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Pulmonary Function, Functional Capacity, Respiratory, and Locomotor Muscle Strength after Severe to Critically Ill COVID-19: A Long-Term Study

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Abstract

Background: The sequelae of post-coronavirus disease 2019 (COVID-19) pneumonia on lung function, exercise capacity, and quality of life were observed in both short-term and long-term. However, the study about the respiratory and locomotor muscle strength in severe and critically ill COVID-19 survivors are still limited. Therefore, we aimed to examine long-term pulmonary function, functional capacities, and respiratory and locomotor body muscle strength in severe to critically ill post-COVID-19 survivors.

Methods: A prospective observational study was conducted in 22 post-COVID-19 pneumonia and healthy adults. Clinical characteristics during admission, pulmonary function, functional capacity, respiratory muscles, and locomotor muscles strength were examined at 1, 3, and 6 months after discharge from the hospital.

Results: The generalized linear mixed model showed that percent predicted of forced expiratory volume in the 1 second (%FEV_1), percent predicted of forced vital capacity (%FVC), maximum inspiratory pressure (MIP), handgrip strength, 6-minute walk distance, and five times sit to stand (5TSTS) were significantly lower in post-COVID-19 pneumonia patients than in healthy subjects during the follow-up period. The percent predicted of maximal voluntary ventilation (%MVV), and locomotor muscle strength were not different between the two groups throughout the follow-up period. Among post-COVID-19 pneumonia patients, %FEV_1, %FVC, %MVV, 5TSTS, locomotor muscle strength significantly improved at three months compared to baseline at 1 month.

Conclusion: Pulmonary function, functional capacity, respiratory, and locomotor muscle strength of survivors from COVID-19 were impaired and recovery was observed after three to six months. These emphasized the need to evaluate the long-term consequences of COVID-19.

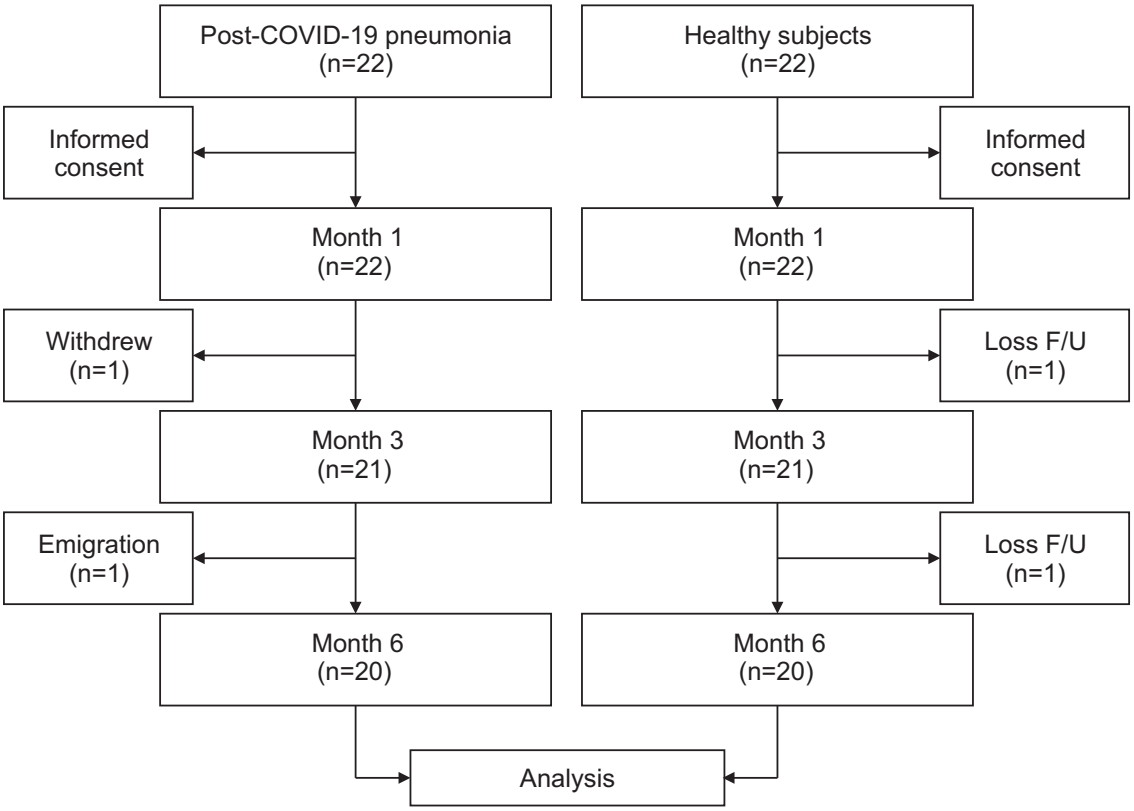
Keywords: COVID-19; Pulmonary Function; Functional Capacity; Muscle Strength

Introduction

The coronavirus disease 2019 (COVID-19) reached a pandemic status in early 2020 causing profound consequences on individual and public health, economic impact, and social disruption[1]. The varying disease severity from asymptomatic to critical illness requiring treatment in the intensive care unit (ICU) might have contributed to the variety of post-acute and long-term sequelae. The physical and/or mental illnesses that developed during or following a confirmed or suspected COVID-19, and which continued for more than 4 weeks was defined as "post-COVID condition or long COVID" according to the Centers for Disease Control and Prevention definition[2]. Typical symptoms include cognitive impairment, headache, sleep problems, exhaustion, joint or muscle pain, cough, and shortness of breath[2,3]. These symptoms cannot be explained by other diagnoses and frequently persist for the first three months after the onset of infection.

