Physical Therapy Management of an Individual With Post-COVID Syndrome: A Case Report

RUNNING HEAD: Post-COVID Syndrome

TOC CATEGORY: COVID-19

ARTICLE TYPE: Case Report

ACCEPTED: March 10, 2020

SUBMITTED: November 24, 2020

REVISED: March 07, 2021

KEYWORDS: COVID-19, Rehabilitation, Cognitive Dysfunction, Posttraumatic Stress Disorder

© The Author(s) 2021. Published by Oxford University Press on behalf of the American Physical Therapy Association. All rights reserved. For permissions, please email: journals.permissions@oup.com

Kirby P. Mayer, DPT, PhD¹ Angela K Steele, PT² Melissa K. Soper, APRN³ Jill D. Branton, RRT² Megan L Lusby, DPT² Anna G Kalema, MD³ Esther E. Dupont-Versteegden, PhD Ashley A. Montgomery, MD³

¹ Department of Physical Therapy, College of Health Sciences, University of Kentucky, Lexington, KY. USA.
² Pulmonary Rehabilitation, Medicine Specialties Clinic, Therapeutic Services, University of Kentucky Healthcare

³ Division of Pulmonary, Critical Care and Sleep Medicine, College of Medicine, University of Kentucky

Corresponding Author:

Kirby P. Mayer, DPT, Ph.D. 900 S. Limestone, CTW 204D

ABSTRACT:

Objective. The purpose of this case report is to present the clinical presentation and physical therapist management for a patient with post-COVID syndrome. Secondarily, the report highlights the importance of assessing cognitive and emotional health in patients with post-COVID syndrome. Methods (Case Description). A 37-year-old woman tested positive for SARS-CoV-2 and developed mild COVID-19 disease but did not require supplemental oxygen or hospitalization. The patient experienced persistent symptoms including dyspnea, headaches, and cognitive fog. On day 62, she participated in an outpatient physical therapist evaluation that revealed deficits in exercise capacity, obtaining 50% of her age-predicted 6-minute walk distance (6MWD). She had minor reductions in muscle strength and cognitive function. Self-reported quality of life (QoL) was 50, and she scored above established cut-off scores for provisional diagnosis of posttraumatic stress disorder (PTSD). **Results.** The patient participated in biweekly physical therapist sessions for 8 weeks, which included aerobic training, strengthening exercises, diaphragmatic breathing techniques, and mindfulness training. Metabolic equivalent for task (METS) levels increased with variability over the course of the program. The patient's muscle strength, physical function, and exercise capacity improved. 6MWD increased by 199 m, equating to 80% of her age-predicted distance. QoL and PTSD scores did not improve. At evaluation after physical therapy, the patient was still experiencing migraines, dyspnea, fatigue, and cognitive dysfunction.

Conclusion. This case report described the clinical presentation and physical therapist management of a person with post–COVID syndrome, a novel health condition for which little evidence exists to guide rehabilitation examination and interventions. Physical therapists should consider cognitive function and emotional health in their plan of care for patients with post–COVID syndromes. **Impact**. This case alerts physical therapists to post–COVID syndrome—which can include debilitating symptoms of decreased aerobic tolerance, anxiety, PTSD, and cognitive dysfunction—and to the role that therapists can play in assessing these symptoms and managing these patients.

[H1] BACKGROUND AND PURPOSE

Individuals testing positive for SARS-COV-2 may have asymptomatic presentations or develop COVID-19 disease ranging from mild to severe presentations. Significant research and media attention have been given to patients that develop critical illness due to severe COVID-19 and require an intensive care unit (ICU) admission.¹ More recently there have been numerous reports of non-critically-ill presentations of COVID-19 developing persistent and debilitating symptoms.^{2,3} Clinicians and researchers are actively studying disease trajectories and recognize an immediate need for "more sophisticated categorization of post-COVID-19 symptoms, including by precise etiology, as this will impact on treatment and rehabilitation decisions.⁴ Recent guidelines recognize "two definitions of post-acute COVID-19 are given: (1) ongoing symptomatic COVID-19 for people who still have symptoms between 4 and 12 weeks after the start of acute symptoms; and (2) post-COVID-19 syndrome for people who still have symptoms for more than 12 weeks after the start of acute symptoms.⁵ A few terms have been introduced to describe persistent symptoms following COVID-19 disease including "post-COVID syndromes" and "Long COVID.⁴³ The purpose of this case report is to present a patient with COVID-19 disease who never required hospitalization that developed persistent symptoms. We will describe physical therapy management to address symptoms of deconditioning, dyspnea and weakness, and we will explore the importance of assessing and addressing deficits in cognitive function and emotional health.

