Footprint of Long-Term Pulmonary Sequelae of Covid 19 on Post Pandemic Pulmonary Status – A Rapid Review

Prof. Dr. Shanmugananth E[1], Prof. Dr Yu Chye Wah[2], Kshtrashal Singh[3], Susmitha Govind[4*]

*shankutty1981@gmail.com1, chyewah@aimst.edu.my2, kshtrashal@aimst.edu.my3, susmitha@aimst.edu.my4**

1 School of Physiotherapy, Sree Balaji Vidyapeeth, Deemed to be University, India,

2,3 School of Physiotherapy, Faculty of Allied Health Professions, AIMST University, Malaysia,

4 School of Physiotherapy, Faculty of Allied Health Professions, AIMST University, Malaysia and Ph.D Scholar, School of Physiotherapy, Sree Balaji Vidyapeeth, Deemed to be University, India

*Corresponding Author: susmitha@aimst.edu.my**

KEYWORDS
Pulmonary Sequelae, Covid 19, Post Pandemic Pulmonary Status

ABSTRACT

Introduction: The long-term pulmonary sequelae of COVID-19 infection and PASC are not known, a considered rehabilitative approach is recommended to yield optimal functional outcomes with a return to pre-morbid functional, avocational, and vocational status. Individuals who are unvaccinated, with pre-existing lung conditions and multiple medical comorbidities are at higher risk of more severe respiratory involvement and prolonged respiratory symptoms.

Methods: Five databases are searched for all the published trials of PR for patients with post-COVID-19 from March 2020 to October 2024. Data were extracted using a standardized form. The risks of bias of included studies were assessed using the Cochrane risk of the bias assessment tool. Data are synthesized where possible. The risk of bias of included studies varied, with major concerns on the risk of blinding of participants and interventions performers.

Discussion: Individuals with chronic lung diseases including chronic obstructive pulmonary disease (COPD), moderate to severe asthma, bronchiectasis, interstitial lung diseases, cystic fibrosis, and pulmonary hypertension, are at increased risk for more severe acute COVID and acute respiratory consequences, as well as post-acute sequelae of COVID-19 (PASC) and persistent respiratory symptoms and disease.

Conclusion: Recovery from post-COVID-19 interstitial lung disease are seen over months but has also been reported to be persistent and, in a minority, progressive.

Keywords: Pulmonary Sequelae, Covid 19, Post Pandemic Pulmonary Status.

Background:

Severe acute respiratory syndrome coronavirus, the infectious agent that causes coronavirus disease 2019 (COVID-19), can infect multiple organ systems triggering an inflammatory response resulting in abnormalities in cellular and organ function. This can result in multiple symptoms and associated functional limitations. Respiratory symptoms in acute COVID-19 and in post-acute sequelae of COVID-19 are common and can range from mild and intermittent to severe and persistent, correlating with functional limitations. Although the long-term pulmonary sequelae of COVID-19 infection and PASC are not known, a considered rehabilitative approach is recommended to yield optimal functional outcomes with a return to pre-morbid functional, avocational, and vocational status. The primary site of entry to the human body of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), the virus that causes coronavirus disease 2019 (COVID-19), is through the upper and lower respiratory tracts. The angiotensin-converting enzyme receptor is the