A large cohort of 1,655 COVID-19 survivors from China reported fatigue and muscle weakness of 63%, and sleep difficulty of 26% at 6 months after acute infection[4]. A smaller study of 300 participants in Turkey reported that approximately 60% of survivors had at least one symptom of long-term COVID, and 40% had at least one rheumatic or musculoskeletal symptom[5]. Another cross-sectional study on ICU survivors reported that 31% of patients were unable to walk 100 me after 1 month of acute infection[6]. However, all the reports were based on questionnaires and interviews. One cross-sectional study included 48 patients with mild to moderate disease severity and found that 30% to 40% handgrip and quadriceps weakness and low physical activity were observed after at least 12 weeks of COVID-19 diagnosis[7]. Our previous studies also found that the sequelae of post-COVID-19 pneumonia on lung function, exercise capacity, and quality of life were observed in both short-term and long-term[8]. However, the study about the respiratory and locomotor muscle strength in severe and critically ill COVID-19 survivors are still limited. Moreover, pulmonary function tests and 6-minute walk test (6-MWT) are useful tools for detection of long-term sequelae of post-COVID-19 pneumonia. Therefore, this study aimed to examine respiratory and locomotor muscle strength in severe and critically ill COVID-19 survivors, as well as the pulmonary function and functional capacities and function

Figure 1. Study flow diagram. COVID-19: coronavirus disease 2019; F/U: follow-up.



outcomes compared to matched healthy people.

Materials and Methods

1. Study design

From December 2021 to October 2022, we conducted a prospective observational study on severe to critically ill COVID-19 pneumonia patients hospitalized in the ICU at the Chiang Mai University Hospital. Omicron variance including BA.1, BA.2, and BA.4/.5 were observed in Thailand during enrollment period. Participants were divided into two groups: post-COVID-19 pneumonia (n=22) and volunteer healthy controls (n=22). All patients were identified from the ICU medical records and provided informed consent. The volunteer healthy subjects were enrolled based on age- and gender-matched.

This study was approved by the Research Ethics Committee of the Faculty of Internal Medicine, Chiang Mai University (Research ID: Study code: 8604 MED-2564-08604, date of approval: 13 December 2021) and filed under Clinical Trials Registry (Study ID: TCTR20220302004).

2. Patients

The inclusion criteria included (1) at least 18 years old; (2) patients were confirmed positive for severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection by real-time polymerase chain reaction using nasal and pharyngeal swab specimens and were diagnosed with pneumonia by clinical and imaging (chest X-ray and/or computed tomography scan); (3) patients were admitted to the ICU and required high flow nasal cannula (HFNC) or mechanical ventilation (MV) either invasive or non-invasive MV. The exclusion criteria included (1) pregnancy; (2) history of neurological dis-

Table 1. Baseline characteristics

Characteristic	Post-COVID-19 pneumonia (n=20)	Healthy subjects (n=20)	p-value
Age, yr	50.9±12.5	51.9±11.9	0.787
Male sex	15 (75.0)	15 (75.0)	1.000
BMI, kg/m^2	27.8±3.8	24.7±2.8	0.005
Smoking status			0.891
Non-smoker	16 (80.0)	17 (85.0)	
Ex-smoker	1 (5.0)	1 (5.0)	
Current-smoker	3 (15.0)	2 (10.0)	
Comorbidities			
Diabetes mellitus	2 (10.0)	0	0.487
Hypertension	5 (25.0)	2 (10.0)	0.407
Diabetes mellitus and hypertension	4 (20.0)	0	0.106
Laboratory, mmol/L			
Potassium	3.9±0.3	3.8±0.5	0.856
Magnesium	1.7±0.1	1.7±0.1	0.097
Phosphorus	3.2±0.7	3.2±0.4	0.773
Calcium	9.4±0.4	9.3±0.4	0.387
CPK	70.7±37.6	159.9±89.9	<0.001
Athlete	0	1 (0.5)	1.000
Exercise, day/wk	0.0 (0.0–0.0)	0.0 (0.0–2.0)	0.055
Exercise duration, min/day	0.0 (0.0–0.0)	0.0 (0.0–17.5)	0.034
Dominant hand			1.000
Right	18 (90.0)	17 (85.0)	
Left	2 (10.0)	3 (15.0)	

Values are presented as mean±standard deviation, number (%), or median (interquartile range).
COVID-19: coronavirus disease 2019; BMI: body mass index; CPK: creatinine phosphokinase.

orders, e.g., previous stroke, neuromuscular disorders, or bedridden status; and (3) terminal illness, e.g., end-stage malignancy.

