volume in 1 s (FEV_1), and maximum voluntary ventilation (MVV) were measured using the Spirolab III electronic spirometer manufactured by Medical International Research (MIR), Rome, Italy. The 6-min walk distances (6MWDs) were compared with normative reference data collected from a population survey of 106 normal healthy volunteers at our center. All 6MWTs were supervised by an experienced physician (QL).

SF-36. The SF-36 includes eight multiple-item domains that assess physical functioning (PF), social functioning (SF), role limitations due to physical problems (role physical [RP]), role limitations due to emotional problem (role emotional [RE]), mental health (MH), bodily pain (BP), vitality (VT), and general health (GH). Scores for each aspect can range from 0 (worst) to 100 (best) with higher scores indicating better HRQoL. The Chinese version of the SF-36 was scanned by smart-phone to complete this survey online, and the results were compared with the normative data collected from an online survey on 243 Chinese adults. Based on that survey, SF-36 domain scores stratified into two age groups (16–40 years and 41–80 years) were available for comparison with those of our patients with COVID-19.

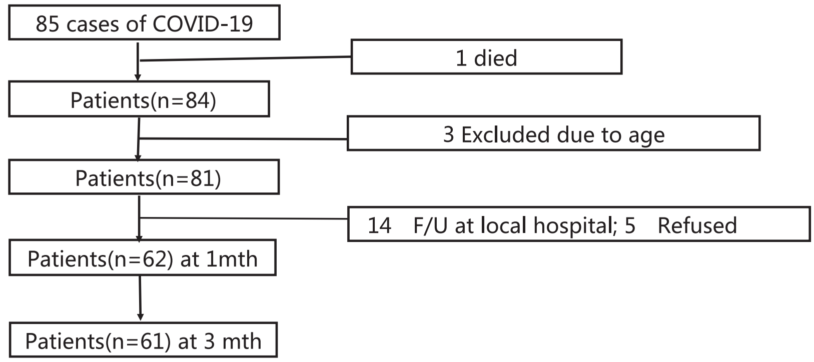

Figure 1. Flow chart of 3-month outcome of discharged patients with COVID-19.
COVID-19, coronavirus disease 2019; F/U, follow up; mth, month.

Statistical analysis

All data were expressed as mean ± SD unless otherwise indicated. Comparisons between groups were performed with unpaired *t* tests for normally distributed continuous variables and Mann–Whitney *U* tests for non-normally distributed continuous variables and Mantel–Haenszel test for categorical variables. Multiple comparisons were done by one-way analysis of variance (ANOVA). Univariate analyses and multivariate analyses were performed to explore the potential correlates of CT scores. With each statistical test, the level used to determine the significance was considered at a p value <0.05.

Results

Among 81 patients, 5 had mild illness, 50 had pneumonia, 23 had severe pneumonia, and 3 had critical illness. The mean length of hospital stay and clinical characteristics for these subgroups at 1- and 3-month follow up are presented in Table 1. Only one patient received mechanical ventilation and died of a severe cerebrovascular accident on hospital day 2; 11 patients had been admitted to the ICU. Oxygen therapy was required in 54 patients, 10 of whom received high-flow nasal cannula oxygen therapy (HFNC). At 1-month follow up, the mean age of 62 patients (77%) was 43.1 years and 35 were male. Demographic details and comorbidities are shown in Table 2. Six patients (10%) were identified to have reactivated infection as evidenced by recurrence of positive RT-PCR test from 2 weeks to 2 months after hospital discharge. At 3-month follow up, 61 patients (75%) were finally enrolled in the study analysis and 1 patient was found to have recurrent of

Table 1. Clinical characteristics of patients with COVID-19 at baseline, 1 month, and 3 months follow up in different severity stages.