best-characterized entry receptor for SARS-CoV-2 and is highly expressed in the lung tissue. Infection of respiratory epithelial cells with SARS-CoV-2 generates a pro-inflammatory immune response including complement activation, the severity of which appears to correlate with the severity of acute COVID-19 lung disease. It is likely that variation in gene expression dictate complement hyperactivity1 and disease severity, accounting for the significant variability in the severity of respiratory disease seen with COVID-19. Mild respiratory symptoms including cough, mild breathing difficulty, and chest discomfort on respiration are very common in acute COVID-19 and are typically self-limiting, resolving over days to weeks. Individuals who are unvaccinated, with pre-existing lung conditions and multiple medical comorbidities are at higher risk of more severe respiratory involvement and prolonged respiratory symptoms. Hypoxemia as evidenced by peripheral pulse oximetry of less than 92% is a marker of more severe disease. Pneumonitis, acute COVID-19 pneumonia, and superimposed bacterial infections are less common. Rarely but most concerning is the progression to acute respiratory distress syndrome (ARDS) with more severe symptoms, significant hypoxemia, and the need for hospitalization including respiratory support. Interstitial lung disease is known long-term pulmonary sequelae of ARDS and reported in over 60%2 of severe acute COVID-19 ARDS survivors. Recovery from post-COVID-19 interstitial lung disease may be seen over months but has also been reported to be persistent and, in a minority, progressive. Patients with acute COVID-19 present with variable clinical symptoms, ranging from a mild upper respiratory tract illness—viral bronchitis—to a severe disease with life-threatening complications exemplified by COVID-19 viral pneumonia, ARDS with acute hypoxic respiratory failure, and susceptibility to secondary bacterial pneumonia. Individuals with milder presentations may still suffer from longer-term complications including persistent pulmonary inflammation and fibrosis. Many individuals with mild acute COVID-19 have mild but persistent and significant symptoms of shortness of breath at rest, dyspnoea on exertion, cough, and chest discomfort despite a negative exam and investigations.

Problem statement:

To study the effects of COVID-19's long-term pulmonary sequelae on post-pandemic pulmonary status as Individuals with chronic lung diseases including chronic obstructive pulmonary disease (COPD), moderate to severe asthma, bronchiectasis, interstitial lung diseases, cystic fibrosis, and pulmonary hypertension, are at increased risk for more severe acute COVID and acute respiratory consequences, as well as post-acute sequelae of COVID-19 (PASC) and persistent respiratory symptoms and disease.

Objectives of the Research:

To study the Footprint of Long Term Pulmonary Sequelae of Covid 19 on Post Pandemic Pulmonary Status.

Review Documents:

1. B Yan, T Freiwald, D Chauss, L Wang, E West, C Mirabelli, CJ Zhang, EM Nichols, N Malik. Science immunology, 2021- Patients with coronavirus disease 2019 (COVID-19) present a wide range of acute clinical manifestations affecting the lungs, liver, kidneys, and gut. Angiotensin-converting enzyme 2 (ACE2), the best-characterized entry receptor for the disease-causing virus SARS-CoV-2, is highly expressed in the aforementioned tissues. However, the pathways that underlie the disease are still poorly understood. Here, we unexpectedly found that the complement system was one of the intracellular pathways most highly induced by SARS-CoV-2 infection in lung

epithelial cells. Infection of respiratory epithelial cells with SARS-CoV-2 generated activated complement component C3a and could be blocked by a cell-permeable inhibitor of complement factor B (CFBi), indicating the presence of an inducible cell-intrinsic C3 convertase in respiratory epithelial cells. Within cells of the bronchoalveolar lavage of patients, distinct signatures of complement activation in myeloid, lymphoid, and epithelial cells tracked with disease severity. Genes induced by SARS-CoV-2 and the drugs that could normalize these genes both implicated the interferon-JAK1/2-STAT1 signaling system and NF-κB as the main drivers of their expression. Ruxolitinib, a JAK1/2 inhibitor, normalized interferon signature genes and all complement gene transcripts induced by SARS-CoV-2 in lung epithelial cell lines but did not affect NF-κB–regulated genes. Ruxolitinib, alone or in combination with the antiviral remdesivir, inhibited C3a protein produced by infected cells. Together, we postulate that combination therapy with JAK inhibitors and drugs that normalize NF-κB signaling could potentially have clinical application for severe COVID-19.

2.Six-month follow-up chest CT findings after severe COVID-19 pneumonia-X Han, Y Fan, O Alwalid, N Li, X Jia, M Yuan, Y Li, Y Cao, J Gu, H Wu, H Shi-Radiology, 2021•pubs.rsna.org- Six-month follow-up CT showed fibrotic-like changes in the lung in more than one-third of patients who survived severe coronavirus disease 2019 pneumonia. These changes were associated with an older age, acute respiratory distress syndrome, longer hospital stays, tachycardia, noninvasive mechanical ventilation, and higher initial chest CT score.

