International Journal of General Medicine | Dovepress

Open Access Full Text Article | REVIEW

A Narrative Review of Impact of Incentive Spirometer Respiratory Training in Long COVID

Yao-Hsiang Chen[1,2], Yu-Shan Hsieh[2]

[1]Department of Nursing, Tri-Service General Hospital Songshan Branch, Taipei City, Taiwan; [2]School of Nursing, National Taipei University of Nursing and Health Sciences, Taipei City, Taiwan

Correspondence: Yu-Shan Hsieh, National Taipei University of Nursing and Health Sciences, No. 365, Ming-te Road, Peitou Dist, Taipei City, 112303, Taiwan, Tel +886-2-28227101, Email 228455300teresa@gmail.com

Abstract: Long COVID refers to symptoms that appear 3 months after initial infection with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), the causative virus of Coronavirus disease 2019 (COVID-19), and last for at least 2 months, not attributable to other diagnoses. This health issue significantly burdens patients' quality of life, the economy, and society. Improving the af-termath of COVID-19 is a crucial global health issue in the post-pandemic era. According to current results, it is evident that developing a simple, low-cost respiratory training method that can be easily used at home by themselves with long Coronavirus disease 2019 symptoms (long COVID) is an important and urgent issue. The incentive spirometer is widely used in physical, speech, and respiratory therapy, as well as in preventing postoperative pulmonary infections and improving sputum clearance. However, to date, the role of incentive spirometer respiratory training in long COVID symptoms is still limited. In this literature review is presented to explore the effectiveness of incentive spirometer respiratory training in alleviating symptoms among individuals recovering from long COVID. We also compile non-invasive assessment methods, with the aim to enable individuals to undergo training and assessments conveniently at home or in the community. In this review, a literature review approach was utilized to explore the effectiveness of incentive spirometer intervention in alleviating long-term COVID symptoms. This study is to synthesize the findings of articles published during January 2019 and December 2023 retrieved from PubMed/CINAHL/MEDLINE/ Google Scholar without re-strictions on study type. We ultimately identified seven articles and have summarized similar past studies. This review could contribute to improving symptoms related to long COVID by incentive spirometer respiratory training and serve as practical reference material for clinical medical staff and provide insights for healthcare policymakers in de-veloping guidelines for future research directions, clinical guidance, and educational strategies in the context of nursing care.

Keywords: COVID-19, long COVID, incentive spirometer respiratory training, respiratory training, incentive Spirometer

Introduction

The coronavirus disease (COVID-19) pandemic, the most significant public health crisis of the 21st century, has rapidly spread worldwide, with more than 7.8 billion confirmed cases by the end of July 2024. In Taiwan, 140.9 million confirmed cases have occurred, as well as instances of reinfection.[1] After Taiwan's COVID-19 expenses were reclassified under the National Health Insurance coverage on March 20, 2023 within just nine months, the expenditure on Western medicine primary care for addressing post-COVID care increased by 0.3 million USD, and hospital medical expenses increased by 10.3 million USD.[2]

In the United Kingdom, statistics indicate that the cost of primary healthcare services within 12 weeks post-COVID-19 infection is approximately £2.44 to £5.72 (3.17 to 7.43 US dollar) per person. Within a year, patients who had contracted COVID-19 experienced a 22.7% increase in primary healthcare consultations. The national cost for primary healthcare consultations to support long-term COVID-19 patients is estimated to be around £23 million, but it could approach £60 million,[3] another statistics from the United States show that the monthly medical expenses increase by an additional $223.60 following a diagnosis of COVID-19.[4] It is evident that the cost incurred by countries for post-treatment of COVID-19 is extremely substantial.

Received: 23 August 2024
Accepted: 5 November 2024
Published: 13 November 2024

However, challenges persist with the emergence of long-term complications associated with COVID-19, termed “long COVID” by the World Health Organization (WHO). Long COVID refers to symptoms that appear 3 months after initial infection with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), the causative virus of COVID-19, and last for at least 2 months, not attributable to other diagnoses. Long COVID has a chronic impact on multiple organ systems, with symptoms including fatigue, cognitive impairment, chest tightness, palpitations, respiratory difficulties, and depression.[5] Statistics from 2021 indicate that up to 80% of individuals experience symptoms related to long COVID, with less than 1% achieving complete recovery within 80 days of SARS-CoV-2 infection.[6] Despite continuous efforts by healthcare professionals to identify suitable treatments, there is currently no confirmed medication to effectively prevent or reduce the sequelae of COVID-19. This health issue significantly burdens individuals’ quality of life, the economy, and society. Improving the aftermath of COVID-19 is a crucial global health issue in the post-pandemic era.[7]

According to current results, it is evident that developing a simple, low-cost respiratory training method that can be easily used at home by those with long COVID symptoms is an important and urgent issue.

In the 1960s, Bartlett et al observed the potential benefits of yawning on postoperative patients’ lungs, leading to the development of the tool to respiratory training. Over the years, it evolved into the incentive spirometer, a tool designed to train inspiratory muscles commonly used in preventive role in atelectasis after cardiac surgery.[8] It guides patients to take maximal inhalation, mimicking deep breaths taken during yawning or sighing, stretching the lungs, and dilating the airways. Alexandra et al stated that it can provide information about the patient’s inspiratory effort by measuring the airflow (FEV1) and air volume (FVC).[9] Due to its low cost and user-friendliness, the training intensity can be adjusted according to the patient’s condition through duration and intensity, ensuring high safety.[9] However, to date, the role of incentive spirometer respiratory training in long COVID symptoms is still limited. Thus, this review presents an extensive exploration of existing literature to explore the effectiveness of incentive spirometer respiratory training in alleviating symptoms among individuals recovering from long COVID. Additionally, non-invasive assessment methods are compiled with the aim to assessment the effect of effectiveness of incentive spirometer respiratory training.

Methods

Definition

Long COVID reflects chronic damage to multiple organ systems, with fatigue and dyspnea being the most prevalent symptom cognitive impairment (commonly described as brain fog), muscle pain, palpitations, anxiety, chest pain, and arthralgia.[5] Even individuals with mild or asymptomatic SARS-CoV-2 infection may experience long COVID symptoms, which encompass a broad range, including fatigue, headache, sleep disturbance, anxiety, and depression, and manifestations in specific organ systems such as cardiovascular and neurological systems. These symptoms may emerge newly after the acute phase recovery from COVID-19 or persist following the initial diagnosis, exhibiting fluctuations over time or relapses. Scholars, such as O’ Mahony et al, note that a substantial number of patients experience long COVID symptoms for more than a year.[10]

Approximately 29% of patients experience shortness of breath 14–21 days after recovery, around 43% continue to have persistent cough, and 20% report lung pain. Patients commonly report chest tightness during speaking or physical activities. These symptoms significantly impact patients’ work and daily activities, leading to lifestyle changes and an increased likelihood of stress, depression, irritability, and insomnia, which represent a substantial cost burden on both primary and secondary healthcare.[11]

Search Strategy

In this review, a literature review approach was utilized to explore the effectiveness of IS intervention in alleviating long-term COVID symptoms. This review is to synthesize the findings of articles published during January 2019 and December 2023 retrieved from PubMed/CINAHL/MEDLINE/ Google Scholar without re-strictions on study type. The search keywords included: COVID-19, COVID, SARS-CoV-2, Post-Acute COVID-19 Syndrome, Dyspnea, pulmonary complications, Incentive Spirometer, breathing training, Pulmonary rehabilitation, Breathing Exercises, and Respiratory rehabilitation. The references were checked, and the titles and abstracts of the references were searched to identify studies that met the following inclusion criteria: (1) participants had COVID-19 with long COVID; (2) quantitative or qualitative measure of the lung function; and (3) reported clinical research (case report, case series, observative study, or clinical trial). After locating the literature that met these criteria, additional material was identified and examined, before being rechecked by the 2-author involved in this study. References were selected and reviewed based on their relevance to the topics covered in this article. Also non-invasive assessment methods are compiled, with the aim to provide insights for future clinical practice to address and improve long COVID symptoms. Results retrieved from Google Scholar were a variety of types of formats: some were media releases, news chapters or personal opinion, many articles retrieved had been published in nonrefereed journals and were therefore excluded. The PRISMA flow chart was presented in Figure 1 (Figure 1).