3. Data collection

Patient characteristics and treatment during admission including age, gender, smoking status, comorbidity, Acute Physiologic and Chronic Health Evaluation II (APACHE II) score at admission, initial sequential organ failure assessment (SOFA) score, day from the onset of illness, co-infecting pathogens, the minimum lymphocyte count, the maximum high-sensitivity C-reactive protein, the duration of MV or HFNC, antiviral agent, vasopressor, sedative drug, immunosuppressive drugs, prone position, and hospital length of stay were recorded.

The schedule of follow-up visits was at 1, 3, and 6 months after discharge from the hospital. At the follow-up appointment, blood chemistries which may affect muscle function interpretation including serum potassium, magnesium, phosphorus, calcium, and creatine kinase were obtained at the first visit. Chest X-ray and pulmonary function test, functional capacity, and respiratory, and locomotor muscle strength were measured at all visits. Pulmonary function including forced expiratory volume in the 1 second (FEV_1), %predicted FEV_1, forced vital capacity (FVC), %predicted FVC, and %FEV_1/FVC, respiratory muscle strength by maximum inspiratory pressure (MIP), and maximal voluntary ventilation (MVV) were measured by an experienced physiotherapist according to European Respiratory Society (ERS)/American Thoracic Society (ATS) guidelines[9]. Functional capacity measured by five times sit to stand (5TSTS) tests and 6-minute walk distance (6-MWD) were also assessed at every visit. For the 5TSTS, all subjects were instructed to stand up completely from seated on armless chair with 45 cm height. The five consecutive times of sit-up and down as fast as possible with their arms crossed over their chest according were instructed according to Buatois et al.[10] The 6-MWT was also assessed according to the ATS guidelines[11,12]. Locomotor muscles including hamstring, quadriceps, and handgrip strength were measured in the same week by well-trained physiotherapists. Handgrip strength was assessed by the Smedley III hand dynamometer according to Vaishya et al.[13] Whereas, quadriceps and hamstring strength were assessed using the isokinetic dynamometer CON-TREX MJ (PHYSIOMED ELEKTROMEDIZIN AG, Schnaittach, Germany) as previously described by O'Sullivan et al.[14]

4. Sample size

Sample size calculation was based on the mean±standard deviation (SD) of MIP between the limbs weakness and no limbs weakness groups in the previous study[6]. The mean±SD of MIP in the limbs weakness and no limbs weakness groups were 37.7±11.8 and 46.1±6.3 cmH_2O, respectively. For three repeated measurements, we need to study at least 30 subjects, 15 in each group to be able to reject the null hypothesis

Table 2. Characteristics of post-COVID-19 pneumonia patients

Characteristic	Post-COVID-19 pneumonia (n=20)
Clinical manifestation	
APACHEII score	4.5 (4.0–8.0)
Initial SOFA score	3.0 (2.0–4.8)
DOI, day	8.0 (6.0–10.0)
Minimal lymphocyte count, cells/mm^3	515.0 (430.0–825.0)
Maximum of high sense CRP, mg/L	143.0 (81.5–249.5)
Management	
Ventilator use	5 (25.0)
Ventilator, day	5.0 (5.0–8.0)
HFNC	15 (75.0)
HFNC, day	3.5 (3.0–5.0)
Remdesivir	19 (95.0)
Favipiravir	1 (5.0)
Antibiotics	15 (75.0)
Corticosteroid	20 (100.0)
Tocilizumab	4 (40.0)
Baricitinib	6 (60.0)
Hemoperfusion	2 (10.0)
Hemoperfusion, day	2.0 (2.0–2.0)
Vasopressor use	1 (5.0)
Sedative/neuromuscular blockage drug	6 (30.0)
Prone position	17 (85.0)
Prone position, day	3.0 (2.0–5.0)
Clinical outcomes	
Hospital length of stay, day	8.5 (7.0–13.5)

Values are presented as median (interquartile range) or number (%).
COVID-19: coronavirus disease 2019; APACHE II: Acute Physiologic and Chronic Health Evaluation II; SOFA: sequential organ failure assessment; DOI: day from the onset of illness; CRP: C-reactive protein; HFNC: high flow nasal cannula.

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Table 3. Pulmonary function, respiratory and locomotor muscle strength, and functional capacities at 1, 3, and 6 months