3.T Liao, D Meng, L Xiong, S Wu, L Yang, S Wang, M Zhou, X He, X Cao, H Xiong, Y Fan. Infectious diseases and therapy, 2022•Springer- Most surviving HCWs, especially female HCWs, still had an abnormal diffusion capacity at 1 year. The physical and psychiatric functions of surviving HCWs were significantly worse than those of the healthy population. Long-term follow-up of pulmonary, physical, and psychiatric functions for surviving HCWs is required.

4. JP Kanne, BP Little, JJ Schulte, A Haramati, LB Haramati Radiology, 2022•pubs.rsna.org- In the 3rd year of the SARS-CoV-2 pandemic, much has been learned about the long-term effects of COVID-19 pneumonia on the lungs. Approximately one-third of patients with moderate-to-severe pneumonia, especially those requiring intensive care therapy or mechanical ventilation, have residual abnormalities at chest CT 1 year after presentation. Abnormalities range from parenchymal bands to bronchial dilation to frank fibrosis. Less is known about the long-term pulmonary vascular sequelae, but there appears to be a persistent, increased risk of venothromboembolic events in a small cohort of patients. Finally, the associated histologic abnormalities resulting from SARS-CoV-2 infection are similar to those seen in patients with other causes of acute lung injury.

5. The role of 6MWT in Covid-19 follow up-M Ferioli, I Prediletto, S Bensai, S Betti, F Daniele, V Di Scioscio, C Modolon, MR Rimond-2021•Eur Respiratory Soc- Worldwide there is an imbalance between the number of patients discharged after Covid-19 and the availability of healthcare resources to follow them after acute illness. Six-minute walking test (6MWT) is a valid and inexpensive measure of exercise capacity for people with chronic lung disease. We used 6MWT during follow-up of patients discharged after Covid-19 to verify if it can be a reliable measure of the disease recovery. During 6MWT we reported walking distance in meters (6MWD), lowest SpO2 when breathing air (SpO2 nadir), desaturation and distance–saturation product (DSP), defined as the product of 6MWD and SpO2 nadir (Table). Data from the first 100 subjects show that 6MWD and DSP at 6 months correlates positively with percent predicted DLCO ($p=0.0001$) and inversely with HRCT severity score at six months ($p<0.05$). In addition, patients with PaO2/FiO2 during

hospitalization (P/F nadir) <200 mmHg performed a statistically significant lower 6MWD, SpO2 nadir and DSP and a larger desaturation during 6MWT at 2 months and a lower SpO2 nadir and a larger desaturation at 6 months compared to patients with a P/F nadir >200 mmHg during hospitalization. In conclusion, 6MWT is a useful test in post-Covid-19 follow-up as it correlates with the severity of acute disease and with functional/radiological impairment in the chronic phase of Covid-19. Furthermore, it shows the progressive improvement in exercise capacity.

6. Use of cardiopulmonary exercise testing to evaluate long COVID-19 symptoms in adults: a systematic review and meta-analysis-MS Durstenfeld, K Sun, P Tahir, MJ Peluso… - JAMA network.2022 - jamanetwork.com- Importance Reduced exercise capacity is commonly reported among individuals with COVID-19 symptoms more than 3 months after SARS-CoV-2 infection (long COVID-19 [LC]).Cardiopulmonary exercise testing (CPET) is the criterion standard to measure exercise capacity and identify patterns of exertional intolerance.

7. Persistent post–COVID-19 interstitial lung disease. An observational study of corticosteroid treatment-KJ Myall, B Mukherjee, AM Castanheira, JL Lam, G Benedetti, SM Mak, R Preston, M Thillai.Annals of the American Thoracic Society, 2021- Following SARS-CoV-2 pneumonitis, a cohort of patients are left with both radiological inflammatory lung disease and persistent physiological and functional deficit. Early treatment with corticosteroids was well tolerated and associated with rapid and significant improvement. These preliminary data should inform further study into the natural history and potential treatment for patients with persistent inflammatory ILD following SARS-CoV-2 infection.

8. Awake prone positioning for COVID-19 acute hypoxaemic respiratory failure: a randomised, controlled, multinational, open-label meta-trial S Ehrmann, J Li, M Ibarra-Estrada, Y Perez, I Pavlov, B McNicholas, O Roca, S Mirza. The Lancet Respiratory Medicine, 2021- Awake prone positioning of patients with hypoxaemic respiratory failure due to COVID-19 reduces the incidence of treatment failure and the need for intubation without any signal of harm. These results support routine awake prone positioning of patients with COVID-19 who require support with high-flow nasal cannula.

