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Respiratory muscle weakness, reduced exercise capacity, and impaired lung functions in long-term post-COVID-19 patients

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ABSTRACT

Background: Many post-COVID-19 patients experienced long-term effects with symptoms lasting for more than three months including fatigue and dyspnea. There is scarce information in the literature on respiratory muscle strength, lung functions, exercise capacity, and the degree of dyspnea in long-term post-COVID-19 patients after two years of recovery.

Objectives: This study aims to assess respiratory muscle function, lung function, exercise capacity, and respiratory symptoms for two years after COVID-19 infection.

Methodology: This is an observational cross-sectional study that included 49 post-COVID-19 patients two years after recovery. Participants were categorized into two groups (hospitalized, n = 18 and non-hospitalized, n = 31). Maximum inspiratory pressure (MIP), maximum expiratory pressure (MEP), a six-minute walk test, and pulmonary function tests, were performed to assess ventilation function and exertion intolerance. The presence of respiratory symptoms was evaluated using the St. George's respiratory questionnaire.

Results: Diffusion impairment was the most common lung function abnormality found among all post-COVID-19 patients (32%) followed by restrictive pattern (19%). Two percent showed small airway disease, and no obstructive patterns were found. A reduced exercise capacity (the six-minute walk distance < 85% of predicted value) was found in 44% of post-COVID-19 patients. Respiratory muscle weakness was reported in twenty post-COVID-19 patients (41%), and MIP and MEP were significantly lower than predicted values ($p < 0.001$). Dyspnea was the most experienced respiratory symptom with (42%) followed by cough (22%) and wheezing (8%).

Conclusion: Our findings showed low exercise capacity, abnormal lung functions, and respiratory muscle weakness in post-COVID-19 patients two years after recovery. We strongly recommend periodic lung function and respiratory muscle testing in symptomatic post-COVID-19 patients.

Keywords: COVID-19, long-COVID-19, maximal respiratory pressures, exercise capacity, six-min walk test, pulmonary function tests

INTRODUCTION

Coronavirus disease 2019 (COVID-19) is an infectious illness caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), leading to widespread morbidity and mortality across the globe [1]. Most people infected with the virus will experience a mild to severe respiratory illness. However, older individuals and those with pre-existing medical conditions, such as cancer, diabetes, cardiovascular disease, or chronic respiratory disorders, are at higher risk of developing severe illness [2].

Recently long-COVID-19 is defined as a chronic condition that occurs after SARS-CoV-2 infection and is present for at least 3 months. Usually, there is a history of suspected or documented SARS-CoV-2 infection, and the symptoms might be newly developed after recovering from an acute COVID-19 infection or continue from the original disease, without being explained by different possible diagnosis. It affects multiple organ systems, with the lungs being the most commonly impacted [3]. Globally, an estimated 65 million people are affected by long-COVID-19, with an incidence rate of 10% among post-COVID-19 patients [4]. According to a meta-analysis study that included 8,517 post-COVID-19 patients after one-year follow-up, fatigue was the most frequently reported symptom (28%), followed by arthromyalgia (26%), depression (23%), and dyspnea (18%) [5].

The lungs are the most affected organ among survivors of COVID-19. In a prospective follow-up study conducted twelve weeks after COVID-19 infection, approximately 85% of patients exhibited one or more abnormal pulmonary function test (PFT) results. Specifically, 52% had abnormal diffusing capacity for carbon monoxide (DLCO), 45% showed a reduced restrictive ventilatory capacity, and 11% had an FEV1/FVC ratio below 0.7, indicating airflow obstruction [6].

In contrast, another prospective cohort study conducted for 3, 6, and 12 months after severe COVID-19 found improved pulmonary function among post-COVID-19 patients. However, 33% of the patients still exhibited impaired lung diffusion at 12 months, along with evidence of persistent physiological and radiographic changes in the lungs [7]. Additionally, many post-COVID-19 patients revealed signs of cardiac dysfunction, muscle weakness, and eventually exercise intolerance which varies depending on the severity of the disease and the time since its onset [8].

Although fatigue, dyspnea, and exercise intolerance are frequent in post-COVID-19 patients, the severity of these symptoms does not seem to correlate with the severity of the original infection [9]. Additionally, the mechanisms of these chronic symptoms are still unclear; vascular abnormalities (peripheral left to right shunt and diminished venous return) endothelial dysfunction, mitochondrial dysfunction, impaired pulmonary function, decreased skeletal muscle mass (sarcopenia), decreased VO2 max and oxygen extraction, and cardiac impairments are possible causes of exercise intolerance in post-COVID-19 patients [10-12].

Numerous follow-up studies have been conducted for three months, six months, and one year after the onset of COVID-19 infection. However, only a few studies have examined the long-term sequelae of COVID-19 beyond two years of recovery. Furthermore, there is ongoing debate regarding the long-term impact of COVID-19 on respiratory muscle strength, PFTs, and exercise capacity in post-COVID-19 patients. Thus, this study aims to assess respiratory muscle function, functional capacity (6-minute walk test), PFT, and respiratory symptoms after two years of COVID-19 infection.

METHODS

Subjects

This is a cross-sectional observational study done at the department of physiology, college of medicine at the Imam Abdulrahman Bin Faisal University between October 2023 and April 2024. Forty-nine post-COVID-19 patients with a documented history of SARS-CoV-2 infection two or more years ago were enrolled by a convenient sampling technique. Patients with known cases of bronchial asthma, chronic obstructive pulmonary disease, cardiac diseases, psychiatric disorders, muscular dystrophy, smokers, and the elderly (more than 65) were excluded. The sample size was determined based on previous similar studies [13-15].