Outcome	Post-COVID-19 pneumonia (n=20)			Healthy subjects (n=20)			p-value
	1st month	3rd month	6th month	1st month	3rd month	6th month	
Pulmonary function testing							
FEV_1, L	2.38±0.56	2.53±0.56	2.61±0.57	2.82±0.78	2.76±0.66	2.93±0.77	0.013
%Predicted FEV_1	86.8±14.7	92.8±15.6	96.0±15.3	97.6±11.9	96.7±12.1	102.2±12.2	0.001
FVC, L	2.79±0.66	2.97±0.62	3.08±0.68	3.39±0.88	3.34±0.77	3.56±0.92	0.001
%Predicted FVC	84.2±15.0	90.5±14.5	93.2±15.0	97.2±12.9	96.2±13.0	102.0±13.4	<0.001
MVV, L/min	103.0±24.3	114.6±30.0	110.0±36.8	108.3±27.7	118.6±30.5	126.5±32.1	0.078
%Predicted MVV	82.3±15.8	90.5±16.3	93.4±16.3	85.5±14.4	93.8±13.8	100.0±12.3	0.108
Functional capacities							
6-MWD, m	426.2±85.5	446.2±89.6	453.0±93.7	533.3±48.2	522.3±55.0	534.6±59.9	<0.001
5TSTS, sec	8.7±1.7	7.2±1.6	7.7±1.6	7.4±1.2	6.5±1.4	6.8±1.4	0.005
Respiratory muscle strength							
MIP, kPa	9.1±3.3	9.0±4.5	9.8±3.9	9.7±3.6	9.9±2.9	9.5±2.5	0.046
%Predicted MIP	86.7±27.2	85.7±36.9	94.0±31.9	95.2±35.6	97.8±28.9	91.9±26.1	0.113
Upper-limb muscle strength							
Handgrip strength	33.6±8.3	32.5±8.7	32.6±8.3	35.0±8.7	35.2±8.7	36.3±9.0	0.021
Lower-limb muscle strength							
Quadriceps							
Torque max, Nm	92.0±28.5	100.5±33.9	95.6±31.8	87.8±29.2	87.3±23.6	87.0±23.7	0.840
Torque max average, Nm	83.0±25.7	92.4±32.6	86.9±30.2	79.9±27.8	77.9±26.5	79.2±22.8	0.908
Torque max average, Nm/kg	1.1±0.3	1.2±0.4	0.7±0.2	1.2±0.4	1.2±0.3	0.8±0.2	0.633
Hamstring							
Torque max, Nm	46.4±14.0	53.8±17.7	56.6±18.9	49.2±17.6	54.2±16.6	53.2±15.9	0.204
Torque max average, Nm	43.0±12.3	46.5±18.5	50.0±18.0	44.9±17.6	50.9±15.6	50.3±16.0	0.149
Torque max average, Nm/kg	0.6±0.2	0.6±0.2	0.7±0.2	0.7±0.2	0.8±0.2	0.8±0.2	0.286

Values are presented as mean±standard deviation. p-value from generalized linear mixed model which comparing between groups adjusted by body mass index and exercise duration.
COVID-19: coronavirus disease 2019; FEV_1: forced expiratory volume in the 1 second; FVC: forced vital capacity; MVV: maximal voluntary ventilation; 6-MWD: 6-minute walk distance; 5TSTS: five times sit to stand; MIP: maximum inspiratory pressure.

that the population means of the post-COVID-19 pneumonia and healthy control groups were equal with a probability (power) of 0.80. The type I error probability associated with this test of this null hypothesis was 0.05 and the correlation between repeated measurements was 0.7.

5. Statistical analysis

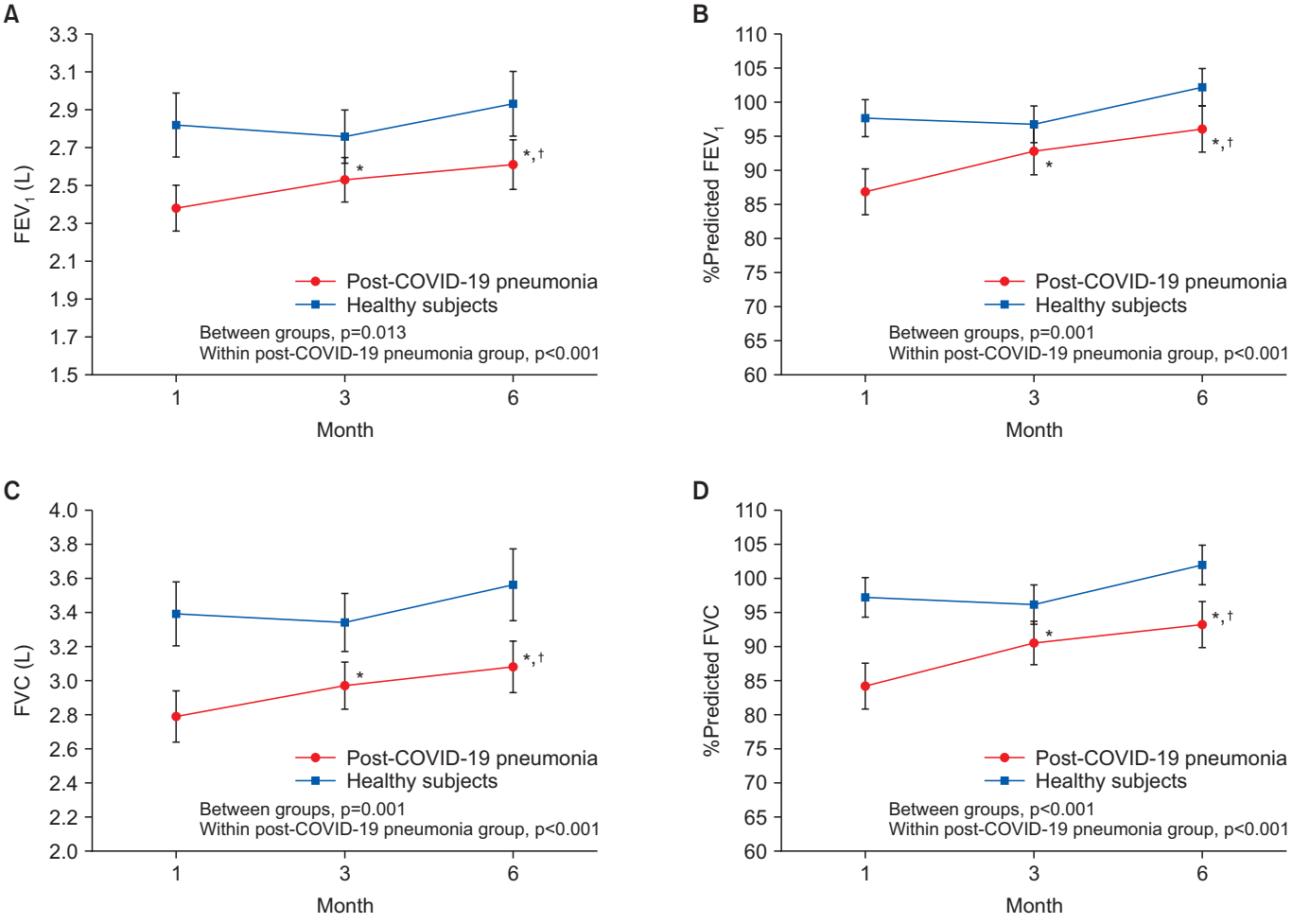
Results for continuous data were expressed as mean±SD or median (interquartile range). Results with proportions were expressed as frequencies and percentages. Independent t-test was used to compare differences between the COVID-19 group and the healthy group. A generalized linear mixed model adjusted by body mass index (BMI) and underlying disease including diabetes mellitus (DM) and hypertension (HT) was used for comparing the parametric data between groups during the study period. Statistical significance was accepted at a $p<0.05$. All statistical analyses were performed using SPSS version 22 (IBM Co., Armonk, NY, USA).