[H1] CASE DESCRIPTION

The patient was a 37-year-old female with no contributing past medical history, who had a positive test on SARS-CoV-2 testing performed routinely by her employer (Day 0). The patient reported a history of anxiety and depression, otherwise she was a healthy and active individual employed full-time as a nurse in an outpatient clinical center. Of importance to this case, the patient was a trail runner and completed 23-kilometer races in the year prior to diagnosis of COVID-19. She developed symptoms 12-days after her positive test with initial complaints of shortness of breath, chills with low-grade fever, decreased appetite, diarrhea, nausea and

daily headaches. Dyspnea progressed over the next week and the patient complained of new onset of intermittent chest pain and palpitations with and without exertion. The patient received care from an infectious disease clinic in an academic medical center with diagnosis of acute upper respiratory infection with suspected pneumonia. She was prescribed an albuterol inhaler for her dyspnea. The patient's symptoms continued to progress and on day 35 she reported new onset of chest tightness, tingling on left side of body, myalgia and increased intensity and duration of migraine-type headache. A Holter monitor was ordered and revealed episodes of tachycardia but otherwise was unremarkable for abnormalities. The patient had continued symptoms of generalized deconditioning, dyspnea with exertion, and persistent migraine headaches despite negative SARS-CoV-2 test on days 25, 38 and 68; she was prescribed prednisone and sumatriptan succinate for treatment of her migraines.

On day 56, eight-weeks after her initial positive SARS-CoV-2 test, she was referred to a cardiologist for persistent palpitations and intermittent chest tightness. Echocardiogram (ECHO) revealed normal cardiac function and structure of the heart. Normal findings on cardiology examination led to the decision to monitor ongoing symptoms that were likely related to post-viral syndrome. The cardiologist referred the patient to physical therapy with an order to "evaluate and treat the patient for deconditioning and complaints of dyspnea with mild exertion." Outpatient physical therapy in a pulmonary rehabilitation clinic was initiated 10 weeks after her initial positive COVID-19 diagnosis.

[H2] Clinical Impression I

Physical rehabilitation, both in the hospital and during acute recovery, is recommended for improving physical function and quality of life in patients with severe COVID-19 developing acute respiratory failure.^{6,7} Recently, there has been a new emphasis of rehabilitation needs for patients with and recovering from mild presentations of COVID-19 that may never require supplemental oxygen or hospitalization.⁸ Due to a purported increased risk of neurological, cardiac, cognitive and emotional health impairments with COVID-19, the patient underwent a comprehensive physical therapy examination that was based on the prior guidelines for ICU survivors⁹ as well as the *COVID-19 Core Outcome Measures* guidelines from the academies and sections of the American Physical Therapy Association.¹⁰

[H2] Initial Examination

At the initial physical therapy examination (day 62), the patient expressed difficulty with instrumental activities of daily living including laundry and household chores and inability to participate in leisure activities including yoga, cycling, swimming, and running. She required extended time off work and endorsed difficulty reintegrating to her level of pre-COVID productivity. At the time of evaluation, patient was working 50% of her full-time schedule. Dyspnea with minimal exertion was the primary complaint and barrier to returning to her active lifestyle; the patient's primary goal was to return to cycling and running. She denied pain, but did report generalized malaise, continued daily headaches. A physical examination was performed including a systems review. Auscultation of the lungs revealed diminished bilateral vesicular breath sounds indicative of diminished air entry and right rhonchi songs that cleared with coughing suggestive of respiratory secretions which aligned with the physician's differential diagnosis and prior treatment of pneumonia. Blood pressure (114/70 mmHg), blood oxygen saturations (99% [SpO₂]), heart rate (59 beats per minute), and respiratory rate (14 breaths per minute) were all within normal physiological range at rest. The patient participated in a battery of tests including muscle strength, lower-extremity muscle power, exercise capacity testing, cognitive testing, and emotional health outcomes; raw scores and references values are provided in the Table. Of note, the patient had minor muscle weakness measured by the Medical Research Council-Sum Score and handgrip dynamometry.¹¹ She also had reductions in lower-extremity (LE) muscle power as measured by unilateral leg-press¹² and time to complete five-time sit-to-stand test.¹³ She presented with difficulty in multi-task performance measured by the difference in timed-up and go (TUG) test with cognitive component (34% difference)¹⁴ and scored a 27/30 on Montreal Cognitive Assessment (MOCA)¹⁵ missing three points for deficits with delayed recall. In addition, the patient's self-reported scores on Impact of Events Scale-Revised (IES-R)¹⁶ were indictive of high levels of distress meeting criteria for provisional diagnosis of post-traumatic stress disorder with hyperarousal being the highest subcomponent (Table). The patient's self-reported health-related quality of life was 50/100 on the EQ-5D-5L Visual Analog Scale.¹⁷ The patient had a 50% deficit in 6-minute walk distance compared to her predicted distance which equates to 312 meters with modified BORG¹⁸ rating of perceived exertion scale of 6 with SpO₂ ranging from 92-98%.¹⁹