Results

Effects of Long COVID-19 on the Respiratory System

The respiratory system is well known to be the most severely affected by acute COVID-19, with patients experiencing sustained respiratory impairment even after discharge. Recovery in the post-acute period also requires more time. Although the exact cause is unclear, respiratory difficulties induced by COVID-19 affect patients' quality of life. Therefore, following recovery from COVID-19, patients require safe and effective rehabilitation strategies to cope with this global health and economic crisis.[12]

Previous studies have demonstrated that pulmonary function tests (PFT) and chest computed tomography results remain abnormal several months after COVID-19 diagnosis, with the most common abnormality being diffusion impairment, followed by restrictive ventilatory impairment.[9] Indeed, combining findings from previous research on SARS-CoV-2 infection, patients may experience persistent respiratory impairment for months or even years after discharge,[10] with issues such as cough, dyspnea, fatigue, and decreased lung function reported up to 8 weeks after recovery. Ma et al, in a systematic review, pointed out that statistical data shows significant differences in lung function tests at 6 and 12 months after contracting COVID-19, with results such as forced expiratory volume in one second < 80%, vital capacity < 80%, and Diffusion capacity of carbon monoxide < 80%.[13]

Previous studies have focused on the prevention and acute-phase treatment of COVID-19. Although organizations such as the WHO, the Chinese Medical Association of Rehabilitation, and the European Respiratory Society/American Thoracic Society have issued COVID-19 recovery guidelines, there remains a lack of specific recommendations for non-

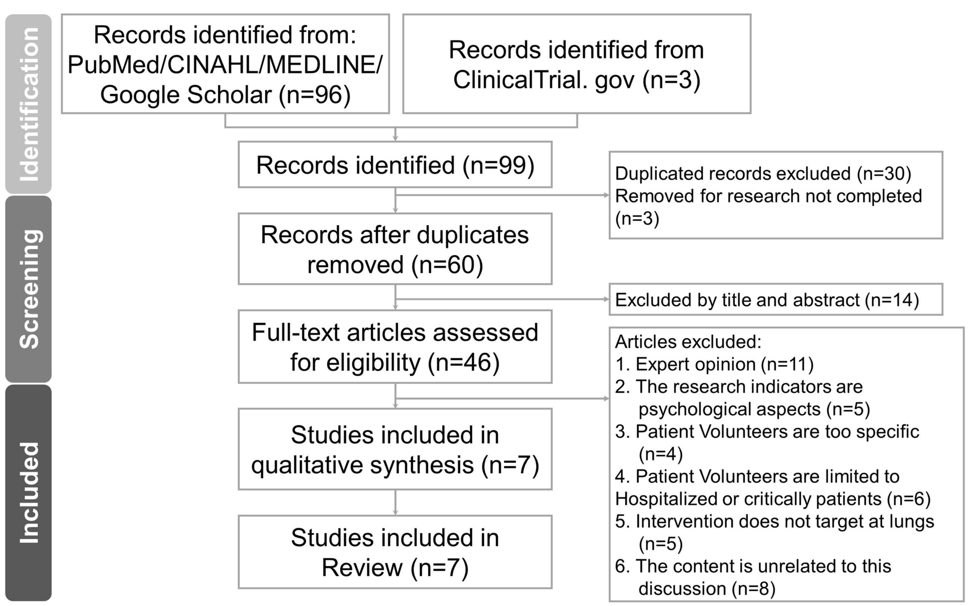

Figure 1 PRISMA flow chart in this study.

invasive treatment and evaluative methods for long COVID. Given that pulmonary respiratory training has been proven to alleviate respiratory difficulty and fatigue while enhancing self-management capabilities in patients with pulmonary diseases (eg, interstitial lung disease and chronic obstructive pulmonary disease), it is also recommended to improve respiratory-related symptoms in long COVID.[11] Existing studies also suggest short-term benefits of pulmonary respiratory training for patients, with no adverse events reported thus far.[14] However, these recommendations are based on expert consensus, and research evidence and clinical data still need to be improved.[3] Continuous research is essential to ensure long-term effectiveness and determine the optimal training methods.[12]

Respiratory Training in Long COVID

Pulmonary Rehabilitation in Long COVID

Previous study show that pulmonary rehabilitation has proven to be beneficial for patients with chronic obstructive pulmonary disease (COPD) and asthma. Within the limited scope of research, evidence suggests that for individuals without contraindications to exercise therapy, using an exercise-based rehabilitation program (adaptive pulmonary rehabilitation) for patients recovering from COVID-19 may be beneficial in alleviating symptoms of respiratory distress. Pulmonary rehabilitation reduces respiratory symptoms and enhances exercise tolerance.[12] Such improvements may be associated with chest expansion and respiratory muscle stretching during deep breathing exercises, leading to more effective breathing patterns, increased respiratory muscle strength, and improved lung compliance in post-recovery impact of COVID-19.[15] Research has demonstrated that Incentive spirometer can significantly improve lung function and reduce complications such as pneumonia and pulmonary insufficiency.[16]

Whole-body intensity training can be challenging for many patients with pulmonary diseases. These patients may find such training extremely difficult, particularly when lung capacity is severely limited. They may also experience exercise-induced hypoxemia/hypercapnia. However, a systematic review suggest that interval (aerobic) training may be slightly more effective than whole-body intensity training.[17] Although aerobic exercise has been greatly beneficial in improving cardiopulmonary fitness in past studies,[15] performing aerobic exercises might be challenging for patients with post-COVID-19 symptoms.

Studies have explored how to best address post-recovery respiratory-related sequelae in patients with COVID-19. Nopp et al conducted a 6-week pulmonary training intervention for COVID-19 survivors in Austria, with the results indicating substantial improvements in exercise capacity, functional status, respiratory difficulty, fatigue, and overall quality of life, significantly enhancing the exercise capacity of patients with long COVID.[18] Moreover, in a randomized controlled trial in China, Liu et al administered a series of respiratory muscle and diaphragmatic training exercises, along with commercial handheld resistance devices for respiratory training, to a group of elderly individuals who had recovered from COVID-19. The results showed significant improvements in lung and respiratory function, quality of life, and anxiety after 6 weeks of respiratory rehabilitation training.[19] Therefore, pulmonary rehabilitation could be an important role for individuals experiencing dyspnea in post COVID-19, with the risk level of training being relatively low.