Results

1. Patient characteristics

A total of 22 post-COVID-19 pneumonia patients and 22 matched healthy adults were enrolled. Two participants from each group were unable to follow the scheduled visits, so the data of 20 participants from each group were completely analyzed. A study flow is shown in Figure 1. The baseline characteristics of all participants are detailed in Table 1. The post-COVID-19 pneumonia group exhibited a higher average BMI com-

Figure 2. Pulmonary functions of post-coronavirus disease 2019 (COVID-19) pnemonia patients compare to matched healthy subjects and comparison within group overtime. Data are presented as mean±standard error of the mean; compare between groups using generalized linear mixed (GLM) adjusted by body mass index and exercise duration. (A) Forced expiratory volume in the 1 second (FEV_1), (B) %predicted FEV_1, (C) forced vital capacity (FVC), and (D) %predicted FVC. In the post-COVID-19 pneumonia group; compare throughout the three visits using GLM model, in the post-COVID-19 pneumonia group. $p<0.017$ *compared to month 1 and †compared to month 3.



pared to the healthy group (27.8±3.8 kg/m^2 vs. 24.7±2.8 kg/m^2, p=0.005). The post-COVID-19 pneumonia group had a higher proportion of DM and HT compared to healthy controls. There were no differences in serum electrolyte values between the two groups, except for creatinine phosphokinase levels, which were higher in the healthy group but remained in the normal range.

The clinical manifestations, treatment during admission, and outcomes of the patients are shown in Table 2. Five patients (25%) required MV during ICU admission, while the others used HFNC. All patients received antiviral medication and systemic corticosteroids with a median dose of 1,411.5 mg equivalent to prednisolone. Two-thirds of patients received empirical antibiotics for possible bacterial co-infection. Only one patient was confirmed bacterial co-infection by positive sputum culture.

2. Pulmonary function and functional capacity

Pulmonary function parameters including FEV_1, %predicted FEV_1, FVC, and %predicted FVC in post-COVID-19 pneumonia patients were significantly lower than matched healthy subjects during the follow-up period. However, all parameters among the post-COVID-19 pneumonia group markedly improved over time (Table 3 and Figure 2). MVV and %predicted MVV were not different between post-COVID-19 pneumonia patients and healthy subjects (Table 3). Functional capacities measured by 6-MWD and 5TSTS were significantly worse in post-COVID-19 pneumonia patients but both parameters significantly improved over time (Figure 3).

The patients with post-COVID-19 pneumonia patients revealed that % the predicted FVC <80% at the first visit was 10/20 (55%), at the second visit was 6/20 (30%), and at the third visit was 3/20 (15%).

3. Respiratory and locomotor muscle strength

The post-COVID-19 pneumonia group had lower respiratory muscle strength measured by MIP. Similarly, upper body muscle strength measured by handgrip strength in post-COVID-19 pneumonia patients was significantly lower than in healthy subjects during the follow-up period. Whereas lower body muscle strength represented by quadriceps and hamstring strength were not different between the two groups. Hamstring strength was slightly lower in the post-COVID-19 pneumonia group compared to the healthy group but significantly improved over the follow-up period (Table 3 and Figure 4).