The Helsinki Declaration was guiding the conduct of this study. The accessed data complies with all applicable privacy and data protection laws. Each participant's informed consent was obtained, and ethical approval was issued by Imam Abdulrahman Bin Faisal University's institutional review board (IRB Number: IRB-UGS-2023-01-385).

Study Protocol

The post-COVID-19 status of all patients was initially determined by reviewing their medical records at King Fahad University Hospital (Al Khobar, Saudi Arabia). Patients who were infected with COVID-19 at least two years ago were selected. Then they were contacted by phone to schedule study appointments. Those who consented to participate underwent the following evaluations:

1. A clinical review and examination to determine eligibility based on the inclusion and exclusion criteria. The St. George's respiratory questionnaire [16] was filled to assess respiratory symptoms.
2. Respiratory muscle functions using a respiratory pressure meter.
3. PFT: Spirometry to evaluate ventilatory function; body plethysmography to measure lung volumes; single-breath technique DLCO.
4. The six-minute walk test (6MWT) to assess functional capacity.

Respiratory Muscle Function

All muscle function tests were conducted using a noninvasive, portable respiratory pressure meter (MicroRPM-CareFusion UK 232 Ltd.). A compact device includes a mouth-pressure manometer with a mouthpiece and a small digital display showing the test results in cm H_2O. The most simple, useful, and noninvasive measures of respiratory muscle strength at the mouth are maximum inspiratory pressure (MIP) and maximum expiratory pressure (MEP) [17, 18].

The reference values of MIP and MEP were estimated using predictive equations for the Arab population established in [19]. Respiratory muscle weakness was defined as % predicted MIP < 70% [20].

Pulmonary Function Test

All PFT measurements (body plethysmographs, spirometry, and DLCO) were done using the Vmax® Encore PFT system, according to the standardized criteria [21]. The data were presented as both absolute values and as percentages of the predicted normal values, which were calculated using the reference equation provided in [22]. Each participant performed three acceptable maneuvers, and the highest value obtained was recorded and used for further analysis [21].

Lung function was classified by a respiratory care specialist according to the American Thoracic Society guidelines, with the following criteria:

1. Normal if both the forced vital capacity (FVC) and the FEV1/FVC ratio fell within the normal range.
2. Obstructive pattern if the FEV1/FVC ratio was less than 70% of the predicted normal value and the FEV1 was less than 80% of the predicted value.
3. Restrictive pattern if the FEV1/FVC ratio was at least 70% of the predicted value, and the total lung capacity (TLC) was less than 80% of the predicted value. If TLC data was unavailable, a restrictive pattern was identified based on an FVC lower than 80% of the expected value.
4. Small airway disease was diagnosed if the forced expiratory flow (FEF) between 25% and 75% of the FVC (FEF 25%-75%) was less than 65% of the predicted normal value.
5. Diffusion impairment was defined as a DLCO of 75% or less of the predicted normal values [21, 23].

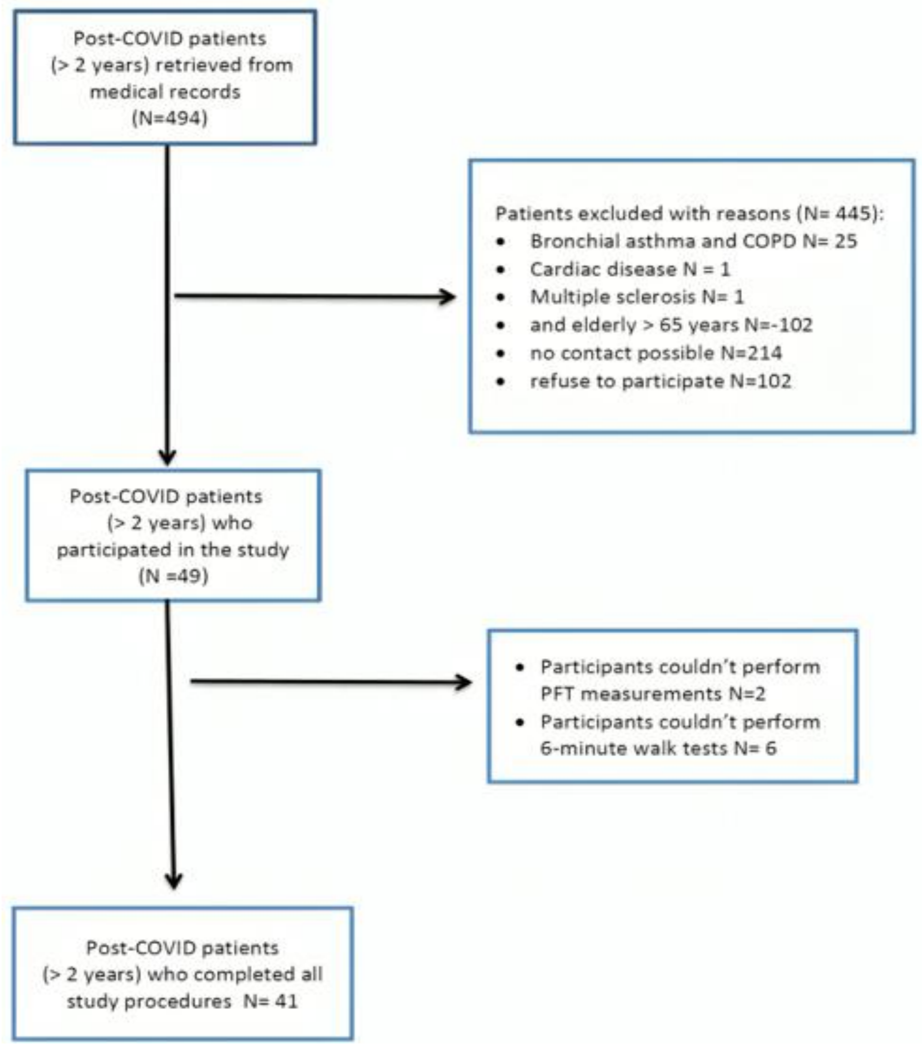

Figure 1. Participant flow charts (Source: Authors' own elaboration)