[H2] Clinical Impression II

The patient has deficits in exercise capacity/aerobic endurance, minor reductions in muscle strength and power, and impairments in emotional health and cognitive function. Thus, the patient agreed to participate in

bi-weekly sessions for 8 weeks (16 sessions) of physical therapy treatment starting 64 days after her initial positive test. The outpatient rehabilitation program including the duration was based on active research at our institution and previous literature in patients surviving an ICU stay.^{20,21} In addition, the physical therapy plan of care was developed to gradually promoted increased physical activity at home as well as consideration for symptoms of distress, PTSD and anxiety related to COVID-19.

[H2] Interventions

The patient attended 15 sessions with (94% attendance, one session missed due to gastrointestinal symptoms) with each session lasting 40-80 minutes. Interventions delivered during treatment and the physiological variables are presented in Figure 1. Rehabilitation sessions were structured to include aerobic training, strength training, and breathing techniques with mindfulness training, and education.

Aerobic training duration and intensities were established based on performance of the six-minute walk. The patient's initial level for aerobic training was determined using calculation of 60-80% of peak heart rate during 6MWT accounting for heart rate reserve as defined by the Karvonen method.^{22,23} Aerobic intensity was progressively increased to maintain workload based on mRPE scale with goal intensity of 4/10 (somewhat hard) and not exceeding 6/10 (Hard). Based on performance on 6-MWT test with peak heart rate of 98 bpm the initial training range was set at 1.5-2.5 METS with heart rate range of 78-86 bpm. The initial aerobic intensity, may be considered low to moderate intensity, was selected as conservative approach with patient having active symptoms and risk of cardiac involvement post COVID. In addition, the patient was highly trained prior to COVID-19 disease and such has a lower peak heart rate was observed during testing. Aerobic exercises included recumbent upper extremity bicycle ergometer (UBE), recumbent cross-training stepper, treadmill walking and jogging as well as dancing (Fig. 1). The patient participated in minimum of 15 minutes of aerobic training at each session with session 7 reaching a maximum of 45 minutes of aerobic training. Of interest to this case, the patient participated in 3 to 6-minute bouts of dancing (line-dancing) to music with cadence of 80 bpm with therapists for aerobic training and mood stimulating therapy at four sessions. Oxygen saturations (SpO₂) were consistently above 94% during aerobic training, except for the one transient drop to 88% SpO₂ during recumbent stepping on the second physical therapy session (Fig. 1). Patient's mean and peak MET levels as well as peak HR and mRPE had a varied progression over the course of 8-weeks (Fig. 1).

Strengthening training was prescribed based on mRPE with initial rating of 5-6/10 performing 10-15 repetitions as per guidelines for deconditioned patients.²⁴ Patients perform 10 to 20 minutes of resistance training with exercises focused on the major muscle groups including multi-joint or compound exercises (eg, leg press).²⁵ Resistance exercises were progressed based on rating of mRPE increasing the load and/or repetitions when an exercise was rated <4/10 on mRPE. At the initial sessions, the patient participated in upper and lower extremity exercises in sitting and standing with 3 lb dumbbells or ankle weights. Exercises progressed slowly to include functional movements including squats and lunges as well increased resistance progressing to 6lb weights by the seventh session. The patient did not engage in strength training after session twelve as the physical therapist provided education for patients to perform independently at home, thus, promoting self-efficacy.