Discussion

This study evaluated long-term pulmonary function, functional capacities, respiratory and locomotor muscle strengths in individuals who survived severe COVID-19 infection compared to matched healthy subjects. Our findings indicated that patients who recovered from severe COVID-19 had reduced FEV_1 and FVC, %predicted FEV_1 and %predicted FVC, MIP, and hand grip strength. The results indicated a smaller lung volume compared to matched healthy subjects. Functional capacities

Figure 3. (A) Six-minute walk distance (6-MWD) and (B) five times sit to stand (5TSTS) of post-coronavirus disease 2019 (COVID-19) pneumonia patients compared to matched healthy subjects and comparison within group overtime. Data are presented as mean±standard error of the mean; compare between groups using generalized linear mixed (GLM) adjusted by body mass index and exercise duration. In the post-COVID-19 pneumonia group; compare throughout the three visits using GLM model, in the post-COVID-19 pneumonia group. *p<0.017 compared to month 1.

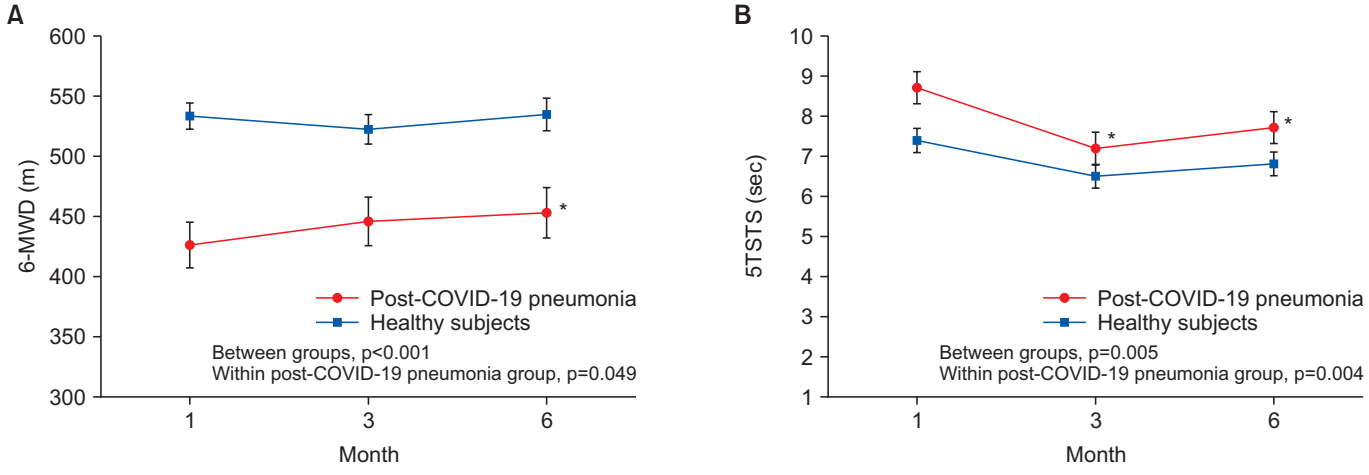
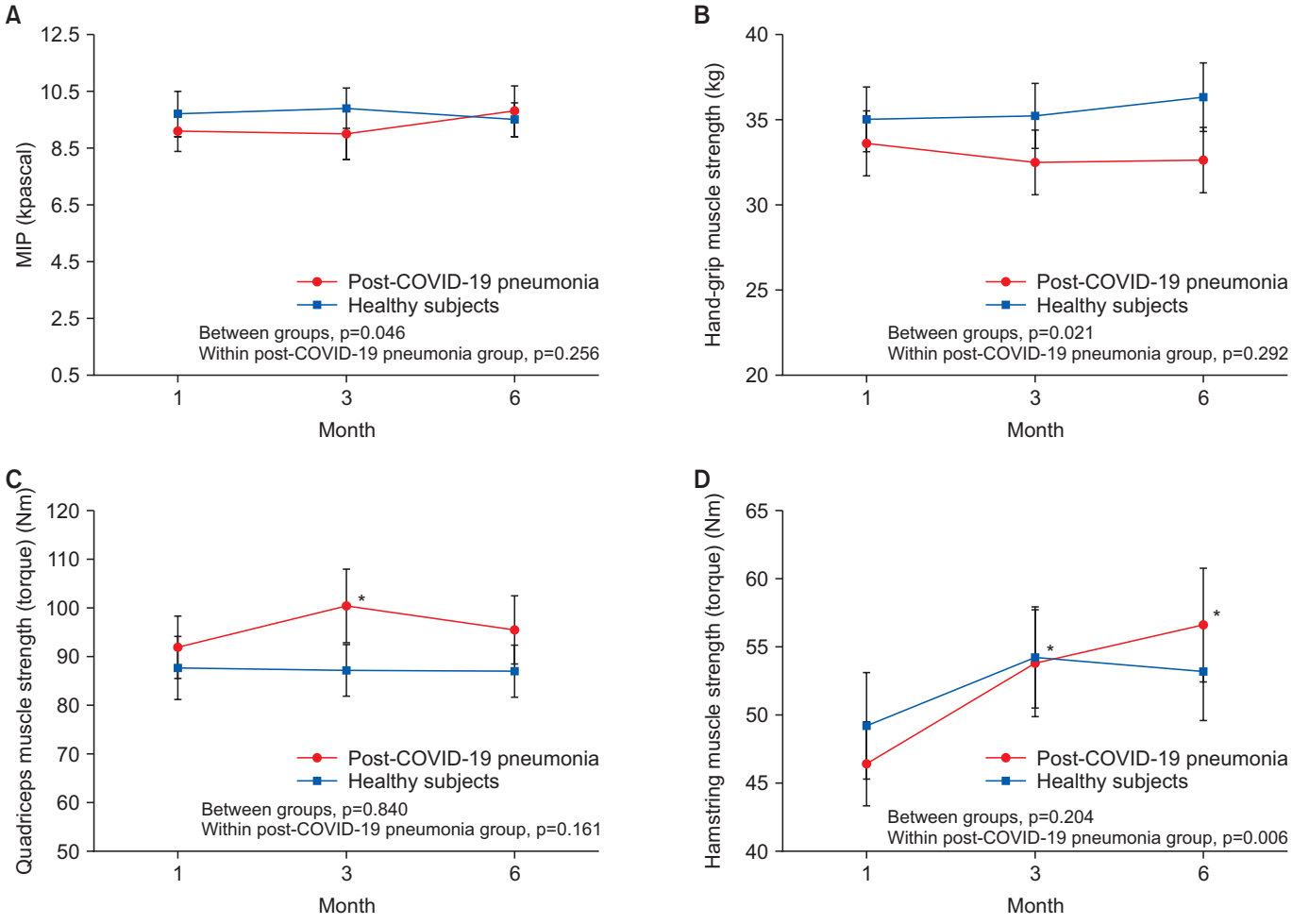