Six-Minute Walk Test

6MWT was conducted in room air under a respiratory care specialist's supervision following a standardized procedure [24]. The test entailed having the subjects walk independently in the clinic hallway for six minutes. The six-minute walk distance (6MWD) is defined as the distance covered over 6 minutes and is used as the primary outcome for functional capacity (exercise tolerance) assessment. For each patient, predicted 6MWD was calculated using a regression equation derived from the Arab population [25]. An abnormal 6MWD result was defined as a decrease of 15% below the predicted values based on age, sex, and height, or by an absolute falling below the established lower limit of normal. The lower limit of normal 6MWD values in healthy adult men and women was set at 153 meters and 139 meters, respectively, below their predicted values [26].

Statistical Analysis

Continuous variables were presented as mean (M) with standard deviation (SD) or median with interquartile range. The unpaired t-test or Mann-Whitney tests were used to compare data with normal and non-normal distribution, respectively. Paired t-test was used to compare the actual measurement with the predicted values. Categorical variables were presented as numbers and percentages and were compared using the Chi-square test. p-value < 0.05 was considered as significant.

RESULTS

Out of 454 individuals who met the eligibility criteria from the retrieved medical records, only 49 were recruited and agreed to participate. Among the recruited post-COVID-19 patients, two participants couldn't perform PFT measurements (spirometry, body plethysmography, and DLCO), and six could not perform 6-minute walk tests. All other participants completed all the tests (**Figure 1**).

Eighteen patients were hospitalized, while 31 received outpatient care during COVID-19 infection. Demographic and clinical characteristics of all participants are described in (**Table 1**).

Diffusion impairment was the most common lung function abnormality found among all post-COVID-19 patients (32%) followed by restrictive pattern (19%). Two percent showed small airway disease, and no obstructive patterns were found. However, no significant differences were reported in the PFT measurements between hospitalized and non-hospitalized post-COVID-19 patients (**Table 2**).

Table 1. Demographic and clinical characteristics of participants

Variable	N-H (N = 31)	H (N = 18)	p
Age (years) M ± SD	38.840 ± 14.799	46.720 ± 14.692	0.078
Sex n (%)			
Male	16 (51.6)	10 (55.6)	0.795
Female	15 (48.4)	8 (44.6)	
BMI (kg/m^2) M ± SD	31.390 ± 8.640	31.210 ± 7.810	0.942
Co-morbidities n (%)			
Diabetes	4 (13.3)	4 (22.2)	0.434
HTN	6 (20.0)	5 (27.8)	0.545
G6PD	1 (3.2)	0 (0.0)	0.452
GERD	1 (3.2)	0 (0.0)	0.452
SLE	0 (0.0)	1 (5.6)	0.192
Hyperthyroidism	1 (3.2)	0 (0.0)	0.452
Hypothyroidism	1 (3.2)	2 (11.1)	0.277
Time (month) M ± SD	38.000 ± 7.321	40.940 ± 2.990	0.119

Note. Data are presented as M ± SD & number (%); N-H: Non-hospitalized; H: Hospitalized; Time: Time since COVID-19 infection; BMI: Body mass index; HTN: Hypertension; G6PD: Glucose-6-phosphate dehydrogenase deficiency; GERD: Gastroesophageal reflux disease; & SLE: Systemic lupus erythematosus

The mean of 6MWD among all post-COVID-19 patients was significantly lower than the predicted values (M ± SD = 403.3 ± 52.8 vs. 467.9 ± 29.8 $p < 0.001$), respectively (**Figure 2**). A reduced exercise capacity (6MWD < 85% of predicted value) was found in 44% of the cases (**Table 2**).

Respiratory muscle weakness has been reported in twenty post-COVID-19 patients (41%) (**Table 2**). The measured MIPs were significantly lower than the predicted values (median [IR]: 55 [21.0] cm H_2O vs 71.8 [15.6] cm H_2O, respectively, $p < 0.001$). Similarly, the measured MEPs were significantly less than the predicted values (median [IR]: 44 [18.7] cm H_2O vs 84 [17.0] cm H_2O, respectively, $p < 0.001$) (part A in **Figure 3**).

No significant difference in both MIP and MEP between hospitalized and non-hospitalized patients (MIP median [IR]: 44.5 [21.0] cm H_2O vs. 59 [22.0] cm H2O, respectively, p = 0.517; MEP median [IR]: 48 [26.3] vs. 44 [15.5] cm H_2O, respectively p = 0.507) (part B in **Figure 3**). According to the St. George's respiratory questionnaire, dyspnea is the most experienced respiratory symptom with 42% followed by cough (22%) and wheezing is the least experienced with 8% (**Figure 4**).