Pulmonary rehabilitation is effective in reducing symptoms and improving health status. However, a study by Tsutsui indicated that some significant barriers to this approach have impeded its implementation in the community. These include variable use of skills by patients and inadequate resources for health professionals.[20]

Exercise-based rehabilitation programs have been reported to attenuate breathlessness in patients recovering from COVID-19.[21] At present, considerable heterogeneity exists between rehabilitation programs, but common components include aerobic/resistance exercise and symptom management. To date, the effectiveness of breathing exercises and retraining post-COVID-19 has not been clearly assessed. One review of breathing exercises for the management of asthma showed positive outcomes.[22] However, another review indicated no evidence to support the use of breathing exercises in patients with dysfunctional breathing.[23] Although the evidence remains insufficient, breathing training is considered to be potentially valuable for people who have difficulty breathing after COVID-19. The recommendations by Singh et al have indicated that further research directions can focus on breathing control, breathing pattern training, and inspiratory muscle training to determine which exercise-based rehabilitation should be delivered.[24]

The management of desaturation post-COVID-19 or in long COVID has not been widely reported to date. However, according to an official American Thoracic Society clinical practice guideline, a pragmatic approach would be to use ambulatory oxygen support in patients who benefit once underlying causes have been managed.[25] Therefore, selecting an appropriate method to train the inspiratory muscles used in pulmonary rehabilitation in post-COVID or long COVID may be important.

Incentive Spirometer Respiratory Training

Incentive spirometer, a tool designed to used in pulmonary rehabilitation. It guides patients to imitate sustained maximum inhalation, mimicking the motion of yawning, providing visual feedback to encourage and assist patients in slow and deep inhalation. This process helps the patient to open collapsed lung spaces, allowing lung expansion and airway clearance, with recent research confirming its effectiveness in increasing the maximal inspiratory volume. Owing to its low cost and user-friendly nature, the training intensity can be adjusted, through duration and intensity, based on the patient's condition, offering high safety.[26]

The incentive spirometer is a handheld mechanical breathing device that uses a one-way valve to prevent exhalation. It consists of a corrugated tube and a nozzle connected to three consecutive plastic chambers, each containing a ball (Figure 2). The external chambers are marked with the minimum flow required to raise the ball internally. The ball rises when the patient performs slow, deep breathing through the nozzle. If the patient breathes too quickly, the balls in the chambers rise to the top, and if breathing is too slow, the balls fall to the bottom. The number of increasing balls measures the volume of inhaled air. When all three balls reach the top of the chambers, the patient's flow rate can reach 1200 mL/sec. After the patient has maximized their inhalation, they are asked to hold the balls in the same position for more than 3 sec. Once inhalation is completed and maintained appropriately, the patient is instructed to remove the nozzle, allowing gravity to return the balls to their original position, completing one cycle of inspiratory training.[26,27] The incentive spirometer is widely used in physical, speech, and respiratory therapy, as well as in preventing postoperative pulmonary infections and improving sputum clearance.

Incentive Spirometer Respiratory Training in COVID-19 and Long COVID

The role of the incentive spirometer in alleviating COVID-19 symptoms is well-known, and numerous studies have also demonstrated its effectiveness in easing breathing difficulties and preventing lung collapse. Patients with COVID-19 may benefit from incentive spirometry via the improving ventilation/perfusion mismatch and alveolar-PaO_2 gradient, which are followed by reduced intrapulmonary shunting and the risk of atelectasis.[28]

Studies have demonstrated that during the COVID-19 pandemic, outpatients who used the incentive spirometer for respiratory exercises daily within 30 days of confirmed recovery experienced a significant increase (of 16%) in maximal inspiratory volume, with no reported reduction in inspiratory volume, coughing, or fever.[16] Furthermore, Garcia et al conducted a pilot study on hospitalized patients with moderate COVID-19 to evaluate whether the use of incentive spirometry demonstrated clinical significance in preventing acute respiratory distress syndrome. As a result, the participants were found to have an improved PaO_2/FiO_2 ratio, improved chest X-ray findings, shorter hospital stays, and earlier improvement of symptoms.[29]

Moreover, in the research on COVID-19 survivors, Srinivasan et al compared a respiratory physiotherapy program based on a combination of pursed lip breathing exercises and a yoga and pranayama form of breathing exercise with breathing

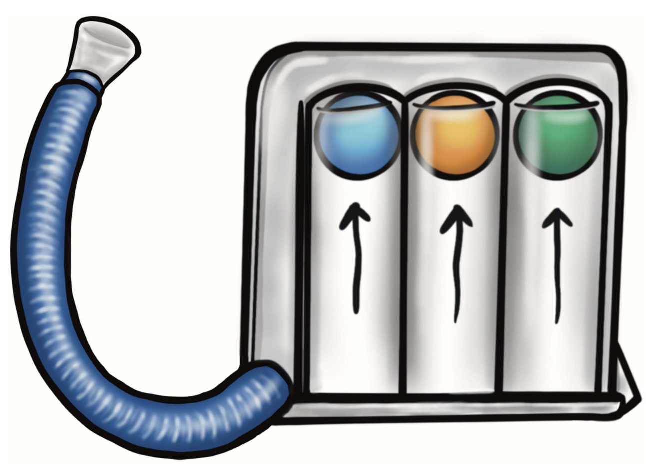

Figure 2 Structure of incentive spirometer.

exercises performed with incentive spirometry in COVID-19 survivors. The results revealed significant improvements in post-test forced expiratory volume in one second (FEV1) in both groups; however, no further training details were provided.[30]

In this section, a literature review is presented some research related to the incentive spirometer in COVID-19 in Table 1 and Supplementary Appendix. The study findings by Gudivada et al suggested that the anxiety/depression scores

Table 1 Characteristics of Included Studies in Incentive Spirometer Respiratory Training

References Study Design	Sample Size	Comparison Groups	Treatment Regimen	Outcomes
Abodonya et al. Saudi Arabia, 2021, quasi-RCT[31]	E: 21; C: 21	E: Inspiratory muscle training ang incentive spirometer exercise C: Incentive spirometer exercise	E: 6 inspiratory cycles with 5min of resisted inspiration, followed by 60-second rest time in each cycle (device-based: threshold PEP) C: NR	1. Pulmonary function (FEV1, FVC, DSI) 2. Exercise capacity (6-MWT) 3. QoL (EQ-5D-3L) 4. Dyspnea severity index (DSI)
Garcia & Sarena. Philippines, 2022, RCT[29]	10	E: Incentive spirometer C: Non- Incentive spirometer	E: Incentive spirometer C: Non- Incentive spirometer	1. Development of ARDS rate 2. Worsening of pneumonia 3. PaO2/FiO2 ratio 4. Length of stay
Srinivasan et al. India, 2021, RCT[30]	48	E: Pursed lip breathing exercise with bhastrika pranayama C: Received Incentive spirometry	E: Pursed lip breathing exercise with bhastrika pranayama for 4–5 seconds 20–25 times C: Received Incentive spirometry 5–10 times	The Pulmonary Function Testing with the FVC & FEV1
Gudivada et al. India, 2023, cross-sectional and open-label randomized interventional design[32]	100	E: Incentive spirometer C: Non- Incentive spirometer	E: Incentive spirometer C: Non- Incentive spirometer	Anxiety/depression scores and lung function
Hsu et al. Taiwan, 2022, case report[33]	NR	NR	Respiratory muscle training, chest expansion, resisted diaphragmatic training, aerobic cycle endurance training, resistance training and home exercises, including incentive spirometer training and lip breathing training.	1. Modified Borg scale (MBS) 2. Modified Medical Research Council (mMRC) 3. Chronic Obstructive Pulmonary Disease assessment test (CAT) 4. Grip strength test 5. SARC-F 6. Short Physical Performance Battery (SPPB) 7. 6-min walk test 8. Incentive spirometer to measure lung volume. 9. Barthel Index (BI) 10. Post-COVID-19 Functional Status scale (PCFS) 11. Fatigue severity scale (FSS) 12. Pittsburgh Sleep Quality Index (PSQI) 13. Beck Anxiety Inventory (BAI) 14. Taiwanese Depression Questionnaire (TDQ) 15. EuroQOL 5-level EQ-5D (EQ-5D-5L) 16. Visual analog scale (VAS) 17. World Health Organization Quality of Life-BREF (WHOQOL-BREF)
Kusumawardani et al. Indonesia, 2023, RCT[34]	E: 10; C: 10	E: Incentive spirometry exercise C: Diaphragmatic breathing exercises.	E: Incentive spirometry exercise C: Diaphragmatic breathing exercises.	1. PEF (L/min) 2. Δ PEF (L/min)
Suharti et al. Indonesia, 2022, single-blind clinical trial[35]	E: 24; C: 21	E: Incentive spirometry C: Diaphragm breathing exercise	E: Incentive spirometry C: Diaphragm breathing exercise	1. 4-meter gait time test (4MGT) 2. 30 sit-to-stand test (30STS)