Phase	Characteristic	Mild illness	Pneumonia	Severe pneumonia	Critical illness
Base line	Case number	5	50	23	3
	Hospital stay (days, mean ± SD)	20.8 ± 7.7	18.1 ± 6.6	15.0 ± 5.6	14.3 ± 1.5
	Chest CT scores (mean ± SD)	0	9.4 ± 5.4	16.6 ± 4.3	22 ± 2.6
1 month follow up	Case number	4	44	13	1
	Chest CT scores (mean ± SD)	0	3.9 ± 4.1	9.5 ± 5.5	15
	6MWD (m)	541 ± 42.8	509 ± 68.8	476 ± 78.5	480
	PFT abnormal number	1	5	1	0
	SF-36 scores	707 ± 78.5	578 ± 171.6	532 ± 215.8	624
3 month follow up	Case number	4	40	16	1
	Chest CT scores (mean ± SD)	0	2 ± 2.5	6 ± 5.6	7
	6MWD (m)	580 ± 26.9	552 ± 54.7	520 ± 66.5	508
	PFT abnormal number	0	3	1	1
	SF-36 scores	707 ± 78.5	581 ± 134.8	436 ± 159.7	365

COVID-19, coronavirus disease 2019; CT, computed tomography; 6MWT, 6-min walk test; PFT, pulmonary function test; SD, standard deviation; SF-36, 36-item short form general health survey.

positive RT-PCR test on day 100 after hospital discharge. At 1 month, 27 (44%) patients had symptoms of cough in 8 (13%), dyspnea in 13 (21%), and fatigue in 7 (11%). At 3 months, 23 (38%) patients had symptoms including cough in 9 (15%), dyspnea in 11 (18%), fatigue in 5 (8%).

Chest CT study

At 1 month, CT findings included bilateral patchy areas of GGO alone in 10 patients (16%), accompanied by septal thickening in 26 patients (42%), or associated with superimposed areas of fibrosis in 6 patients (10%); 19 patients (31%) manifested no relevant intrathoracic abnormalities. At 3 months, CT findings included bilateral patchy areas of GGO alone in 9 patients (15%), accompanied by septal thickening in 20 patients (34%), or associated with superimposed areas of fibrosis in 3 patients (5%); 29 patients (46%) had no relevant intrathoracic findings. The mean CT scores for disease severity subgroups at baseline, 1 month, and 3-month follow-up visits are shown in Table 1. Chest CT scores were significantly and progressively improved at 3 months (3.0 ± 4.5) *versus* at 1 month (5.0 ± 5.1, $p < 0.01$) both compared with the in-hospital study (11 ± 6.8, $p < 0.01$) as shown in Figure 2. Only old age ($p = 0.024$, OR 20.85, 95% CI 1.51–288.74) and the use of steroids during hospitalization ($p = 0.013$, OR 28.27, 95% CI 2.05–390.05) were found to be independent factors associated with high CT score at 3 months (Tables 3 and 4).

6MWD and PFT

The mean 6MWD was reduced significantly at 1 month when compared with normal subjects, and partly improved at 3 months (Table 5). Overall, the mean 6MWD at 1-month was 495 m [standard deviation (SD) 84 m] in male patients older than 40 years, and 544 m (SD 56 m) in male patients aged 40 years and younger. In female patients, the 6MWD was 448 m (SD 92 m) in those older than 40 years and 513 m (SD 59 m) in the 40 years and younger population. These values were significantly lower compared with those of healthy comparison groups (569 ± 69 m, 645 ± 40 m, 537 ± 74 m, 611 ± 61 m, respectively; $p < 0.01$). At 3-month follow up, the 6MWD of both male and female patients who were below

Table 2. Clinical characteristics of patients with COVID-19 at baseline, 1 month, and 3 months follow up.