<u>Breathing techniques</u> focused on controlled diaphragmatic breathing with cues for relaxation and mindfulness to reduce anxiety and improve overall mood.²⁶ The patient completed these exercises at four supervised sessions with education to complete at home on daily basis. Diaphragmatic breathing techniques were combined with general core and trunk exercises in sitting, quadruped, or standing. One example prolonged expiration with seated trunk flexion and slow inspiration with trunk extension. Similar concepts were utilized with patient performing controlled breathing activities during core exercises in the quadruped position for lumbar extension and flexion with core activation eg, cat-cow exercise, child's pose, and bird-dog exercises. The goal of these techniques was not to improve core stability, but rather to increase chest wall expansion with increased attention to diaphragmatic breathing while engaging core musculature. Core stability is purported to be a vital component of efficient respiratory muscle activation²⁷ with previous findings demonstrating that core stabilization exercises with breathing are more effective in improving pulmonary function.²⁸ Breathing techniques were embedded in the program focusing on reducing dyspnea, stress and anxiety while improving quality of life.²⁹

Supplemental home exercise plan: The patient participated in home exercise plan including a walking program, resistance exercises, and breathing techniques. The patient was instructed to perform a walking program or supplemental other aerobic exercises (cycling and swimming) at home targeting at least 30 minutes per day with mRPE \leq 4 to be completed 3 days per week which equated to 5 days of aerobic training per week (2 supervised, 3 unsupervised). The patient was instructed to perform 20-30 minutes of resistance

training with an elastic resistance band at home completing 3 sets of 15 repetitions at least 3 times per week (Fig. 2). The patient was also educated to perform diaphragmatic breathing each day as well as at any time the patient experienced anxiety or distress. She gradually increased time participating in exercises and activities at home, which peaked at week 6 and reduced in weeks 7 and 8, Figure 2. In addition, the patient reported return to participation in yard-work including potting plants and mowing during week 3 and aerobic training on her stationary bicycle. She was able to return to swimming for aerobic training at week 7.

[H2] PARTICIPATION IN PHYSICAL THERAPY TREATMENT

The patient completed her treatment program on day 120 of her clinical course and there were no adverse events reported during physical rehabilitation treatment. However, the patient experienced bouts of reduced participation in physical rehabilitation with worsening symptoms of headaches, dyspnea and fatigue. Physical rehabilitation sessions demonstrated fluctuating pattern with some days the patient able to participate in longer durations at higher intensities (session 8), while other sessions were limited due to aforementioned symptoms (session 9, Fig. 1). Periods of reduced participation in rehabilitation correlated to reduced activity at home with the patient reporting feelings of exhaustion lasting 2-3 days after trying to progress her home activities. The patient's course and symptoms over her 8-weeks of physical therapy treatment varied leading to multiple sessions being shortened or requiring reduction on exercise intensities and more rest periods (sessions 9, 13, 15). The patient was educated about activity progression and energy conservation throughout the program with focus on preventing over-exertion.

[H1] OUTCOMES

Following physical rehabilitation, the patient participated in outcome testing 120 days after initial diagnosis; findings are summarized in the Table. In general, physical measures of muscle strength, muscle power and physical function improved. Of note, the patient increased her distance on 6-minute walk test to 511 meters, an increase of 199 meters, but still 80% of her age-predicted distance. Cognitive functioning appeared to be slightly improved or unchanged with the patient continuing to have deficits with delayed recall and a difference of 21% on the Time-up and Go Test with cognitive component (TUG-cog) suggesting continued difficulty with multi-tasking. Despite improvements in physical function, scores on emotional and HrQOL questionnaires were the same or worse with all subcomponents of the IES-R increasing (higher scores indicting more signs of

distress, intrusion, avoidance, and hyperarousal). On day 153, the patient was referred to neurology and imaging of the head was performed for ongoing symptoms including daily migraines, left-sided tingling and cognitive fog. Magnetic resonance imaging revealed mild amount of scattered small T2 hyperintense foci in the bilateral cerebral white matter and subcortical distribution, nonspecific in nature, similar to patients with migraines. At the time of this report, the patient continues to have daily migraines, fatigue and dyspnea that are worse with exertion, cognitive deficits, and left-sided parasthesias. The continued presence of symptoms four months after initial diagnosis led to continue medical follow-up with patient being referred for cognitive rehabilitation led by an occupational therapist.