Table 2. Comparison of PFT measurements between hospitalized and non-hospitalized post-COVID-19 patients with pulmonary function impairment patterns among whole cohort

Variable	N-H	H	p
PFT measurements (M ± SD)			
FEV1 liters	2.69 ±0.90	2.68±0.69	0.972
FVC liters	3.51 ± 0.96	3.55 ± 0.76	0.897
FEV1/FVC	76.3 ± 15.2	76.13 ±13.37	0.964
PEF L/sec	4.78 ±2.65	4.28 ±1.89	0.514
FEF25-75 L/sec	2.8 ± 1.18	2.84 ±1.2	0.903
TLC liters	5.45 ±1.14	4.94 ± 0.99	0.135
VC liters	3.69 ± 0.91	3.52 ± 0.84	0.538
DLCO mmol/kPa.min	7.48 ±1.79	6.71 ±1.98	0.185
Impairment patterns N (%)			
Obstructive		0 (0.0)	
Restrictive		9 (19.0)	
Diffusion impairment		15 (32.0)	
Small airways disease		1(2.0)	
Reduced exercise capacity*		19 (44.0)	
Respiratory muscle weakness*		20 (41.0)	

Note. Data are presented as M ± SD & number (%); N-H: Non-hospitalized; H: Hospitalized; *Reduced exercise capacity is defined as 6MWD < 85% of predicted value; *Respiratory muscle weakness was defined as % predicted MIP < 70%; FEV1: Forced expiratory volume in 1 s; FEF25-75%: FEF at 25-75% of FVC; PEF: Peak expiratory flow; & VC: Vital capacity

DISCUSSION

This cross-sectional study of post-COVID-19 patients two years after recovery identified a significant reduction in DLCO, TLC, and/or FVC below the normal predicted values in about one-fourth of post-COVID-19 patients reflecting diffusion impairment and restrictive lung patterns, respectively. Around 40% of post-COVID-19 patients exhibited reduced exercise capacity (6MWD < 85% of predicted value) with a significant reduction in MIP below normal predicted values indicating respiratory muscle weakness. About 42% of post-COVID-19 patients showed persistent dyspnea followed by cough (22%) after two years.

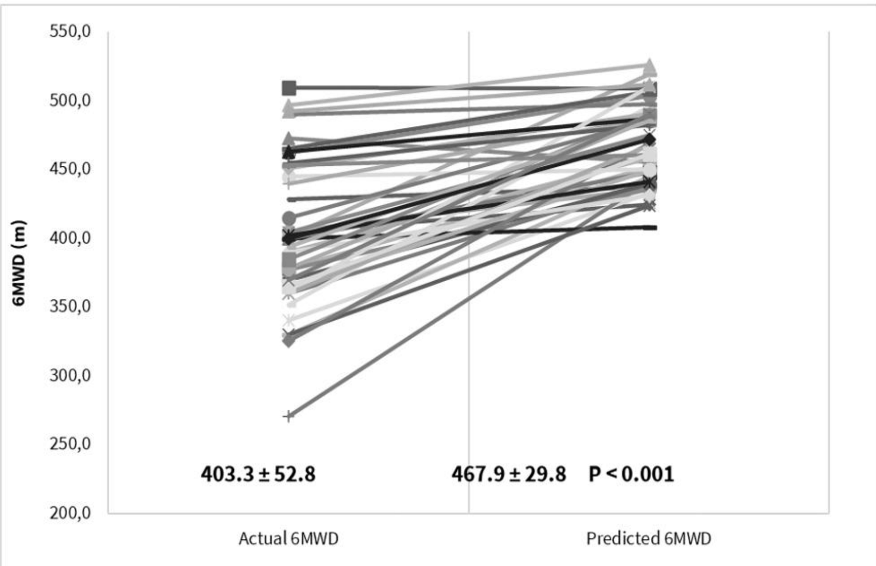

Figure 2. Actual (M ± SD, 403.3 ± 52.8) and predicted (M ± SD, 467.9 ± 29.8) 6MWD of the whole sample (43 patients who completed 6MWT) and p < 0.001 (paired t-test) (Source: Authors' own elaboration)