9. Benefits of pulmonary rehabilitation in COVID-19: a prospective observational cohort study R Gloeckl, D Leitl, I Jarosch, T Schneeberger, C Nell, N Stenzel, CF Vogelmeier, K Kenn. ERJ open research, 2021- Our study shows that pulmonary rehabilitation is a feasible, safe and effective therapeutic option in COVID-19 patients independent of disease severity.

10. Modeling lung perfusion abnormalities to explain early COVID-19 hypoxemia-J Herrmann, V Mori, JHT Bates, B Suki-Nature communications, 2020- Early stages of the novel coronavirus disease (COVID-19) are associated with silent hypoxia and poor oxygenation despite relatively minor parenchymal involvement. Although speculated that such paradoxical findings may be explained by impaired hypoxic pulmonary vasoconstriction in infected lung regions, no studies have determined whether such extreme degrees of perfusion redistribution are physiologically plausible, and increasing attention is directed towards thrombotic microembolism as the underlying cause of hypoxemia. Herein, a mathematical model demonstrates that the large amount of pulmonary venous admixture observed in patients with early COVID-19 can be reasonably explained by a combination of pulmonary embolism, ventilation-perfusion mismatching in the noninjured lung, and normal perfusion of the relatively small fraction of injured lung. Although underlying perfusion heterogeneity exacerbates existing shunt and ventilation-perfusion mismatch in the model, the reported hypoxemia severity in early COVID-19 patients is not replicated without either extensive

perfusion defects, severe ventilation-perfusion mismatch, or hyperperfusion of nonoxygenated regions.

11. Outpatient pulmonary rehabilitation in patients with long COVID improves exercise capacity, functional status, dyspnea, fatigue, and quality of life-S Nopp, F Moik, FA Klok, D Gattinger, M Petrovic, K Vonbank, AR Koczulla, C Ay, RH Zwick. Respiration, 2022- In patients with long COVID, exercise capacity, functional status, dyspnea, fatigue, and quality of life improved after 6 weeks of personalized interdisciplinary pulmonary rehabilitation. Future studies are needed to establish the optimal protocol, duration, and long-term benefits as well as cost-effectiveness of rehabilitation.

12. Effects of a comprehensive pulmonary rehabilitation in severe post-COVID-19 patients. M Spielmanns, AM Pekacka-Egli, S Schoendorf, W Windisch, M Hermann-International journal of environmental research and public health, 2021- Comprehensive PR in PG is very effective according to the results in FIM, 6-MWT and FT. Therefore, we recommend PR following severe post-COVID-19 infections.

13. Effect of pulmonary rehabilitation for patients with post-COVID-19: a systematic review and meta-analysis- The review showed that PR could improve exercise capacity measured by 6-MWT among patients with mild-to-moderate lung impairment after COVID-19. The interpretation of effects on lung function, dyspnea, and QoL should be cautious due to inadequate and conflicting data reported across studies.

14. Jason H Maley 1, George A Alba 2, John T Barry 3, Matthew N Bartels 4, Talya K Fleming 5, Christina V Oleson 6, Leslie Rydberg 7, Sarah Sampsel 8, Julie K Silver 9, Sabrina Sipes 10, Monica Verduzco-Gutierrez 11, Jamie Wood 12, Joseph D Zibrak 1, Jonathan Whiteson 13-Multidisciplinary collaborative consensus guidance statement on the assessment and treatment of breathing discomfort and respiratory sequelae in patients with post-acute sequelae of SARS-CoV-2 infection (PASC) 2022- Large numbers of individuals who have been infected with SARS-CoV-2, the virus responsible for COVID-19, continue to experience a constellation of symptoms long past the time that they have recovered from the acute stages of their illness. Often referred to as “long COVID,” these symptoms, which can include fatigue, shortness of breath, palpitations, cognitive dysfunction (“brain fog”), sleep disorders, fevers, gastrointestinal symptoms, anxiety, depression, and others, can persist for months and can range from mild to incapacitating. Although still being defined, these effects can be collectively referred to as postacute sequelae of SARS-CoV-2 infection (PASC). 1 The magnitude of this problem is not yet known, but given the millions of individuals worldwide who have had, or will have, COVID-19, the societal impacts are likely to be profound and long lasting. 2-5 It is widely acknowledged that systematic study is needed to develop an evidence-based approach for caring for patients with PASC. At present, there is a dearth of rigorous scientific evidence regarding effective assessment and treatment of PASC that prevents the creation of evidence-based clinical guidelines. However, the US health system is currently seeing an increase in the number of patients presenting with PASC, and there is an urgent need for clinical guidance in treating these patients. The goal of this, and future statements, is to provide practical guidance to clinicians in the assessment and treatment of patients presenting with PASC.