Characteristic	Baseline (*n* = 81)	1 month (*n* = 62)	3 months (*n* = 61)	F/X^2	*p*
Age-years, mean (±SD)	45 (15)	43.1 (15.5)	43.5 (15.9)	0.495	0.610
Male, *n* (%)	47 (58)	35 (56)	33 (54)	0.435	0.804
Current smoking history, *n* (%)	9 (11)	7 (11)	8 (13)	0.207	0.902
Comorbidities, *n* (%)	30 (37)	23 (37)	25 (41)	1.224	0.542
Severe/critical patients, *n* (%)	27 (33.3)	14 (23)	17 (28)	1.618	0.445
Oxygen therapy, *n* (%)	42 (51.9)	28 (45)	29 (47)	0.540	0.763
Steroid treatment, *n* (%)	32 (39.5)	24 (39)	25 (41)	0.073	0.964
White blood cells (<4 × 109/l), *n* (%)	18 (22.2)	14 (23)	16 (26)	0.476	0.788
Lymphocytes (<1.1 × 109/l), *n* (%)	44 (54.3)	35 (56)	32 (52)	0.214	0.899

COVID-19, coronavirus disease 2019; SD, standard deviation.

40 years old was still significantly lower than that of healthy comparison groups (578 ± 46 m, 563 ± 47 m, $p < 0.05$). At 3 months, the 6MWD of female patients older than 40 years was improved compared with that at 1 month. The mean 6MWD (m) in the respective disease severity subgroups at 1- and 3-month follow up are shown in Table 1.

Overall, pulmonary function parameters were well recovered at 1-month follow up except for one patient who was unable to adequately perform the test due to chest discomfort. At 3-month follow up, one patient was unable to adequately perform PFT because of tooth loss, another patient manifested worse PFT resulting from a 10-kg weight gain over a 2-month interval. At 1 month, seven patients (11%) manifested abnormal pulmonary function; the frequency of discharged patients with lung function parameters <80% of predicted values were as follows: FEV_1 [5 (8%)], FVC [7 (11%)], MVV [4 (6%)]. At 3-month follow up, the pulmonary function results were abnormal in six patients (10%) and included: FEV_1 [5 (8%)], FVC [6 (10%)], MVV [2 (3%)]. The number of patients who manifested abnormal pulmonary function in the different disease severity subgroups at 1- and 3-month follow up is presented in Table 1.

SF-36

SF-36 scores at both 1 and 3 months were significantly impaired in domains of RP and SF compared with normal age-matched subjects, and that of additional RE in 41–64 years group ($p < 0.01$). The domain of PF in the 18- to 40-year-old group was impaired compared with normal subjects ($p < 0.01$). Domains of BP and MH were significantly impaired in the 41–64 year-old group, and domain of RE in the 18–64 year-old group compared with normal age-matched subjects ($p < 0.05$). Although some physical and social functioning domains were below the control value, scores for the GH domain were not changed significantly (Figure 3). The total SF-36 scores in the different disease severity subgroups at 1- and 3-month follow up are shown in Table 1. At 3-month follow up, domains of PF and RE in the 18–40 year-old group and domains of BP, RE, and MH in the 40–64 year-old group were not significantly impaired compared with normal subjects compared with 1-month follow up. Domain of RP was improved significantly compared with that of 1-month follow up in the elder group ($p < 0.01$).

Discussion

To the best of our knowledge, this is the first prospective study to explore 3-month outcomes in recovered patients with COVID-19. This cohort study has shown that chest CT abnormalities were still present in one half of COVID-19 survivors at 3 months and worse chest CT scores were independently associated with older age and steroid administration during hospitalization. Impaired