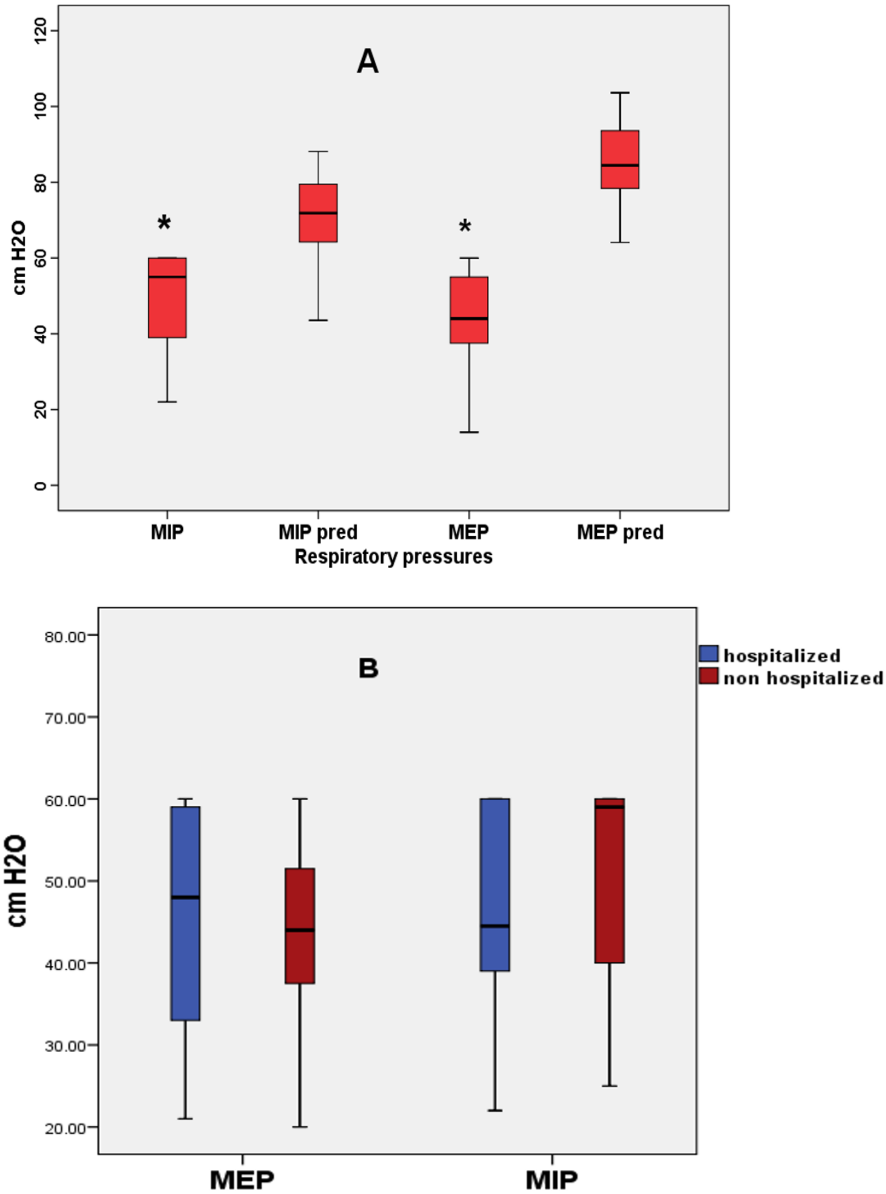

Figure 3. Comparison of (A) MIP and MEP with the predicted values and (B) MIP and MEP between hospitalized and non-hospitalized patients (Source: Authors' own elaboration)

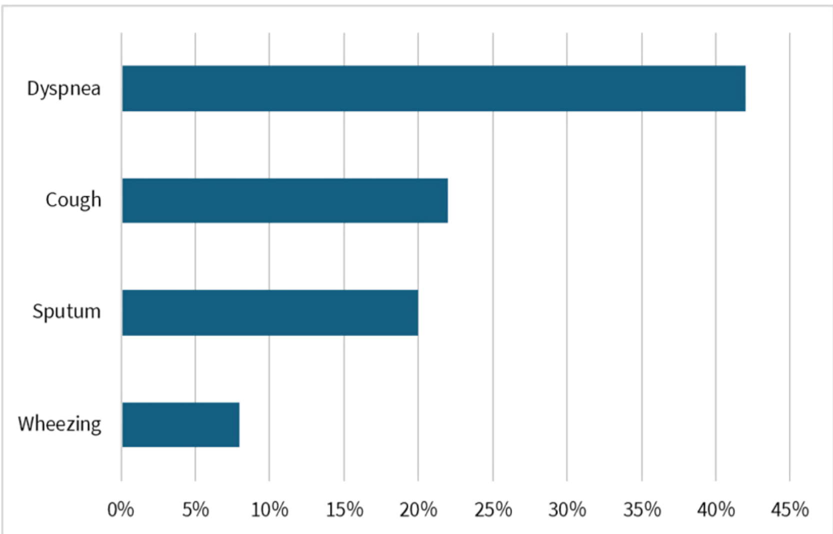

Figure 4. Percentage of patients having respiratory symptoms according to the St. George's respiratory questionnaire (Source: Authors' own elaboration)

This study is one of a few studies that observed patients after two years of COVID-19 infection, and the first in Saudi Arabia to track COVID-19 patients for this duration. A significant reduction in DLCO, FVC, and TLC below the normal values was documented in hospitalized and non-hospitalized patients. This aligns with a recent systematic review and meta-analysis, which included 30 studies with follow-up periods ranging from 6 to 12 months. The most common abnormality observed in PFT was impaired diffusion capacity affecting 35% of patients, followed by 13% of restrictive pulmonary dysfunction determined as reduced FVC/TLC [27]. Another recent systematic review and multicenter cohort study found that low DLCO (diffusion impairment) was more commonly observed 3-6 months after acute COVID-19 than low FVC (restrictive pattern) [28].

Similarly, around two-thirds of individuals who recovered from COVID-19 showed impaired diffusion capacity 12 months after discharge. Although diffusion capacity improved during the first 6 months of post-hospitalization, no further improvement was seen thereafter [29]. Furthermore, a persistent defect in DLCO with impaired gas diffusion was observed in about 47% of COVID-19 patients 2-6 months after admission, followed by a restrictive pattern (14%) [30]. These lung function impairments were also reported at a two-year follow-up longitudinal cohort study of COVID-19 survivors. A significantly higher proportion of post-COVID-19 patients showed lung diffusion impairment (65%), reduced residual volume (62%), and reduced TLC (39%), with no airflow obstruction, compared to matched controls [31]. In contrast, some studies had also reported obstructive impairment with small airway involvement. However, airway obstruction was neither frequent nor detected during early periods after recovery and improved thereafter[14].