15. An online breathing and wellbeing programme (ENO Breathe) for people with persistent symptoms following COVID-19: a parallel-group, single-blind .KEJ Philip, H Owles, S McVey, T Pagnuco, K Bruce, H Brunjes, W Banya, J Mollica, A Lound. The Lancet Respiratory Medicine, 2022- Our findings suggest that an online breathing and wellbeing programme can improve the

mental component of HRQoL and elements of breathlessness in people with persisting symptoms after COVID-19.

Methodology

Five databases are searched for all the published trials of PR for patients with post-COVID-19 from March 2020 to October 2024. Data are extracted using a standardized form. The risks of bias of included studies were assessed using the Cochrane risk of the bias assessment tool. The risk of bias of included studies varied, with major concerns on the risk of blinding of participants and interventions performers.

Study Design and Sampling Method

This study is a cross-sectional study design using an internet based survey for five databases are searched for all the published trials of PR for patients with post-COVID-19 from March 2020 to October 2024.

Sample size and population

This study employs a convenient sampling method, a strategic choice that capitalizes on the accessibility of database. To quantify the extent of the sampling, the research employs the sophisticated Qualtrics Statistical Application (Carrie A. Miller et al., 2020). This tool enables the researchers to calculate an estimated sample size that is statistically significant.

Selection Criteria

The entire database is meticulously chosen based on specific inclusion and exclusion criteria. These criteria are essential for identifying database that is most appropriate for the research, ensuring they match the scientific objectives of the study. This careful selection is vital for reducing potential biases, and enhancing the study's relevance and practicality. Establishing clear and relevant inclusion criteria is key to ensuring the sample population is uniform, which, in turn, supports the accuracy and reliability of the research outcomes.

Inclusion Criteria

- Patients aged 45-65 years who were positive RT-PCR for SARS-CoV-2
- Free available data base only from march 2020 onwards

Exclusion criteria

- Paid and subscription base data base.

Data entry and analysis

The data analysis is performed by using SPSS. Descriptive statistic is used for data analysis. Tabulation and computation of frequencies and percentages are calculated on selected variables.

Results: Large numbers of articles supported that individuals who have been infected with SARS-CoV-2, the virus responsible for COVID-19, continue to experience a constellation of symptoms long past the time that they have recovered from the acute stages of their illness. Often referred to as “long COVID,” these symptoms, which can include fatigue, shortness of breath, palpitations, cognitive dysfunction (“brain fog”), sleep disorders, fevers, gastrointestinal symptoms, anxiety, depression, and others, can persist for months and can range from mild to incapacitating. Although still being defined, these effects can be collectively referred to as post-acute sequelae of SARS-

CoV-2 infection (PASC). It is widely acknowledged that there is currently an increase in the number of patients presenting with PASC, and there is an urgent need for clinical guidance in treating these patients.

Discussion: Individuals with chronic lung diseases including chronic obstructive pulmonary disease (COPD), moderate to severe asthma, bronchiectasis, interstitial lung diseases, cystic fibrosis, and pulmonary hypertension, are at increased risk for more severe acute COVID and acute respiratory consequences, as well as post-acute sequelae of COVID-19 (PASC) and persistent respiratory symptoms and disease.

Conclusion: Recovery from post-COVID-19 interstitial lung disease may be seen over months but has also been reported to be persistent and, in a minority, progressive.