Abbreviations: E, experiment group; C, control group; PEP, positive expiratory pressure; FEV1, forced expiratory volume in one second; FVC, forced vital capacity; 6-MWT, 6-min walk test; QoL, quality of life; Eq-5D-3L, EuroQuality-5Dimensions-3Levels questionnaire; DSI, dyspnea severity index; mMRC dyspnea score, modified British Medical Research Council dyspnea score; PEF, peak expiratory flow;; NR, not reported.

of COVID-19 survivors were significantly decreased with 4 weeks of incentive spirometry exercises compared to standard of care alone. Incentive spirometer-based breathing exercises for psychosomatic rehabilitation in COVID-19 survivors with persistent pulmonary dysfunction could release the dyspnea. The study indicated that clinicians must be mindful of improvements in anxiety and depression with incentive spirometer, in addition to gains in respiratory function of COVID-19 survivors.[32] In another study by Curci et al,[36] participants were managed with both breathing exercises with the pep bottle (forced inhalation/exhalation) and use of an incentive spirometer (30 min/set, 2 times a day for the duration of hospitalization); the Barthel Index, modified Medical Research Council Dyspnea Scale, 6-Minute Walking Test, Borg Rating of Perceived Exertion Scale, arterial blood gas analysis, and serum levels of laboratory markers showed improvement in the participants' post-acute COVID-19 status.[30] Interestingly, in the study by Gudivada et al, 100 patients with COVID-19 with pulmonary dysfunction were randomized (incentive spirometry vs controls), and anxiety/depression scores and lung function were reevaluated after 4 weeks. Not only was the lung function was improved but the anxiety/depression rates were also reduced with incentive spirometer-based exercises.[37]

In a case study by Hsu et al, a female patient who was severely ill and functionally dependent and required long-term oxygen therapy after recovery from COVID-19 with acute respiratory failure and extensive pulmonary fibrosis was evaluated. After two months of comprehensive pulmonary rehabilitation program, and was advised to use incentive spirometry at home daily, her physical performance, pulmonary function parameters, and activities of daily living rapidly improved.[33] Furthermore, Kusumawardani et al compared ten COVID-19 survivors in an experimental group who performed incentive spirometry exercise and ten survivors in a control group who performed diaphragmatic breathing exercises. Both exercises were performed five times daily, with ten repetitions each for four weeks.[37]

The results indicated a significant increase in peak expiratory flow in the experimental group. Incentive spirometry exercise could be an alternative therapy to improve the pulmonary function of COVID-19 survivors[34] (Figure 3).[29–35]

At present, few studies have investigated the symptoms of long COVID or in COVID-19 survivors. Moreover, establishing the role of incentive spirometry in subsequent rehabilitation treatment remains a critical issue. The use of an incentive spirometer in long-term COVID may represent a worthwhile cost-saving intervention.[38] However, it is important to ensure proper training and technique. The use of an incentive spirometer in patients with long COVID patients may help improve how clinical nurses care for this patient population. In addition to determining the role of the incentive spirometer in long COVID, it is also important to effectively assess its effectiveness.

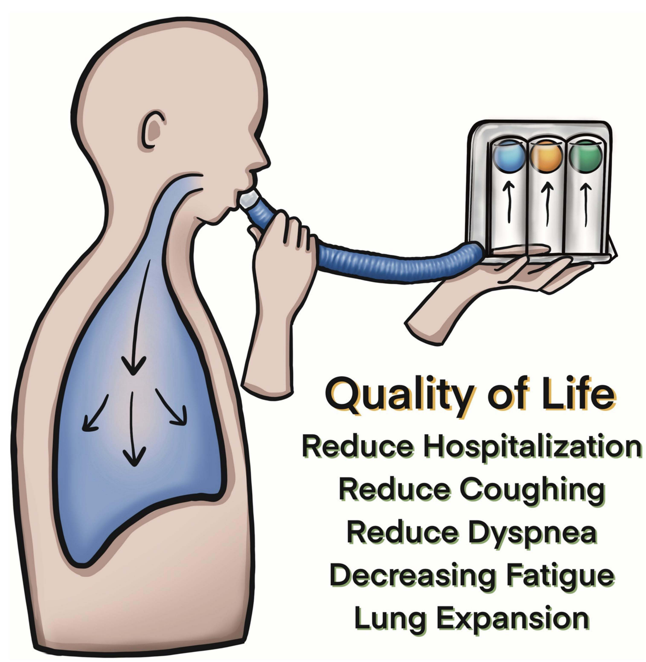

Figure 3 Benefits of Incentive Spirometer respiratory rehabilitation.

However, several studies have been published that take the opposite view as to whether incentive spirometer actually has benefits in patients with COVID-19.

Other Opinions Related to Incentive Spirometry for Patients with COVID-19 and Long COVID

Studies from both China[39] and Italy[40] have suggested that to avoid aggravating respiratory distress, early respiratory rehabilitation should not be initiated. For critical inpatients, the early performance of pulmonary rehabilitation is also not recommended.[41] Even in the acute phase, incentive spirometry, respiratory muscle training, and aerobic exercise are not recommended to avoid lung injury.[40] However, in the post-acute phase, inspiratory muscle training should be included if the inspiratory muscles are weak.[42] In fact, there are still no significant results demonstrating organ injury resulting from incentive spirometry, and incentive spirometry has been successfully used in a variety of other diseases involving lung injury.[28]

Seyller et al recommend incentive spirometry might not be the best intervention in COVID-19 or long COVID because of the lack of trials. However, the potential for it to be a cost-saving measure should be considered.[38]

Although these different opinions and results that incentive spirometry training may or may not has benefit in COVID-19, the studies all indicated that more randomized-controlled trials are necessary to further assess the use of incentive spirometry in patients with COVID-19 and survivors.

To provide clinical medical staff with an assessment of the effectiveness of respiratory training, in the following paragraphs, a literature review is presented to introduce a series of methods to evaluate the effectiveness of noninvasive breathing training.