[H1] DISCUSSION

The findings in this case report demonstrate that individuals diagnosed with COVID-19 who never require hospitalization may still be at risk of impairments in physical function, cognition and emotional health. The patient described in this case report continues to have debilitating symptoms 6-months after mild COVID-19 disease. We present this case report to highlight the severity of symptoms and demonstrate the arduous recovery some patients are facing despite never requiring an admission to the hospital. Moreover, we emphasize the need for ongoing physical and cognitive rehabilitation to address deficits developed as a result of COVID-19. In particular, we suggest that physical therapy treatment may improve post-viral symptoms of deconditioning and weakness, and potentially interventions such as diaphragmatic breathing, dancing, and mindfulness training may stimulate mood, reduce anxiety and support recovery. Eight-weeks of physical rehabilitation was associated with increased physical function and exercise capacity. However, six-minute walk test remained below her age-predicted value. Moreover, the patient's emotional health and quality of life scores did not improve following physical rehabilitation treatment likely due to post-viral syndrome referred to as post-COVID syndrome that continues to plague the patient.

The intractable symptoms experienced by the patient in this case are consistent with prior reports outlining "debilitating persistent symptoms."³ The presence of daily symptoms months after the patient's initial positive test with subsequent negative test for SARS-CoV-2 may explain continued poor scores on distress and HrQOL questionnaires. For reference, the patient's scores on the distress questionnaire (IES-R) are similar to patient surviving critical illness due to acute respiratory failure.³⁰ Recent research demonstrates that the COVID-19 pandemic can have "direct neuropsychiatric consequences and indirect effects on mental

health.^{*31} Physiologically, coronavirus is purported to lead to cerebral and brainstem dysregulation and, or tissue damage³², potentially due to invasion of SARS CoV-2 through the olfactory system or the bloodstream, or indirectly by systemic proinflammatory response increasing risk of neurologic involvement.³³ The patient in this case would meet criteria for a provisional diagnosis of post-traumatic stress disorder (>33/88 on IES-R).¹⁶ Additionally, the patient experienced debilitating daily migraines which have continued to time of this report. Headaches are a commonly reported neurologic symptom in patients with COVID-19 and post-viral illnesses, with the pathophysiology thought to be related to immune or inflammatory responses.³⁴ Neuroimaging performed six-months after initial exposure revealed nonspecific changes thought to be consistent with migraines. The frequency and severity of the patient's migraines in combination with ongoing distress continued to affect her normal life routines.

The primary purpose of this case report was to present of physical therapy management for a nonhospitalized patient recovering from COVID-19. Previous studies demonstrate that exercise training can improve cardiorespiratory and physical function for patients with SARS³⁵ and physical rehabilitation and exercise interventions are recommended for patients with and recovering from COVID-19.⁷ The treatment program was associated with improved performance on physical measures on post-examination, but limited improvements were noted in emotional health and cognitive function. This may partially be explained by the fluctuating pattern of interventions that were likely related to over-exertion leading to malaise and increasing frequency of fatigue. Acute fatigue is one of the primary symptoms of COVID-19 in hospitalized and nonhospitalized patient populations.² In this case, the patient reported trends of increasing symptom intensities and regression of her functionality after periods of over-exertion, potentially similar to post-exertional malaise that is often reported with chronic fatigue syndrome.³⁶ Thus, the post-viral symptoms may have a physiological impact on recovery that warranted modification of rehabilitation to optimize recovery. Modification in this case included reduced session duration with more focus on diaphragmatic breathing and mindfulness techniques while providing education on monitoring mRPE during activities at home to maintain low to moderate intensities. Physical rehabilitation as well as exercise activity in general are known to have a positive impact on cognitive function, emotional health and quality of life in a variety of patient populations including patients with community-acquired pneumonia.³⁷ However, the patient in this case report did not have improved scores on IES-R and HRQoL even despite a focus on reducing anxiety. We may speculate that current state of the

pandemic with large periods of isolation and restrictions may also contributed to lower scores.³⁸ The patient exhibited minor improvements in cognition evident in small improvements on the MOCA as well as the TUGcog. Scores on TUG and TUGcog were similar to "non-fallers" in studies previously assessing performance in older adults.¹⁴ The difference between TUG and TUGcog scores is quantified as the "cognitive cost" with the patient having a deficit of 34% on initial examination that improved to deficit of 21%. Improvements are noted, but the deficits also suggest the patient has continued difficulty with dual-task performance, although references values are not available for TUG-cog in her age group. Therefore, we suggest physical therapy treatment may be important to address deficits in muscle strength and cardiorespiratory endurance in patients with post-COVID syndromes, but additional research is required to study effectiveness including optimal delivery.