References

1. Yan B., Freiwald T., Chauss D., et al. SARS-CoV-2 drivesJAK1/2-dependent local complement hyperactivation. Sci. Immunol. 2021;6:eabg0833. [PMC free article] [PubMed] [Google Scholar]
2. Han X., Fan Y., Alwalid O., et al. Six-month Follow-up Chest CT Findings after Severe COVID-19 Pneumonia. Radiology. 2021;299(1):E177–E186. [PMC free article] [PubMed] [Google Scholar]
3. Lewis K.L., Helgeson S.A., Tatari M.M., et al. COVID-19 and the effects on pulmonary function following infection: a retrospective analysis. EClinicalMedicine. 2021;39:101079. [PMC free article] [PubMed] [Google Scholar]
4. Liao T., Meng D., Xiong L., et al. Long-term effects of COVID-19on health care workers 1-year post-discharge in Wuhan. Infect Dis Ther. 2021:1–19. [PMC free article] [PubMed] [Google Scholar]
5. Kanne J.P., Little B.P., Schulte J.J., et al. Long-Term Lung Abnormalities Associated with COVID-19 Pneumonia. Radiology. 2022 doi: 10.1148/radiol.221806. [PMC free article] [PubMed] [CrossRef] [Google Scholar]
6. Banzett R.B., O'Donnell C.R., Guilfoyle T.E., et al. Multidimensional dyspnea profile: an instrument for clinical and laboratory research. Eur Respir J. 2015;45(6):1681–1691. [PMC free article] [PubMed] [Google Scholar]
7. Mahler D.A., Horowitz M.B. Perception of breathlessness during exercise in patients with respiratory disease. Med Sci Sports Exerc. 1994;26:1078–1081. [PubMed] [Google Scholar]
8. Bestall J.C., Paul E.A., Garrod R., et al. Usefulness of the Medical Research Council (MRC) dyspnoea scale as a measure of disability in patients with chronic obstructive pulmonary disease. Thorax. 1999;54:581–586. [PMC free article] [PubMed] [Google Scholar]
9. Hlatky M.A., Boineau R.E., Higginbotham M.B., et al. A brief self-administered questionnaire to determine functional capacity (the Duke activity status index) Am J Cardiol. 1989;64(10):651–654. [PubMed] [Google Scholar]
10. ATS Statement: Guidelines for the Six-Minute Walk Test. Am J Respir Crit Care Med. 2002;166:111–117. [PubMed] [Google Scholar]
11. Ferioli M., Prediletto I., Bensai S., et al. The role of 6MWT in Covid-19 follow up. Eur Respir J Suppl. 2021;58(suppl 65):OA4046. [Google Scholar]