Non-Invasive Assessment Methods in Long COVID Symptoms

Hemoglobin and Oxygen Levels

While respiratory medicine guidelines focus on arterial partial pressure of oxygen (PaO_2) and arterial oxygen saturation (SaO_2), the arterial oxygen content (CaO_2) is the parameter that is most relevant to oxygen delivery to tissues. CaO_2 represents the amount of oxygen delivered to tissues per unit of blood volume. When breathing room air, almost all oxygen in the blood is bound to hemoglobin (Hb), and each gram of blood Hb, when fully saturated, can transport approximately 1.34 mL of oxygen. Therefore, CaO_2 can be calculated as $Hb \times SaO_2 \times 1.34/100$ (mL/dL), where SaO_2 is expressed as a percentage. Studies indicate that CaO_2 is primarily determined by Hb, with an increase in Hb of 1 g/dL leading to a 1.10-fold increase in CaO_2. The correlation between SaO_2 and CaO_2 is less evident. Thus, in a prolonged adaptive state, Hb is a crucial determinant of CaO_2, allowing the pulmonary function to be estimated.[43]

Post-COVID-19 Functional Status (PCFS) Scale

Considering the substantial number of COVID-19 survivors globally, scholars such as Klok believe that there is a need for a simple and reproducible tool to differentiate those recovering slowly or incompletely to assist in the rational allocation of medical resources and standardized research assessments. Hence, the PCFS scale is an ordinal for assessing patients' comprehensive functional limitations. This scale can track patients' improvement over time, answer clinically meaningful questions, and serve academic research purposes. Assessment methods include patient self-reports or formal standardized interviews. The PCFS scale was initially designed to monitor recovery at discharge, 4 and 8 weeks post-discharge, and assess various sequelae at 6 months.[44] Although the Chinese version of the PCFS scale has not undergone validity testing, previous studies have affirmed its applicability in evaluating the impact of post-COVID-19 functional status and detecting functional limitations associated with various persistent symptoms.[45,46]

Six-Minute Walk Test (6MWT)

The 6MWT, which was officially introduced by the American Thoracic Society in 2002, is an exercise test designed to monitor a patient's physical condition. Initially used for patients with cardiopulmonary issues, the test has found widespread application in assessing patients with various diseases over time because it not only evaluates aerobic capacity and endurance but also provides information on other systems during physical activity, including the pulmonary and cardiovascular systems, neuromuscular units, and body metabolism, offering valuable insights into functional capacity.[47]

The 6MWT is a safe test with minimal complications and requires no complex equipment or techniques. During the test, patients are instructed to walk back and forth along a flat, unobstructed 30-m path for 6 min. This metric can be used to determine treatment responses and predict the incidence and mortality rates of chronic respiratory diseases.[47] A literature analysis by Bellet et al found strong test–retest reliability in studies evaluating repeated 6-min walk distances. In another study by Ferioli et al, the 6MWT was used to evaluate low SpO_2 or desaturation. Data from the participants showed that the 6MWT and saturation and distance–saturation product at 6 months were correlated positively with the percent predicted low SpO_2 or desaturation. These results indicate that the 6MWT is a useful test in post-COVID-19 follow-up as it correlates with the severity of acute disease in the chronic phase of COVID-19.[48]

Among eight articles assessing the standard concurrent validity of the 6MWT, four demonstrated moderate to high correlations between the 6-min walk distance and maximal power, oxygen consumption, and maximum metabolic equivalents during symptom-limited exercise tests.[49] In a previous meta-analysis, Chen et al also used the 6MWT as an outcome measure to evaluate inspiratory muscle training in patients with COVID-19.[50] The 6MWT is also a simple method that can be used to evaluate the effectiveness of respiratory training in long COVID.

Dyspnoea-12 (D-12) Scale

The D-12 scale, introduced in 2010, employs a multidimensional approach to evaluate dyspnea, particularly its sensory and emotional dimensions. Comprising 12 descriptors of dyspnea, the scale divides item scores into sub-scores representing physical and emotional domains, allowing for a more comprehensive assessment of the impact of dyspnea on patients.[51]

The D-12 scale, which was specifically designed to assess various sensations of dyspnea, consists of 12 questions, each scored by intensity ranging from 0 for mild symptoms to 3 for severe symptoms. The total score is the sum of all the item scores, with six questions addressing the sensory aspects of dyspnea and another six addressing the emotional aspects. The D-12 scale serves as a valuable tool for assessing the severity of dyspnea and has become a standard instrument for measuring dyspnea severity in international trials.[51]

The D-12 scale can assess a patient's current experiences of dyspnea in daily life and has been widely used for at least a decade, with demonstrated reliability and effectiveness in measuring various dimensions of dyspnea in different populations[52–54] and languages.[51,52,55,56] The Chinese version of the scale, which has been assessed for its reliability and validity by Choi et al, showed high internal consistency in the physical domain (Cronbach's alpha = 0.88) and moderate item-total correlations ranging from 0.37 to 0.65. Similarly, the emotional domain displayed high internal consistency (Cronbach's alpha = 0.91).[52] The results by Milne et al indicated that dyspnea in patients post-COVID-19 is associated with abnormal pulmonary gas exchange and deconditioning as well as anxiety, depression, and post-traumatic stress.[57] Long COVID can cause symptoms of anxiety and depression; therefore, the D-12 scale can be used to simultaneously assess changes in patients' respiratory and emotional symptoms.

However, the study by Philip et al indicated that in patients post-COVID-19 who received an online breathing and wellbeing program intervention, the D-12 scale score showed decreasing, but there was no improvement in body composition. Philip et al suggested that the experience of dyspnea and its emotional impact were lessened; however, future research is needed to elucidate the mechanisms of influence.[58]

Another study performed measurements using both the 6MWT and D-12 scale to compare the effect of respiratory exercises in patients with COVID-19. It is obvious that the 6MWT and D-12 scale can be used in patients with COVID-19 to evaluate the effectiveness of the intervention.[59]

A previous study comparing the D-12 scale with other tools also suggested that although the Borg Breathlessness Scale or MRC dyspnea scale are commonly used, the D-12 scale could explore the multidimensional components of breathlessness such as sensations of breathlessness, air hunger, or chest tightness.[24]

Long COVID Symptoms and Impact Tools

In 2021, Tran et al constructed the long COVID symptom and impact tools based on responses from an open-ended questionnaire survey of 492 individuals experiencing long-term COVID symptoms to establish a convenient tool for patients' self-assessment. The questionnaire comprised five open-ended questions, initially exploring the actual symptoms that patients were experiencing. Subsequently, the researchers assessed the impact of long-term COVID on patients' lives based on their descriptions. Finally, the participants rated their perception of the effects of long-term COVID on a scale from 0 to 10.

The tool was validated in 1022 participants, and the scores exhibited strong correlations with health-related quality of life (EQ-5D-5L) (r^2 = –0.45 and r^2 = –0.59, respectively), PCFS (r^2 = –0.39 and r^2 = –0.55), and MYMOP2 (r^2 = –0.40 and r^2 = –0.59). The tools constructed on the basis of patients' lived experiences proved useful for monitoring long COVID symptoms.[60]

Discussion

Long COVID, also known as chronic or post-acute sequelae of SARS-CoV-2 infection (PASC), is characterized by enduring symptoms and impairments persisting beyond 2–3 months following the acute phase resolution of COVID-19, with these manifestations not explainable by alternative diagnoses. Long COVID is characterized by a spectrum of clinical manifestations impacting multiple organ systems. These include, but are not limited to, pulmonary, cardiovascular, gastrointestinal, endocrine, and neuropsychiatric involvements.[61,62] The condition presents a diverse array of symptoms affecting these systems, reflecting its systemic and multifaceted nature.