Figure 4. (A) Maximum inspiratory pressure (MIP), (B) handgrip, (C) quadriceps, and (D) hamstring muscles strength of post-coronavirus disease 2019 (COVID-19) pneumonia patients compared to matched healthy subjects and comparison within groups over time. Data are presented as mean±standard error of the mean; compare between groups using generalized linear mixed (GLM) adjusted by body mass index and exercise duration. In the post-COVID-19 pneumonia group; compare throughout the three visits using GLM model, in the post-COVID-19 pneumonia group. *p<0.017 compared to month 1.



that included 6-MWD was approximately 100 m lower than the matched healthy controls. Similarly, the post-COVID-19 patients required a longer time to finish five times from sitting-to-standing. However, these parameters demonstrated improvement within 3 to 6 months.

The current study's results were comparable with a previous study by Salem et al.[15] which found that 50% of patients with COVID-19 pneumonia exhibited impaired lung function resulting from restrictive lung impairment. A recent meta-analysis of seven studies included 380 lung functions within the first 3 months of post-COVID-19 and identified a 15% restrictive lung impairment[16]. Another systematic review evaluated short and long-term rates of post-acute sequelae of COVID-19, focused on three studies, reported a 10% prevalence of restrictive lung impairment[17]. Disparities in the prevalence of pulmonary restriction among survivors of COVID-19 pneumonia could be attributed to differing evaluation timings, ranging from shortly before discharge to several months post-discharge, as well as variations in disease severity. The primary mechanism believed to contribute to restrictive lung function is the fibrotic changes that develop in the lungs following the acute COVID-19 infection. The viral-induced lung injury caused by COVID-19 prompts the recruitment and activation of fibroblasts, heightening the risk of pulmonary fibrosis in post-COVID-19 patients[18]. Nonetheless, our study revealed a trend of improvement in restrictive lung impairment over time. This suggests that the majority of individuals who have recovered from COVID-19 are unlikely to experience permanent restrictive lung impairment or extensive fibrotic changes.

Obvious impaired functional capacity was observed in our participants. These findings were supported by a previous study by Anastasio et al.[19] which evaluated patients with pneumonia from SARS-CoV-2 infection at 4 months after diagnosis. They reported a reduction of 6-MWD among patients who had exertional dyspnea without other differences in pulmonary function. Another cohort study, involving 1,733 patients with severe COVID-19 pneumonia, found 29% of patients had a median 6-MWD below the normal range at 6 months after infection[4]. One study from Chile demonstrated short-term impaired functional capacity of patients with post-COVID-19 using one minute sit to stand. Only 83% of patients could complete the test, with an average of 20 repetitions per minute, in which 90% of patients' performances were under the reference value[20]. Our study was the first report of impaired 5TSTS in post-severe COVID-19 patients compared to healthy controls. The 5TSTS has been established as a dependable method for evaluating functional capacity, displaying a strong correlation with the 6-MWD in terms of assessing balance and muscle strength[21]. The 5TSTS is more convenient, requires a shorter time to complete the test, and can be performed in a limited space. Moreover, our study confirmed that 5TSTS can be used to evaluate functional capacity and improvement over time.