12. Balady G.J., Ross A., Sietsema K., et al. on behalf of the American Heart Association Exercise, Cardiac Rehabilitation, and Prevention Committee of the Council on Clinical Cardiology; Council on Epidemiology and Prevention; Council on Peripheral Vascular Disease; Interdisciplinary Council on Quality of Care and Outcomes Research. Clinician's Guide to cardiopulmonary exercise testing in adults: a scientific statement from the. Am Heart Assoc. 2010;122(2):191–225. [Google Scholar]
13. Durstenfeld M.S., Sun K., Tahir P., et al. Use of Cardiopulmonary Exercise Testing to Evaluate Long COVID-19 Symptoms in Adults: A Systematic Review and Meta-analysis. JAMA Netw Open. 2022;5(10):e2236057. [PMC free article] [PubMed] [Google Scholar]
14. Centers for Medicare & Medicaid Services. National Coverage Determination (NCD) for Home Use of Oxygen (240.2). Publication Number100-3; Version 1; Effective Date of this Version October 27, 1993. Available at: https://www.cms.gov/medicare-coverage-database/details/ncd-details.aspx?NCDId=169.Accessed September 3, 2021.
15. Myall K.J., Mukherjee B., Castanheira A.M., et al. Persistent Post-COVID-19 Interstitial Lung Disease. An Observational Study of Corticosteroid Treatment. Ann Am Thorac Soc. 2021;18(5):799–806. [PMC free article] [PubMed] [Google Scholar]
16. Salvi S.S., Ghorpade D., Dhoori S., et al. Role of anti-fibrotic drugs in the management of post-COVID-19 interstitial lung disease: A review of literature and report from an expert working group. Lung India. 2022;39(2):177–186. [published correction appears in Lung India. 2022;39(3):310] [PMC free article] [PubMed] [Google Scholar]
17. King C.S., Mannem H., Kukreja J., et al. Lung Transplantation for Patients With COVID-19. Chest. 2022;161(1):169–178. [PMC free article] [PubMed] [Google Scholar]
18. Whiteson J.H., Xavier Escalón M. Susan Maltser, Monica Verduzco-Gutierrez MD Demonstrating the vital role of physiatry throughout the health care continuum: Lessons learned from the impacts of the COVID-19 pandemic on inpatient rehabilitation. PM R. 2021;13:6 554–562. [PMC free article] [PubMed] [Google Scholar]
19. Langer T., Brioni M., Guzzardella A., et al. Prone position in intubated, mechanically ventilated patients with COVID-19: a multi-centric study of more than 1000 patients. Crit Care. 2021;25:128. [PMC free article] [PubMed] [Google Scholar]
20. Ehrmann S., Li J., Ibarra-Estrada M., et al. Awake prone positioning for COVID-19 acute hypoxaemic respiratory failure: a randomised, controlled, multinational, open-label meta-trial. Lancet Respir Med. 2021;9:1387–1395. [PMC free article] [PubMed] [Google Scholar]
21. Corcoran J.R., Herbsman J.M., Bushnik T., et al. Early Rehabilitation in the Medical and Surgical Intensive Care Units for Patients With and Without Mechanical Ventilation: An Interprofessional Performance Improvement Project. PM R. 2017;9(2):113–119. [PubMed] [Google Scholar]
22. Battaglini D., Robba C., Caiffa S., et al. Chest physiotherapy: An important adjuvant in critically ill mechanically ventilated patients with COVID-19. Respir Physiol Neurobiol. 2020;282:103529. [PMC free article] [PubMed] [Google Scholar]
23. Gloeckl R., Leitl D., Jarosch I., et al. Benefits of pulmonary rehabilitation in COVID-19: a prospective observational cohort study. ERJ Open Res. 2021;7(2):00108–02021. [PMC free article] [PubMed] [Google Scholar]
24. Herrmann J., Mori V., Bates J.H.T., et al. Modeling lung perfusion abnormalities to explain early COVID-19 hypoxemia. Nat Commun. 2020;11:4883. [PMC free article] [PubMed] [Google Scholar]

25. NIH COVID-19 Treatment Guidelines. Oxygenation and Ventilation for Adults. Available at: https://www.covid19treatmentguidelines.nih.gov/management/critical-care-for-adults/oxygenation-and-ventilation-for-adults/. Accessed April 20, 2023.
26. Centers for Medicare & Medicaid Services. National Coverage Determination – Home Use of Oxygen. Available at: https://www.cms.gov/medicare-coverage-database/view/ncd.aspx?NCDId=169. Accessed September 27, 2021.
27. Nopp S., Moik F., Klok F., et al. Outpatient Pulmonary Rehabilitation in Patients with Long COVID Improves Exercise Capacity, Functional Status, Dyspnea, Fatigue, and Quality of Life. Respiration. 2022;101:593–601. [PMC free article] [PubMed] [Google Scholar]
28. Spielmanns M., Pekacka-Egli A.-M., Schoendorf S., et al. Effects of a Comprehensive Pulmonary Rehabilitation in Severe Post-COVID-19 Patients. Int J Environ Res Publ Health. 2021;18(5):2695. [PMC free article] [PubMed] [Google Scholar]
29. Chen H., Shi H., Liu X., et al. Effect of Pulmonary Rehabilitation for Patients With Post-COVID-19: A Systematic Review and Meta-Analysis. Front Med. 2022;9:837420. [PMC free article] [PubMed] [Google Scholar]
30. Centers for Medicare and Medicaid Services. Changes to the pulmonary rehabilitation (PR) benefit. 12/31/2021 Available at: https://www.aarc.org/wp-content/uploads/2022/06/aarc-medicare-pulmonary-rehabilitation-update-2022.pdf. Accessed December 31, 2021.