The rehabilitation program was prescribed based on patients surviving acute respiratory failure and patients that are deconditioned.^{20,21} The initial intensities, therefore, may be considered conservative especially the low-intensity aerobic training. This was intentional due to the purported risk of cardiac and neurologic complications with COVID-19 as well as the relative unknown about the impairments with post-COVID syndromes. The optimal timing and duration of treatment are pertinent clinical questions. It is possible that starting earlier in the course of her illness may have impacted outcomes, but the referral was provided nearly 2 months after her symptom onset. It is also possible that the duration was suboptimal and she may have benefitted from more sessions. However, she was self-sufficient with her home exercise plan and it was mutually decided to discontinue supervised sessions with the option to return to clinic, if needed. The decision to stop in-person sessions was supported by the patient's high healthcare literacy and that she was actively seeking treatment for emotional and cognitive impairments. Moreover, the patient returned to cycling and swimming in the later weeks of her treatment program reaching one of her initial goals. The case report highlights the need to provide individualized physical therapy treatment to address patient specific impairments with attention to patient specific goals.

[H1] Conclusion

This case report highlights that younger individuals with no pre-existing health issues that have recovered from an initial SARS-COV-2 infection may be at risk for long-term impairments, referred to as post-COVID syndrome. We present this case to demonstrate that rehabilitation clinicians need to consider

physiological response to exercise and the implications of post-exertional malaise and fatigue as well as emotional and cognitive function in their management of patients with post-COVID syndromes.

Author Contributions

Concept/idea/research design: K.P. Mayer, A.K. Steele, E.E. Dupont-Versteegden, A.A. Montgomery

Writing: K.P. Mayer, M.K. Soper, M.L Lusby, E.E. Dupont-Versteegden, A.A. Montgomery

Data collection: K.P. Mayer, A.K. Steele, M.K. Soper, J.D. Branton, M.L Lusby,

Data analysis: K.P. Mayer

Project management: K.P. Mayer, A.K. Steele

Fund procurement: K.P. Mayer

Providing participants: K.P. Mayer, A.K. Steele, M.K. Soper, A.A. Montgomery

Providing facilities/equipment: A.A. Montgomery

Providing institutional liaisons: M.K. Soper

Consultation (including review of manuscript before submitting): A.K. Steele, M.K. Soper, J.D. Branton, M.L Lusby, A.G. Kalema, E.E. Dupont-Versteegden, A.A. Montgomery

Ethics Approval: This study was approved by the University of Kentucky's Institutional Review Board (no. 59097). The patient provided informed consent as well as written consent to publish findings.

Funding: This publication was supported by a grant from the National Center for Research Resources and the National Center for Advancing Translational Sciences, National Institutes of Health (UL1TR001998). The content is solely the responsibility of the authors and does not necessarily represent the official views of NIH.

ROLE OF THE FUNDING SOURCE: The funders played no role in the design, conduct, or reporting of this study. The content is solely the responsibility of the authors and does not necessarily represent the official views of the National Institutes of Health.

Disclosure

The authors completed the ICMJE Form for Disclosure of Potential Conflicts of Interest and reported

no conflicts of interest.