The primary mechanism believed to contribute to restrictive lung impairment is alveolar injury. COVID-19 has the potential to damage the alveoli and activate profibrotic pathways, similar to those seen in idiopathic pulmonary fibrosis, which can ultimately lead to pulmonary fibrosis, particularly in individuals with a genetic predisposition. Although treatments aimed at mitigating COVID-19-induced lung damage may help alleviate some of these effects, the long-term outcomes are still uncertain. As a result, post-COVID-19 patients are at increased risk of developing pulmonary fibrosis [32, 33]. In contrast, abnormalities in diffusion capacity appear to be more closely linked to endothelial damage in the lungs, rather than to the diffusive properties of the alveolar membrane itself [34].

Also, this study reported a reduced exercise capacity (6MWD < 85% of predicted value) in about 44% of post-COVID-19 patients. Patients with post-COVID-19 syndrome experience decreased maximal and submaximal physical performance, along with limitations in their quality of life. A recent longitudinal follow-up study reported that it persistently reduced 6MWD in about 8% of COVID-19 survivors at two years compared to (14%) six months after the initial infection [31]. Additionally, 25% of post-COVID-19 patients showed less than 75% of the predicted 6MWD value [35]. Another study showed a significant reduction in functional capacity and increased exertional desaturation among patients with persistent dyspnea compared to patients without persistent dyspnea [36].

Numerous studies have explored the potential mechanisms behind the long-term decline in exercise capacity among post-COVID-19 patients. Several factors contributing to this reduction were identified, including impaired pulmonary function, decreased skeletal muscle mass (sarcopenia), and evidence of respiratory muscle dysfunction [12].

The current study showed a significant reduction in the MIP and MEP than the predicted values in hospitalized and non-hospitalized patients. This is consistent with the results reported in [37], where reduced MIP were found in hospitalized patients (88%), and non-hospitalized patients (65%). Also impaired respiratory muscle function was linked to exercise-induced oxygen desaturation, limited exercise tolerance, low physical activity, and reduced score on the post-COVID-19 functional status scale [38]. Another study found significant impairment in inspiratory muscle function, even though lung function tests and chest imaging (CT or X-ray) appeared normal. A reduction in MIP was closely linked to the severity of dyspnea, regardless of the time elapsed since the acute phase of COVID-19 [38].

Additionally, postmortem findings in critically ill patients with COVID-19 showed evidence for SARS-CoV-2 viral RNA in the diaphragm with activation of fibrosis pathways (fibroblast growth factor signaling) [39]. Besides growing pieces of evidence about pulmonary parenchymal and cardiac complications, exercise intolerance in patients with long-COVID-19 may also stem from other factors, including impaired respiratory muscle function and sarcopenia of skeletal muscles [12].

Nearly 40% of our patients had dyspnea after 2 years of COVID-19. Several studies reported similar findings with a predominance of persistent dyspnea among post-COVID-19 patients followed by cough [35]. Dyspnea was reported in 49% of patients at 3 months and in 46% at 12 months after recovering from COVID-19. About 24% of patients experienced a significant deterioration in their dyspnea symptoms [40].

Limitations of the Study and Future Research

The relatively small sample size due to challenges in reaching participants for follow-up after two years represents a potential limitation to the current study, which limited the generalization of the results and may not fully represent the true incidence of the long-term functional impairment. The cross-sectional design adds a further limitation to concluding a causal relationship. Thus, we recommend employing longitudinal studies with a larger sample size to elucidate the causal relationship between COVID-19 and the long-term sequelae at different time intervals.

CONCLUSION

In conclusion, about forty percent of post-COVID-19 patients had persistent dyspnea, low exercise capacity, and respiratory muscle weakness two years after recovery, with significant lung restriction and reduced diffusion capacity. This study points towards the implication of respiratory muscle dysfunction as a novel aspect of COVID-19 sequelae that might explain the associated restrictive pulmonary impairment and reduced exercise capacity. Thus, we strongly advocate for yearly lung function testing follow-up and proper rehabilitation programs designed for post-COVID-19 patients to monitor the progression of the disease and avoid any undesirable consequences

Author contributions: AMS: conceptualization, methodology, formal analysis, writing the original draft, & supervision; **NAK**: methodology, investigation, writing the original draft, & supervision; **MAO & MAH & NA & HA & AAO**: methodology, Investigation, formal analysis, & writing the original draft; **AAH & KA & LA**: data curation, supervision, & writing original draft; **TY**: conceptualization, methodology, writing the original draft, & supervision. All authors have agreed with the results and conclusions.

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Ethical statement: The authors stated that the study was approved by the Institutional Review Board at Imam Abdulrahman Bin Faisal University on 17 October 2023 with approval number IRB-UGS-2023-01-385. Written informed consents were obtained from the participants.

Declaration of interest: No conflict of interest is declared by the authors.

Data sharing statement: Data supporting the findings and conclusions are available upon request from the corresponding author.