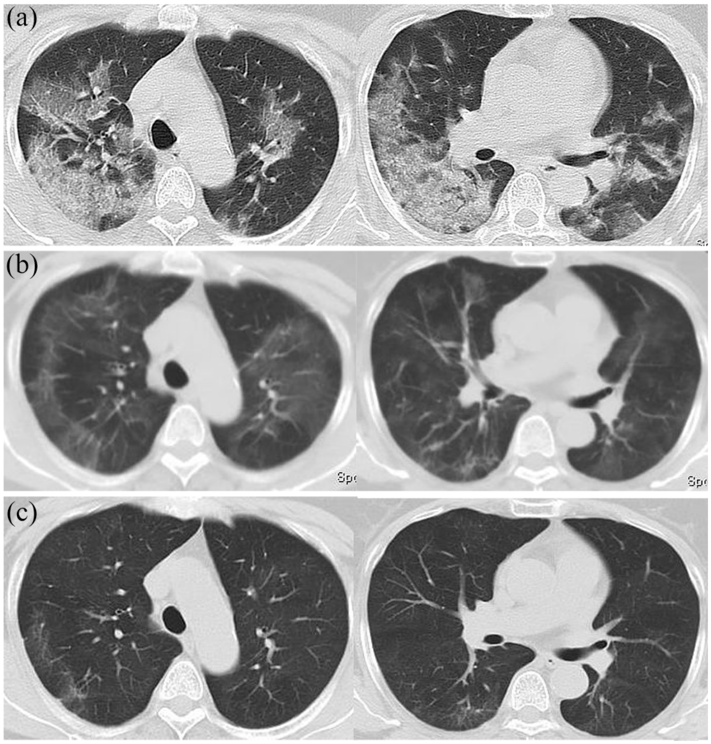

Figure 2. Chest CT images of patient with COVID-19 in hospital and 1 and 3 months after discharge. (a) CT image on day 6 after symptom onset showing worsening of bilateral GGOs with mixed linear opacities. (b) CT images showing improvement in bilateral GGOs at 4 weeks follow up. (c) CT images showing the near-complete resolution of bilateral GGOs at 3-month follow up after discharge.
CT, computed tomography; COVID-19, coronavirus disease 2019; GGO, ground-glass opacity.

pulmonary function was found in about 10% of recovered patients, while 6MWD and SF-36 were significantly worse compared with those of healthy age-matched control subjects at 3 months.

The importance of chest CT for the diagnosis of COVID-19 infection at early stage and assessment the treatment effects has been demonstrated.[12,13] The sequelae of this emerging viral pneumonia at recovery stage are limited.[8,14–16] Liu et al. found that lung damage due to COVID-19 could be reversible for most patients at 1 month.[17] In our study, abnormal CT findings were still present in 54% of survivors at 3-months follow up. However, most patients manifested progressively improved CT scores at 3 months. These are similar to the results reported by Liu and colleagues from Wenzhou, China.[17]

The lung damage in COVID-19 is reported to be associated with a cytokine storm induced by SARS-CoV-2, which has similarities to SARS-CoV.[18–20] Wang *et al.* investigated 12 recovered patients with SARS in Taiwan, over 80% of them manifested high-resolution CT (HRCT) abnormalities at 60 days after discharge.[21] Moreover, the higher HRCT scores correlated with increased cellularity of bronchoalveolar lavage fluid (BALF).[21] Thus, persistence of lung inflammation during the early recovery period may be associated with the delayed resolution of SARS. As several SARS studies have reported, radiologic abnormalities are rather common among survivors, and were observed in about 80% and 30% of patients at 3-months and 1-year follow up, respectively.[22,23] Compared with SARS, COVID-19 appears to be associated with a more prompt resolution on chest CT during the recovery phase. Although our cohort comprised a modest number of patients, it does demonstrate relatively good outcomes based on chest imaging.

Similar to previous reports, mild pulmonary function abnormalities were present in less than 20% of patients at 1- and 3-month follow up.[24] This might explain the persistent cough and dyspnea symptoms noted in some patients after discharge. A recent study reported 110 discharged patients with COVID-19 in Guangzhou, China. The mean age was 49.1 years old and 19 of them had severe pneumonia. Pulmonary function impairment included low DLCO% in 51 cases (47.2%), FEV_1% in 15 (13.6%), FVC% in 10 (9.1%); these results are similar to our findings. Furthermore, their study showed a significant difference in diffusing-capacity measurements among the different groups of severity. There was no significant difference among the discharged survivors with different severity pneumonia in regard to other pulmonary function measures (e.g., FEV_1, FVC, FEV_1/FVC).[15]