In comparison to healthy subjects, respiratory muscle strength assessed by MIP as well as upper body muscle strength assessed by handgrip dynamometer revealed a significant decrease among post-severe COVID-19 pneumonia patients. Interestingly, the lower body muscle strength including quadriceps and hamstring muscles were not different from matched healthy subjects. These results contrasted with a previous study, which reported handgrip and quadriceps weakness (assessed by handheld dynamometer) in 39% and 35% of post-mild to moderate COVID-19 patients[7]. The inconsistent results may occur from the difference in the included patients' age and gender and the instrument used to assess muscle strength. The current study chose a standard isokinetic dynamometer for accurate evaluation of the lower body muscle strength. Our study found a reduction in muscle strength that was observed in the upper limbs but not in the lower limbs when compared between survived severe COVID-19 infection and healthy subjects. Previous study suggested that the upper limbs muscle weakness could be affected by many factors, e.g., specific muscle fiber types, muscle mass, muscle volume, and malnutrition[22].

The pathogenesis of muscle weakness in COVID-19 survivors is mainly from direct virus-induced cellular damage and inflammation. The SARS-CoV-2 viruses enter into cells via angiotensin-converting enzyme 2 (ACE2) receptors on cell membranes and then destroy host cells[23-26]. The myopathic change was found in various muscles of post-COVID-19 infection, thus this explains physical fatigue[27]. In addition, survivors of acute respiratory failure can experience muscle weakness due to prolonged MV, sedation, neuromuscular blocking medications, corticosteroids, and hypoxia, all of which can exacerbate post-infectious respiratory and body muscle strength impairment[28,29]. Avgeri et al.[30] conducted a study that investigate the lung function and exercise capacity in COVID-19 when compared to non-COVID-19 patients following ICU discharge. They found differences between COVID-19 and non-COVID-19 ICU patients in terms of lung function and 6-MWD over 1 year of follow-up. The improvement was greater in COVID-19 patients. They hypothesized that these differences in the improvement may be due to a specific impact of COVID-19 on lung function and exercise performance in these patients[30]. To restore lung function, muscle strength, and exercise capacity in subjects with post-COVID-19 infection, the cardiopulmonary rehabilitation has been introduced. Previous studies underscored that the cardiopulmonary rehabilitation program including strength and endurance exercises can improved lung function parameters, muscle strength, and exercise performance in patients recovering from COVID-19[31-33].

Based on the single-center study, several limitations have been found. Firstly, the majority of included patients received HFNC and only five patients required MV. We could not demonstrate the difference in lung function, functional capacity, and muscle strength between non-MV and HFNC groups. Secondly, muscle strength and exercise performance can be affected by the use of neuromuscular blockage. However, there was a small sample size (six patients) who were prescribed with sedative/neuromuscular blockage in this study. Unfortunately, we could not demonstrate the difference in lung function, functional capacity, and muscle strength between neuromuscular blockage usages. Thirdly, as a department concerned with infection control, the assessment of expiratory muscle strength during the acute phase following COVID-19 was restricted. Thus, we did not assess maximal expiratory pressure during the follow-up period. Moreover, although the mean MIP in the post-COVID-19 pneumonia group seemed to be significantly lower than healthy subjects, the clinically significant effect might not be revealed. The MIP of –80 cmH_2O usually excluded the clinically important inspiratory muscle weakness based

on the statement of ATS/ERS[34]. Fourthly, normal values of body muscle strength of Thai people have never been established. The body muscle strength of the healthy control group may not indicate the normal values in the overall population. Fifthly, difference in BMI between groups were observed. However, the generalized linear mixed model adjusted by BMI was used for dealing this issue. Lastly, there was no baseline data of outcome measurements, making it difficult to accurately determine the extent of improvement from the initial condition. However, healthy controls were included for comparison.

In conclusion, pulmonary function, functional capacity, respiratory, and locomotor muscle strength of survivors of severe and critically ill COVID-19 were significantly impaired when compared to matched healthy subjects. However, recovery was observed within 3 to 6 months. Existing evidence highlights the potential adverse consequences of long COVID-19 on the body, but it is important to note that recovery can be achieved through follow-up efforts. Given these findings, it is imperative to consider the exploration of potential benefits of rehabilitation to mitigate the compromise of pulmonary function, functional capacities, and muscle strength, and enhance the well-being and health outcomes among post-COVID-19 survivors.

Authors' Contributions

Conceptualization: all authors. Methodology: all authors. Formal analysis: Ngamsutham T, Chiawong W, Tajarernmuang P. Data curation: Ngamsutham T, Chiawong W, Tajarernmuang P. Funding acquisition: Tajarernmuang P. Validation: Ngamsutham T, Chiawong W, Tajarernmuang P. Investigation: all authors. Writing - original draft preparation: Ngamsutham T, Chiawong W, Dacha S, Tajarernmuang P. Writing - review and editing: all authors. Approval of final manuscript: all authors.

Conflicts of Interest

No potential conflict of interest relevant to this article was reported.

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