REFERENCES

1. Antar AAR, Peluso MJ. CROI 2024: Acute and post-acute COVID-19. Top Antivir Med. 2024;32(4):523-41.
2. Chairul AN, Arif NMA, Astria NN, Setyarina I, Reviany VN. Curcumin from curcuma longa L. as dual inhibitors against Indonesian SARS-CoV-2 isolates: A molecular docking study. Pharmacogn J. 2023;15(1):228-32. https://doi.org/10.5530/pj.2023.15.34
3. Davis HE, McCorkell L, Vogel JM, Topol EJ. Long COVID: major findings, mechanisms and recommendations. Nat Rev Microbiol. 2023;21(3):133-46. https://doi.org/10.1038/s41579-022-00846-2 PMid:36639608 PMCid:PMC9839201
4. Ballering AV, van Zon SKR, olde Hartman TC, Rosmalen JGM. Persistence of somatic symptoms after COVID-19 in the Netherlands: An observational cohort study. Lancet. 2022;400(10350):452-61. https://doi.org/10.1016/S0140-6736(22)01214-4 PMid:35934007
5. Han Q, Zheng B, Daines L, Sheikh A. Long-term sequelae of COVID-19: A systematic review and meta-analysis of one-year follow-up studies on post-COVID symptoms. Pathogens. 2022;11(2):269. https://doi.org/10.3390/pathogens11020269 PMid:35215212 PMCid:PMC8875269
6. Shah AS, Wong AW, Hague CJ, et al. A prospective study of 12-week respiratory outcomes in COVID-19-related hospitalisations. Thorax. 2021;76(4):402-4. https://doi.org/10.1136/thoraxjnl-2020-216308 PMid:33273023
7. Wu X, Liu X, Zhou Y, et al. 3-month, 6-month, 9-month, and 12-month respiratory outcomes in patients following COVID-19-related hospitalisation: A prospective study. Lancet Respir Med. 2021;9(7):747-54. https://doi.org/10.1016/S2213-2600(21)00174-0 PMid:33964245
8. Serviente C, Decker ST, Layec G. From heart to muscle: Pathophysiological mechanisms underlying long-term physical sequelae from SARS-CoV-2 infection. J Appl Physiol. 2022;132(3):581-92. https://doi.org/10.1152/japplphysiol.00734.2021 PMid:35019775 PMCid:PMC8873035
9. Ferreira EVM, Oliveira RKF. Mechanisms of exercise intolerance after COVID-19: New perspectives beyond physical deconditioning. J Bras Pneumol. 2021;47(5):e20210406. https://doi.org/10.36416/1806-3756/e20210406 PMid:34878057 PMCid:PMC9013534
10. Soares MN, Eggelbusch M, Naddaf E, et al. Skeletal muscle alterations in patients with acute COVID-19 and post-acute sequelae of COVID-19. J Cachexia Sarcopenia Muscle. 2022;13(1):11-22. https://doi.org/10.1002/jcsm.12896 PMid:34997689 PMCid:PMC8818659
11. Joseph P, Singh I, Oliveira R, et al. Exercise pathophysiology in myalgic encephalomyelitis/chronic fatigue syndrome and postacute sequelae of SARS-CoV-2: More in common than not? Chest. 2023;164(3):717-26. https://doi.org/10.1016/j.chest.2023.03.049 PMid: 37054777 PMCid:PMC10088277
12. Ribeiro Baptista B, d'Humières T, Schlemmer F, et al. Identification of factors impairing exercise capacity after severe COVID-19 pulmonary infection: A 3-month follow-up of prospective COVulnerability cohort. Respir Res. 2022;23:68. https://doi.org/10.1186/s12931-022-01977-z PMid:35317815 PMCid:PMC8938727
13. Logue JK, Franko NM, McCulloch DJ, et al. Sequelae in Adults at 6 Months After COVID-19 Infection. JAMA Netw Open. 2021;4(2):e210830-e. https://doi.org/10.1001/jamanetworkopen.2021.0830 PMid:33606031 PMCid: PMC7896197
14. Salem AM, Al Khathlan N, Alharbi AF, et al. The long-term impact of COVID-19 pneumonia on the pulmonary function of survivors. Int J Gen Med. 2021;14:3271-80. https://doi.org/10.2147/IJGM.S319436 PMid:34267545 PMCid: PMC8276825
15. van Voorthuizen EL, van Helvoort HAC, Peters JB, van den Heuvel MM, van den Borst B. Persistent exertional dyspnea and perceived exercise intolerance after mild COVID-19: A critical role for breathing dysregulation? Phys Ther. 2022;102(10):pzac105. https://doi.org/10.1093/ptj/pzac105 PMid:35900016 PMCid:PMC9384552
16. Ferrer M, Villasante C, Alonso J, et al. Interpretation of quality of life scores from the St George's respiratory questionnaire. Eur Respir J. 2002;19(3):405-13. https://doi.org/10.1183/09031936.02.00213202 PMid: 11936515
17. Gil Obando LM, López López A, Avila CL. Normal values of the maximal respiratory pressures in healthy people older than 20 years old in the City of Manizales–Colombia. Colomb Med. 2012;43(2):119-25. https://doi.org/10.25100/cm.v43i2.1141
18. Evans JA, Whitelaw WA. The assessment of maximal respiratory mouth pressures in adults. Respir Care. 2009;54(10):1348-59.
19. Bairapareddy KC, Augustine A, Alaparthi GK, et al. Maximal respiratory pressures and maximum voluntary ventilation in young Arabs: Association with anthropometrics and physical activity. J Multidiscip Healthc. 2021;14:2923-30. https://doi.org/10.2147/JMDH.S333710 PMid:34703244 PMCid:PMC8524059
20. Hamazaki N, Kamiya K, Matsuzawa R, et al. Prevalence and prognosis of respiratory muscle weakness in heart failure patients with preserved ejection fraction. Respir Med. 2020;161:105834. https://doi.org/10.1016/j.rmed.2019.105834 PMid:31783270
21. Graham BL, Steenbruggen I, Miller MR, et al. Standardization of spirometry 2019 update. An official American Thoracic Society and European Respiratory Society technical statement. Am J Respir Crit Care Med. 2019;200(8):e70-88. https://doi.org/10.1164/rccm.201908-1590ST PMid:31613151 PMCid:PMC6794117
22. Hankinson JL, Odencrantz JR, Fedan KB. Spirometric reference values from a sample of the general U.S. population. Am J Respir Crit Care Med. 1999;159(1):179-87. https://doi.org/10.1164/ajrccm.159.1.9712108 PMid: 9872837