In a series of 55 SARS patients in Hong Kong at 2-year follow up, about 15% were found to have a restrictive ventilatory defect and 50% patients had impaired diffusion capacity.[25] Other studies also showed similar results in the recovery period of SARS patients.[23,26] Compared with these studies on SARS, pulmonary function impairment was less in our cohort of COVID-19 patients. Regarding the pulmonary fibrosis resulting from viral pneumonia in the recovery phase, diffusion capacity would be expected to be more affected compared with lung volume in most patients. Therefore, it would be preferable to combine

Table 3. Comparison of the characteristics of 61 patients with COVID-19 at 3-month follow up.[a]

	CT 3M>0 (*N*=29)	CT 3M=0 (*N*=32)	X^2	*p*
Age (%)			12.884	0.000
⩽40	24	12		
>40	5	20		
Gender (%female)	15	18	0.125	0.723
Current smoker (%)	4	2	0.976	0.323
Lymphocyte (%)			6.039	0.014
⩾1.1	9	12		
<1.1	20	20		
White blood cells (%)			0.660	0.417
⩾4.0	20	25		
<4.0	9	7		
Cough (%)	6	2	2.784	0.095
Difficulty breathing (%)	8	4	2.191	0.139
Oxygen therapy (%)	21	8	13.713	0.000
Hormones used (%)	15	6	7.327	0.007
Underlying disease (%)	16	9	4.601	0.032
Critically ill patients (%)	13	4	7.909	0.005

[a]Continuous variables were compared using Wilcoxon scores (Mann–Whitney *U* test), and categorical variables were compared using the Mantel–Haenszel test.
COVID-19, coronavirus disease 2019; CT, computed tomography.

Table 4. Multivariate analysis of predictors of abnormal CT score on 3-month follow up.

	OR	95 CI%	*p*
Age >40 years	7.080	[1.410, 35.540]	0.017
Lymphocyte $<1.1\times10^9$/l	1.228	[0.303, 4.969]	0.774
Oxygen therapy	2.673	[0.500, 14.290]	0.250
Steroid treatment	7.148	[1.394, 39.500]	0.024
Severe/critical patients	0.647	[0.090, 4.663]	0.647
Underlying disorders	1.370	[0.352, 5.333]	0.650

CI, confidence interval; CT, computed tomography; OR, odds ratio.

FEV_1 with DLCO in identifying pulmonary function impairment with higher sensitivity.[23]

At 1-month, the 6MWD was significantly reduced in our patients when compared with corresponding

Table 5. Comparison of 6MWD in different groups on 1- and 3-month follow up.

Groups	Male > 40 year	Male ⩽ 40 year	Female > 40 year	Female ⩽ 40 year
1 month	495 ± 84**	544 ± 56**	448 ± 92**	513 ± 59**
3 months	536 ± 73	578 ± 46**	518 ± 42***	563 ± 47*
Normal (*n*)	569 ± 69 (28)	645 ± 40 (26)	537 ± 74 (26)	611 ± 61 (26)

*Significant at $p < 0.05$, **significant at $p < 0.01$, compared with normal population; ***significant at $p < 0.01$, compared with 3-month population.
6MWD, 6-min walk distance.

age-matched healthy subjects, and gradually improved by 3-month follow up. Given the relatively well-preserved lung function in most of our patients, the reduced 6MWD may be related to extrapulmonary factors such as physical deconditioning and psychological effects. Previous studies have shown that 6MWD was substantially lower among ARDS and SARS survivors.[27–29] The 6MWD of 97 survivors in Hong Kong was 464 m (SD, 87 m) at 3 months and 502 m (SD, 97 m) at 6 months. The 500 m distance of our 6MWD at 1 month was similar to that of SARS survivors at 6 months after discharge. The performance in our cohort was better than that of SARS survivors in Hong Kong.[28] These observations seem to indicate more prompt recovery of COVID-19 patients compared with those with SARS. Similarly, the evolution of findings on physical examination, pulmonary-function testing, 6MWT, and quality-of-life evaluation has been previously described for survivors of ARDS. Poorer HRQL compared with the healthy population, mild residual radiographic and functional abnormalities, and extrapulmonary deficits after ARDS have been reported, persisting for more than 1 year in some cases.[29–31]