Furthermore, diagnostic and assessment tools such as chest X-rays, the PCFS scale, the 6MWT, the D-12 questionnaire, Long COVID symptom and impact assessment instruments, as well as hemoglobin and oxygen saturation measurements, are instrumental in evaluating pulmonary function, exercise tolerance, and changes in oxygen saturation as required. In cases where patients exhibit cardiopulmonary symptoms such as chest pain, palpitations, or syncope, diagnostic modalities including electrocardiography, cardiac troponin levels, N-terminal pro-brain natriuretic peptide measurements, echocardiography, or more comprehensive cardiac evaluations are essential to assess cardiac function. Management of underlying pathologies indicated by these "red flags" should take precedence to mitigate safety concerns before intervention.[63]

In previous study, we have indeed observed the positive effects of IS on the PCFS scale,[33] the 6MWT,[31] exercise ability,[35] the Dyspnea severity index,[31] and overall quality of life.[33]

This review highlights the role of incentive spirometry in alleviating COVID-19 symptoms, with some research validating its effectiveness in easing respiratory distress and preventing lung collapse. The use of an incentive spirometer for respiratory exercises can significantly increase the maximal inspiratory volume while reducing symptoms like dyspnea and coughing.[16] Even in hospitalized patients with moderate COVID-19, respiratory training using an incentive spirometer has shown improvements in the PaO2/FiO2 ratio,[29] Pulmonary function (FEV1, FVC, PEF),[30,31,34] anxiety/depression scores,[33,37] and chest X-rays.[29] This not only reduces the length of hospital stay but also facilitates early symptom improvement.[29] Similarly, the study by Srinivasan et al indicates that after the intervention, there was a significant increase in FVC and FEV1 in patients with long COVID.[30] Gudivada et al also conducted an intervention using an incentive spirometer in patients with post-COVID PFT abnormalities. The results showed that after four weeks of intervention, 50% of the patients recovered normal lung function, whereas only 33% of the control group, who did not receive the intervention, regained normal lung function.[37] Kusumawardani et al and Suharti et al compared diaphragmatic breathing exercises and the using incentive spirometer, finding that although both improved lung function, the incentive spirometer had a greater impact on patients compared to diaphragmatic breathing exercises.[31,35]

This elucidates that the incentive spirometer is an efficacious tool for respiratory rehabilitation, instrumental in re-expanding collapsed alveolar structures, enhancing pulmonary expansion, and promoting clearance of the airways.

Contemporary research corroborates its role in augmenting maximal inspiratory capacity. Owing to its cost-effectiveness and ease of operation, the incentive spirometer allows for individualized adjustments in training intensity—both in duration and force—congruent with the patient's clinical status, whilst upholding an elevated safety profile. Nonetheless, patients enduring Long COVID are counseled to vigilantly observe the emergence, persistency, and severity of symptom exacerbations, in addition to recognizing their physiological constraints. This is aimed at concurrently managing symptom flare-ups and incrementally intensifying rehabilitative activities. Execution of such methodologies permits patients to equilibrate physical exertion with rest, thereby optimizing their recuperative journey without inducing undue strain.

Presently, empirical evidence regarding the application of incentive spirometry in ameliorating Long COVID symptoms remains limited. Given its substantiated efficacy in alleviating respiratory symptoms during the acute

COVID-19 phase, there is a pressing need for further investigative endeavors to ascertain its utility in the long-term management of symptoms, particularly in ambulatory patient populations. As widely acknowledged, the respiratory system is profoundly affected by the acute symptoms of COVID-19. Patients often experience persistent respiratory impairments even after discharge, and the recovery period in the post-acute phase tends to be prolonged. Considering the increasing prevalence of non-hospitalized, mild COVID-19 cases, establishing a simple yet effective respiratory training regimen that can be conducted at home is crucial to mitigate the long-term effects of COVID-19 on patients with chronic conditions. This literature review aims to explore the effectiveness of incentive spirometer respiratory training in alleviating symptoms among individuals recovering from long COVID. Also, non-invasive assessment methods are recommended with the aim to enable individuals' patients to undergo training and assessments conveniently at home or in the community. However, this paper still has many research limitations. Firstly, COVID-19 remains an emerging infectious disease. Although there has been extensive research since 2019, there is still a lack of literature on its chronic sequelae and long-term rehabilitation strategies. Additionally, to date, studies on the use of incentive spirometers in COVID-19 or long COVID patients remains insufficient, and there is a lack of long-term effectiveness studies involving generational research. Secondly, few studies have focused solely on the use of incentive spirometers for long COVID. Thirdly, most papers are based on single case reports.

Conclusion

In conclusion, convenient, simple, and highly safe training measures and interventions are crucial for patients in the community requiring long-term care. The duration of Long COVID can extend from several months to several years. For clinical and community healthcare professionals, as well as caregivers, providing a method that allows for ongoing rehabilitation and minimizes hospital visits is of significant value. Our findings will contribute to a better understanding of the efficacy of incentive spirometer respiratory training in improving symptoms related to long COVID, serve as practical reference material for clinical practitioners, and provide insights for healthcare policymakers in developing guidelines for future research directions, clinical guidance, and educational strategies in the context of nursing care.

Abbreviations

COVID-19, Coronavirus disease 2019; long COVID, long Coronavirus disease 2019 symptoms; PCFS, Post-COVID-19 functional status scale; 6MWT, Six-minute walk test; D-12, Dyspnoea-12 scale; WHO, World Health Organization; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2.

Acknowledgments

Thanks to the painter Hsiao-Han Chang for providing the assistance to us.

Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

Funding

This work was support by Tri-service General Hospital Songshan Branch (Grant number is TSGH-SS_D_113004).

Disclosure

The authors declare no conflicts of interest in this work.

References

1. Taiwan Centers for Disease Control. National Severe Special Infectious Pneumonia (Case Definition Version Prior to March 19, 2023) Domestic and Imported Case Statistics Table. Ministry of Health and Welfare. 2023. Available from: https://nidss.cdc.gov.tw/nndss/disease?id=19CoV.