23. Stanojevic S, Kaminsky DA, Miller MR, et al. ERS/ATS technical standard on interpretive strategies for routine lung function tests. Eur Respir J. 2022;60(1):2101499. https://doi.org/10.1183/13993003.01499-2021 PMid:34949706
24. ATS Committee on Proficiency Standards for Clinical Pulmonary Function Laboratories. ATS statement: Guidelines for the six-minute walk test. Am J Respir Crit Care Med. 2002;166(1):111-7. https://doi.org/10.1164/ajrccm.166.1.at1102 PMid:12091180
25. Alameri H, Al-Majed S, Al-Howaikan A. Six-min walk test in a healthy adult Arab population. Respir Med. 2009; 103(7):1041-6. https://doi.org/10.1016/j.rmed.2009.01.012 PMid:19230640
26. Enright PL, Sherrill DL. Reference equations for the six-minute walk in healthy adults. Am J Respir Crit Care Med. 1998;158(5 Pt 1):1384-7. https://doi.org/10.1164/ajrccm.158.5.9710086 PMid:9817683
27. Lee JH, Yim JJ, Park J. Pulmonary function and chest computed tomography abnormalities 6-12 months after recovery from COVID-19: A systematic review and meta-analysis. Respir Res. 2022;23(1):233. https://doi.org/10.1186/s12931-022-02163-x PMid:36068582 PMCid:PMC9446643
28. Cornelissen MEB, Leliveld A, Baalbaki N, et al. Pulmonary function 3-6 months after acute COVID-19: A systematic review and multicentre cohort study. Heliyon. 2024;10(6): e27964. https://doi.org/10.1016/j.heliyon.2024.e27964 PMid:38533004 PMCid:PMC10963328
29. Kang A, Regmi B, Cornelissen C, et al. Persistence of diffusion capacity impairment and its relationship with dyspnea 12 months after hospitalization for COVID-19. J Clin Med. 2024;13(5):1234. https://doi.org/10.3390/jcm13051234 PMid:38592095 PMCid:PMC10931668
30. Long Q, Li J, Hu X, Bai Y, Zheng Y, Gao Z. Follow-ups on persistent symptoms and pulmonary function among post-acute COVID-19 patients: A systematic review and meta-analysis. Front Med (Lausanne). 2021;8:702635. https://doi.org/10.3389/fmed.2021.702635 PMid:34540862 PMCid:PMC8448290
31. Huang L, Li X, Gu X, et al. Health outcomes in people 2 years after surviving hospitalisation with COVID-19: A longitudinal cohort study. Lancet Respir Med. 2022;10(9): 863-76. https://doi.org/10.1016/S2213-2600(22)00126-6 PMid:35568052
32. Fumagalli A, Misuraca C, Bianchi A, et al. Pulmonary function in patients surviving to COVID-19 pneumonia. Infection. 2021;49(1):153-7. https://doi.org/10.1007/s15010-020-01474-9 PMid:32725597 PMCid:PMC7386387
33. Singh SJ, Baldwin MM, Daynes E, et al. Respiratory sequelae of COVID-19: Pulmonary and extrapulmonary origins, and approaches to clinical care and rehabilitation. Lancet Respir Med. 2023;11(8):709-25. https://doi.org/10.1016/S2213-2600(23)00159-5 PMid:37216955
34. Imeri G, Conti C, Caroli A, et al. Gas exchange abnormalities in Long COVID are driven by the alteration of the vascular component. Multidiscip Respir Med. 2024;19(1):938. https://doi.org/10.5826/mrm.2024.938 PMid:38577738 PMCid:PMC10968839
35. Polese J, Ramos AD, Moulaz IR, et al. Pulmonary function and exercise capacity six months after hospital discharge of patients with severe COVID-19. Braz J Infect Dis. 2023; 27(4):102789. https://doi.org/10.1016/j.bjid.2023.102789 PMid:37442195 PMCid:PMC10403708
36. Cortés-Telles A, López-Romero S, Figueroa-Hurtado E, et al. Pulmonary function and functional capacity in COVID-19 survivors with persistent dyspnoea. Respir Physiol Neurobiol. 2021;288:103644. https://doi.org/10.1016/j.resp.2021.103644 PMid:33647535 PMCid:PMC7910142
37. Hennigs JK, Huwe M, Hennigs A, et al. Respiratory muscle dysfunction in long-COVID patients. Infection. 2022;50(5): 1391-7. https://doi.org/10.1007/s15010-022-01840-9 PMid:35570238 PMCid:PMC9108020
38. Nagel C, Olschewski H, Sorichter S, et al. Impairment of Inspiratory Muscle Function after COVID-19. Respiration. 2022;101(11):981-9. https://doi.org/10.1159/000527361 PMid:36310021
39. Shi Z, de Vries HJ, Vlaar APJ, et al. Diaphragm pathology in critically Ill patients with COVID-19 and postmortem findings from 3 medical centers. JAMA Intern Med. 2021;181(1):122-4. https://doi.org/10.1001/jamainternmed.2020.6278 PMid:33196760 PMCid:PMC7670391
40. Grewal JS, Carlsten C, Johnston JC, Shah AS, Wong AW, Ryerson CJ. Post-COVID dyspnea: Prevalence, predictors, and outcomes in a longitudinal, prospective cohort. BMC Pulm Med. 2023;23(1):84. https://doi.org/10.1186/s12890-023-02376-w PMid:36907855 PMCid:PMC10008721