The physical component status scores of PF and GH in SF-36 were not significantly decreased in our cohort. Although viral pneumonia could result in inflammatory lung damage, most of our patients had normal or mild pulmonary impairment at 3-month follow up. The mental component scores of SF, RE, and MH were significantly worse in 41–64 year-old group compared with the normal controls. This finding could be explained by the worse chest CT scores in older patients, and greater stresses in family and work roles. Previous studies on SARS at 24-months also demonstrated significant impairments in all SF-36 domains for the age group 41–64 years.[25] In addition, it might reflect the enormous psychological trauma and mood disturbance during the long hospitalization and isolation period. In this cohort, every patient had to stay in the hospital for about 2 weeks. After that, the quarantine protocol in China required a 2-week isolation at a designated location and subsequently at home. In total, the 6-week long journey following discharge that these patients with COVID-19 had to endure was alone, away from family members for most of the time. Psychological support and further follow up should be provided for these patients.

The association between older age and worse chest CT scores at 3 months is similar to findings during the acute phase of COVID-19 reported in other studies.[32,33] An earlier study enrolled 22,512 patients with COVID-19 and demonstrated the mortality rate to be increased with older age among COVID-19 patients in Italy.[34] Another study showed patients with fibrosis seen in follow-up CT studies at 15 days after discharge to be older, with longer hospitalization, higher rate of ICU admission, compared with those without fibrosis.[35] Similarly, our study also showed the CT scores in 41–80-year group to be significantly worse compared with those in 16- to 40-year-old group.

Steroids have been prescribed widely in patients with severe viral pneumonia in recent decades, although the role of this treatment remains controversial. During the 2003 SARS outbreak in Hong Kong, steroids were associated with better prognosis but a higher rate of secondary infections.[36] In a recent Chinese COVID-19 protocol,[9] the recommended dose (equivalent of methylprednisolone 1–2 mg/kg/day) and duration (3–5 days) were relatively lower than those used in the SARS epidemic. There was concern that the anti-inflammatory effects of steroids might lead to slower resolution of pneumonia and poorer CT scores. Thus, it would be of interest to perform additional studies on the long-term outcomes to