2. TaiwanMinistryofHealthandWelfare. Hospital and Clinic statistics. 2023. Available from: https://www.mohw.gov.tw/mp2.html.
3. Tufts J, Guan N, Zemedikun DT, et al. The cost of primary care consultations associated with long COVID in non-hospitalised adults: a retrospective cohort study using UK primary care data. *BMC Prim Care*. 2023;24(1):245. doi:10.1186/s12875-023-02196-1
4. Koumpias AM, Schwartzman D, Fleming O. Long-haul COVID: healthcare utilization and medical expenditures 6 months post-diagnosis. *BMC Health Serv Res*. 2022;22(1):1010. doi:10.1186/s12913-022-08387-3
5. Koc HC, Xiao J, Liu W, Li Y, Chen G. Long COVID and its Management. *Int J Biol Sci*. 2022;18(12):4768–4780. doi:10.7150/ijbs.75056
6. Cabrera Martimbianco AL, Pacheco RL, Bagattini ÂM, Riera R. Frequency, signs and symptoms, and criteria adopted for long COVID-19: a systematic review. *Int J Clin Pract*. 2021;75(10):e14357. doi:10.1111/ijcp.14357
7. Jimeno-Almazán A, Pallarés JG, Buendía-Romero Á, et al. Post-COVID-19 Syndrome and the Potential Benefits of Exercise. *Int J Environ Res Public Health*. 2021;18(10):5329. doi:10.3390/ijerph18105329
8. Gale GD, Sanders DE. The Bartlett-Edwards incentive spirometer: a preliminary assessment of its use in the prevention of atelectasis after cardio-pulmonary bypass. *Can Anaesth Soc J*. 1977;24(3):408–416. doi:10.1007/BF03005115
9. Hristara-Papadopoulou A, Tsanakas J, Diomou G, Papadopoulou O. Current devices of respiratory physiotherapy. *Hippokratia*. 2008;12 (4):211–220.
10. OM L, Buwalda T, Blair M, et al. Impact of Long COVID on health and quality of life. *HRB Open Res*. 2022;5:31. doi:10.12688/hrbopenres.13516.1
11. van Kessel SAM, Olde Hartman TC, Lucassen P, van Jaarsveld CHM. Post-acute and long-COVID-19 symptoms in patients with mild diseases: a systematic review. *Fam Pract*. 2022;39(1):159–167. doi:10.1093/fampra/cmab076
12. Davis HE, Assaf GS, McCorkell L, et al. Characterizing long COVID in an international cohort: 7 months of symptoms and their impact. *EClinicalMedicine*. 2021;38:101019. doi:10.1016/j.eclinm.2021.101019
13. Ma Y, Deng J, Liu Q, Du M, Liu M, Liu J. Long-Term Consequences of COVID-19 at 6 Months and Above: a Systematic Review and Meta-Analysis. *Int J Environ Res Public Health*. 2022;19(11):1.
14. Ahmed I, Mustafaoglu R, Yeldan I, Yasaci Z, Erhan B. Effect of Pulmonary Rehabilitation Approaches on Dyspnea, Exercise Capacity, Fatigue, Lung Functions, and Quality of Life in Patients With COVID-19: a Systematic Review and Meta-analysis. *Arch Phys Med Rehabil*. 2022;103 (10):2051–2062. doi:10.1016/j.apmr.2022.06.007
15. Poon ET, Zheng C, Wong SH. Effect of Wearing Surgical Face Masks During Exercise: does Intensity Matter? *Front Physiol*. 2021;12:775750. doi:10.3389/fphys.2021.775750
16. Toor H, Kashyap S, Yau A, et al. Efficacy of Incentive Spirometer in Increasing Maximum Inspiratory Volume in an Out-Patient Setting. *Cureus*. 2021;13(10):e18483. doi:10.7759/cureus.18483
17. Troosters T, Janssens W, Demeyer H, Rabinovich RA. Pulmonary rehabilitation and physical interventions. *Eur Respir Rev*. 2023;32(168):220222. doi:10.1183/16000617.0222-2022
18. Nopp S, Moik F, Klok FA, et al. Outpatient Pulmonary Rehabilitation in Patients with Long COVID Improves Exercise Capacity, Functional Status, Dyspnea, Fatigue, and Quality of Life. *Respiration*. 2022;101(6):593–601. doi:10.1159/000522118
19. Liu K, Zhang W, Yang Y, Zhang J, Li Y, Chen Y. Respiratory rehabilitation in elderly patients with COVID-19: a randomized controlled study. *Complement Ther Clin Pract*. 2020;39:101166. doi:10.1016/j.ctcp.2020.101166
20. Tsutsui M, Gerayeli F, Sin DD. Pulmonary Rehabilitation in a Post-COVID-19 World: telerehabilitation as a New Standard in Patients with COPD. *Int J Chron Obstruct Pulmon Dis*. 2021;16:379–391. doi:10.2147/COPD.S263031
21. Zheng B, Daines L, Han Q, et al. Prevalence, risk factors and treatments for post-COVID-19 breathlessness: a systematic review and meta-analysis. *Eur Respir Rev*. 2022;31(166):220071. doi:10.1183/16000617.0071-2022
22. Santino TA, Chaves GS, Freitas DA, Fregonezi GA, Mendonça KM. Breathing exercises for adults with asthma. *Cochrane Database Syst Rev*. 2020;3(3):Cd001277. doi:10.1002/14651858.CD001277.pub4
23. Jones M, Harvey A, Marston L, O'Connell NE. Breathing exercises for dysfunctional breathing/hyperventilation syndrome in adults. *Cochrane Database Syst Rev*. 2013;2013(5):Cd009041. doi:10.1002/14651858.CD009041.pub2
24. 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):709–725. doi:10.1016/S2213-2600(23)00159-5
25. Jacobs SS, Krishnan JA, Lederer DJ, et al. Home Oxygen Therapy for Adults with Chronic Lung Disease: an Official American Thoracic Society Clinical Practice Guideline. *Am J Respir Crit Care Med*. 2020;202(10):e121–e41. doi:10.1164/rccm.202009-3608ST
26. Eltorai AEM, Baird GL, Eltorai AS, et al. Perspectives on Incentive Spirometry Utility and Patient Protocols. *Respir Care*. 2018;63(5):519–531. doi:10.4187/respcare.05872
27. Sum SK, Peng YC, Yin SY, et al. Using an incentive spirometer reduces pulmonary complications in patients with traumatic rib fractures: a randomized controlled trial. *Trials*. 2019;20(1):797. doi:10.1186/s13063-019-3943-x
28. Seyller H, Gottlieb M, Colla J. A breath of fresh air: the role of incentive spirometry in the treatment of COVID-19. *Am J Emergency Med*. 2021;48:369. doi:10.1016/j.ajem.2021.01.084
29. Garcia AC, Sarenas J. Blowing in the Wind: use of Incentive Spirometry in Preventing Acute Respiratory Distress Syndrome for Patients with Moderate COVID. *Eur Respir J*. 2022;60(suppl 66):268.
30. Srinivasan V, Kandakurti PK, Alagesan J, et al. Efficacy of pursed lip breathing with bhastrika pranayama vs incentive spirometry in rehabilitating post Covid 19 follow up-a randomized control study. *Turkish J Physiother Rehab*. 2021;32:1.
31. Abodonya AM, Abdelbasset WK, Awad EA, Elalfy IE, Salem HA, Elsayed SH. Inspiratory muscle training for recovered COVID-19 patients after weaning from mechanical ventilation: a pilot control clinical study. *Medicine*. 2021;100(13):e25339. doi:10.1097/MD.0000000000025339
32. Gudivada KK, Tikka SK, Bonthala Y, Miryala SK, Ch RP, Garre S. Association Between Post-COVID Pulmonary Dysfunction and New-Onset Anxiety and Depression and the Impact of Incentive Spirometer-Based Exercises. *Prim Care Companion CNS Disord*. 2023;25(5). doi:10.4088/PCC.23m03490
33. Hsu W-L, Chang Y-W, Horng Y-S, Hsu Y-T, Wu P-S. The successful rehabilitation of a 75-year-old female with debilitating long COVID: a case report. *JFormos Med Assoc*. 2022;121(7):1342–1347. doi:10.1016/j.jfma.2022.01.016
34. Kusumawardani RI, Tinduh D, Poerwandari D, Melaniani S, IA M. The effectiveness of incentive spirometry exercise on pulmonary function in COVID-19 survivors: a randomized controlled trial study. *Bali Medical Journal*. 2023;12(1):539–544. doi:10.15562/bmj.v12i1.3956