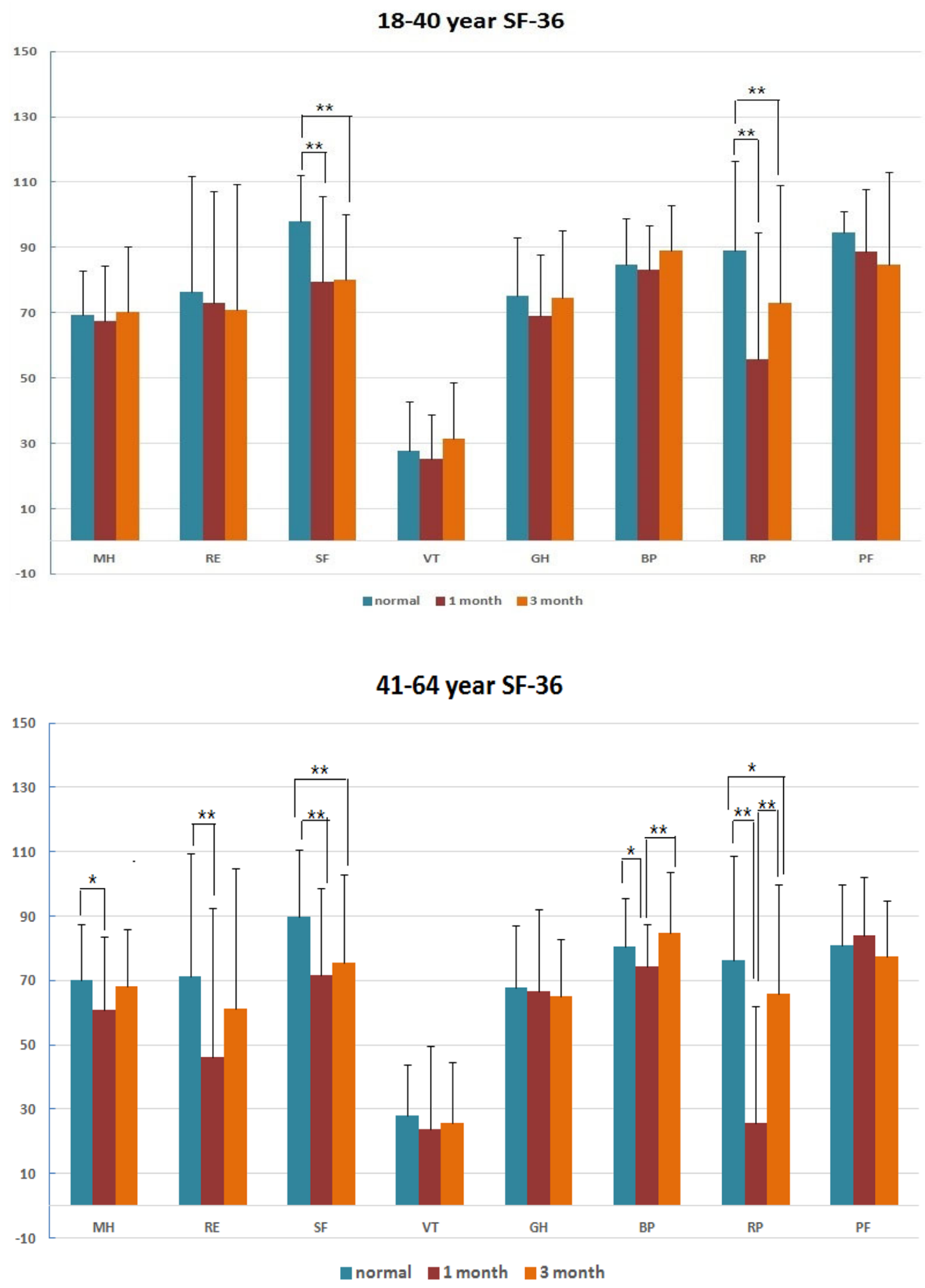

Figure 3. HRQoL (SF-36) of COVID-19 survivors at 1 and 3 months after discharge in comparison with normal subjects.
*Significant at $p < 0.05$, **significant at $p < 0.01$.
CT, computed tomography; COVID-19, coronavirus disease 2019; HRQoL, health-related quality-of-life; SF-36, 36-item short form general health survey.

determine the optimal dose/duration of steroids in the treatment of patients with COVID-19.

There are several limitations of this study. Firstly, some patients manifested positive results of virus RT-PCR testing during follow up and were not suitable to undergo physical exercise such as PFT testing in the active period of COVID-19, especially at 1 month after discharge. Secondly, diffusing capacity was not measured in this study due to concerns regarding potential transmission during PFT performance. However, severely reduced pulmonary gas exchange can be assessed by pulse oxygen oximetry. All the patients manifested oxygen saturation above 93% at 3 months. In addition, 6MWD was performed to assess exercise capacity for all patients in this cohort. Thirdly, the number of patients in this cohort enrolled from a single center was relatively modest, which may limit extrapolation of our data. Investigating of the long-term outcomes of COVID-19 survivors will provide additional insights.

Conclusions

At 3 months after discharge, chest CT abnormalities were present in one half of patients who had recovered from COVID-19; worse chest CT scores were independently associated with older age and steroid administration during hospitalization. Modest residual impairments were noted in pulmonary function, whereas exercise capacity and SF-36 were significantly lower than those of the general population. A support program and further follow-up assessments may be needed in the care of recovered COVID-19 patients.

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Conflict of interest statement

The authors declare that there is no conflict of interest.

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Supplemental material

The reviews of this paper are available via the supplemental material section.

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