35. Suharti A, Nur Hidayati E, Yusviani H. Comparative effect of incentive spirometry and diaphragm breathing to functional capacity in COVID-19 patient in an isolated ward. *Bali Medical Journal*. 2022;11(3):1415–1419. doi:10.15562/bmj.v11i3.3579
36. Curci C, Negrini F, Ferrillo M, et al. Functional outcome after inpatient rehabilitation in postintensive care unit COVID-19 patients: findings and clinical implications from a real-practice retrospective study. *Eur J Phys Rehabil Med*. 2021;57(3):443–450. doi:10.23736/S1973-9087.20.06660-5
37. Garre KKGSKTYBSKMRPa S. Association Between Post-COVID Pulmonary Dysfunction and New-Onset Anxiety and Depression and the Impact of Incentive Spirometer-Based Exercises. *The Primary Care Companion*. 2023;25:479272.
38. Seyller H, Gottlieb M, Colla J. The Role of Incentive Spirometry for Patients with COVID-19. *Am J Emerg Med*. 2021;47:292–293. doi:10.1016/j.ajem.2021.05.034
39. Zhao HM, Xie YX, Wang C. Recommendations for respiratory rehabilitation in adults with coronavirus disease 2019. *Chin Med J*. 2020;133(13):1595–1602. doi:10.1097/CM9.0000000000000848
40. Lazzeri M, Lanza A, Bellini R, et al. Respiratory physiotherapy in patients with COVID-19 infection in acute setting: a Position Paper of the Italian Association of Respiratory Physiotherapists (ARIR). *Monaldi Arch Chest Dis*. 2020;90(1). doi:10.4081/monaldi.2020.1285.
41. Rehabilitation. CAoRMRRCoCAoRMCRGoCSoPMa. Recommendations for respiratory rehabilitation of coronavirus disease 2019 in adult. *Zhonghua jie he he hu xi za zhi = Zhonghua jiehe he huxi zazhi = Chinese journal of tuberculosis and respiratory diseases*. 2020;43(4):308–314. doi:10.3760/cma.j.cn112147-20200228-00206
42. Sheehy LM. Considerations for Postacute Rehabilitation for Survivors of COVID-19. *JMIR Public Health Surveill*. 2020;6(2):e19462. doi:10.2196/19462
43. Rizvi A, Macedo P, Babawale L, et al. Hemoglobin Is a Vital Determinant of Arterial Oxygen Content in Hypoxemic Patients with Pulmonary Arteriovenous Malformations. *Ann Am Thorac Soc*. 2017;14(6):903–911. doi:10.1513/AnnalsATS.201611-872OC
44. Klok FA, Boon G, Barco S, et al. The Post-COVID-19 Functional Status scale: a tool to measure functional status over time after COVID-19. *Eur Respir J*. 2020;56(1):2001494. doi:10.1183/13993003.01494-2020
45. Machado FVC, Meys R, Delbressine JM, et al. Construct validity of the Post-COVID-19 Functional Status Scale in adult subjects with COVID-19. *Health Qual Life Outcomes*. 2021;19(1):40. doi:10.1186/s12955-021-01691-2
46. Benkalfate N, Eschapasse E, Georges T, et al. Evaluation of the Post-COVID-19 Functional Status (PCFS) Scale in a cohort of patients recovering from hypoxemic SARS-CoV-2 pneumonia. *BMJ Open Respir Res*. 2022;9(1). doi:10.1136/bmjresp-2021-001136.
47. Agarwala P, Salzman SH. Six-Minute Walk Test: clinical Role, Technique, Coding, and Reimbursement. *Chest*. 2020;157(3):603–611. doi:10.1016/j.chest.2019.10.014
48. Ferioli M, Prediletto I, Bensai S, et al. The role of 6MWT in Covid-19 follow up. *Eur Respir J*. 2021;58(suppl 65):OA4046.
49. Bellet RN, Adams L, Morris NR. The 6-minute walk test in outpatient cardiac rehabilitation: validity, reliability and responsiveness--a systematic review. *Physiotherapy*. 2012;98(4):277–286. doi:10.1016/j.physio.2011.11.003
50. Chen Y, Liu X, Tong Z. Can inspiratory muscle training benefit patients with COVID-19? A systematic review and meta-analysis. *J Med Virol*. 2023;95(8):e28956. doi:10.1002/jmv.28956
51. Williams MT, Lewthwaite H, Paquet C, et al. Dyspnoea-12 and Multidimensional Dyspnea Profile: systematic Review of Use and Properties. *J Pain Symptom Manage*. 2022;63(1):e75–e87. doi:10.1016/j.jpainsymman.2021.06.023
52. Choi TCM, Chan LLY, Tsang HC, et al. Adaptation and validation of the Chinese version of Dyspnoea-12 scale in individuals with chronic obstructive pulmonary disease. *Clin Respir J*. 2021;15(10):1081–1087. doi:10.1111/crj.13411
53. Banzett RB, O'Donnell CR, Guilfoyle TE, et al. Multidimensional Dyspnea Profile: an instrument for clinical and laboratory research. *Eur Respir J*. 2015;45(6):1681–1691. doi:10.1183/09031936.00038914
54. Banzett RB, Moosavi SH. Measuring dyspnoea: new multidimensional instruments to match our 21st century understanding. *Eur Respir J*. 2017;49(3):1602473. doi:10.1183/13993003.02473-2016
55. Amado Diago CA, Puente Maestu L, Abascal Bolado B, et al. Translation and Validation of the Multidimensional Dyspnea-12 Questionnaire. *Arch Bronconeumol*. 2018;54(2):74–78. doi:10.1016/j.arbres.2017.08.001
56. Nishimura K, Oga T, Nakayasu K, et al. Comparison between tools for measuring breathlessness: cross-sectional validation of the Japanese version of the Dyspnoea-12. *Clin Respir J*. 2021;15(11):1201–1209. doi:10.1111/crj.13427
57. Milne KM, Cowan J, Schaeffer MR, et al. Exercise responses and mental health symptoms in COVID-19 survivors with dyspnoea. *ERJ Open Res*. 2023;9(3):606–2022. doi:10.1183/23120541.00606-2022
58. Philip KEJ, Owles H, McVey S, et al. An online breathing and wellbeing programme (ENO Breathe) for people with persistent symptoms following COVID-19: a parallel-group, single-blind, randomised controlled trial. *Lancet Respir Med*. 2022;10(9):851–862. doi:10.1016/S2213-2600(22)00125-4
59. Gonzalez-Gerez JJ, Saavedra-Hernandez M, Anarte-Lazo E, Bernal-Utrera C, Perez-Ale M, Rodriguez-Blanco C. Short-Term Effects of a Respiratory Telerehabilitation Program in Confined COVID-19 Patients in the Acute Phase: a Pilot Study. *Int J Environ Res Public Health*. 2021;18(14):7511. doi:10.3390/ijerph18147511
60. Tran V-T, Riveros C, Clepier B, et al. Development and Validation of the Long Coronavirus Disease (COVID) Symptom and Impact Tools: a Set of Patient-Reported Instruments Constructed From Patients Lived Experience. *Clinl Infect Dis*. 2021;74(2):278–287. doi:10.1093/cid/ciab352
61. Nalbandian A, Sehgal K, Gupta A, et al. Post-acute COVID-19 syndrome. *Nat Med*. 2021;27(4):601–615. doi:10.1038/s41591-021-01283-z
62. Soriano JB, Murthy S, Marshall JC, Relan P, Diaz JV. A clinical case definition of post-COVID-19 condition by a Delphi consensus. *Lancet Infect Dis*. 2022;22(4):e102–e7. doi:10.1016/S1473-3099(21)00703-9
63. WHO. *WHO Guidelines Approved by the Guidelines Review Committee. Clinical Management of COVID-19: Living Guideline*. Geneva: World Health Organization; 2022.