References

- 1. Richardson S, Hirsch JS, Narasimhan M, et al. Presenting Characteristics, Comorbidities, and Outcomes Among 5700 Patients Hospitalized With COVID-19 in the New York City Area. *Jama*. 2020.
- Tenforde MW KS, Lindsell CJ, et al. Symptom Duration and Risk Factors for Delayed Return to Usual Health Among Outpatients with COVID-19 in a Multistate Health Care Systems Network — United States, March–June 2020. MMWR Morb Mortal Wkly Rep 2020. 2020;69:993-998.
- 3. Rubin R. As Their Numbers Grow, COVID-19 "Long Haulers" Stump Experts. Jama. 2020;324(14):1381-1383.
- 4. Halpin S, O'Connor R, Sivan M. Long COVID and chronic COVID syndromes. *J Med Virol.* 2020:10.1002/jmv.26587.
- 5. Venkatesan P. NICE guideline on long COVID. *The Lancet Respiratory Medicine*. 2021;9(2):129.
- 6. Simpson R, Robinson L. Rehabilitation following critical illness in people with COVID-19 infection. *American journal of physical medicine & rehabilitation.* 2020.
- 7. Falvey JR, Ferrante LE. Flattening the disability curve: Rehabilitation and recovery after COVID-19 infection. *Heart & Lung: The Journal of Cardiopulmonary and Acute Care.*
- 8. Wade DT. Rehabilitation after COVID-19: an evidence-based approach. *Clinical medicine (London, England).* 2020;20(4):359-365.
- 9. Needham DM, Sepulveda KA, Dinglas VD, et al. Core Outcome Measures for Clinical Research in Acute Respiratory Failure Survivors. An International Modified Delphi Consensus Study. *American journal of respiratory and critical care medicine*. 2017;196(9):1122-1130.
- 10. Martin R, Botkin R, Campbell A, et al. COVID-19 Core Outcome Measures, APTA Academies and Sections Consensus Statement. COVID-19 Practice Resources Web site. <u>https://www.apta.org/your-practice/outcomes-measurement/covid-19-core-outcome-measures</u>. Published 2020. Updated 10/21/2020. Accessed 10/22/2020.

- 11. Parry SM, Berney S, Granger CL, et al. A new two-tier strength assessment approach to the diagnosis of weakness in intensive care: an observational study. *Critical Care*. 2015;19(1):52.
- 12. Mayer KP, Welle MM, Evans CG, et al. Muscle Power is Related to Physical Function in Patients Surviving Acute Respiratory Failure: A Prospective Observational Study. *Am J Med Sci.* 2020.
- 13. Ramírez-Vélez R, Pérez-Sousa MA, Venegas-Sanabria LC, et al. Normative Values for the Short Physical Performance Battery (SPPB) and Their Association With Anthropometric Variables in Older Colombian Adults. The SABE Study, 2015. *Front Med (Lausanne).* 2020;7:52.
- 14. Hofheinz M, Mibs M. The Prognostic Validity of the Timed Up and Go Test With a Dual Task for Predicting the Risk of Falls in the Elderly. *Gerontol Geriatr Med.* 2016;2:2333721416637798-2333721416637798.
- 15. Carson N, Leach L, Murphy KJ. A re-examination of Montreal Cognitive Assessment (MoCA) cutoff scores. International Journal of Geriatric Psychiatry. 2018;33(2):379-388.
- 16. Bienvenu OJ, Williams JB, Yang A, Hopkins RO, Needham DM. Posttraumatic stress disorder in survivors of acute lung injury: evaluating the Impact of Event Scale-Revised. *Chest.* 2013;144(1):24-31.
- 17. Nolan CM, Longworth L, Lord J, et al. The EQ-5D-5L health status questionnaire in COPD: validity, responsiveness and minimum important difference. *Thorax.* 2016;71(6):493-500.
- 18. Kendrick KR, Baxi SC, Smith RM. Usefulness of the modified 0-10 Borg scale in assessing the degree of dyspnea in patients with COPD and asthma. *J Emerg Nurs.* 2000;26(3):216-222.
- 19. Enright PL, Sherrill DL. Reference Equations for the Six-Minute Walk in Healthy Adults. *American journal of respiratory and critical care medicine*. 1998;158(5):1384-1387.
- 20. Denehy L, Skinner EH, Edbrooke L, et al. Exercise rehabilitation for patients with critical illness: a randomized controlled trial with 12 months of follow-up. *Critical care (London, England).* 2013;17(4):R156.
- 21. Mayer KP, Steele AK, Joshi RR, et al. Optimizing Outcomes With Physical Therapy Treatment for IndividuALs Surviving an Intensive Care Units Admission for COVID-19 (OPTIMAL)—A Protocol for a Single Center Prospective Study. *Cardiopulmonary physical therapy journal*. 2020;Publish Ahead of Print.
- 22. Holland AE, Hill K, Alison JA, et al. Estimating peak work rate during incremental cycle ergometry from the 6minute walk distance: differences between reference equations. *Respiration; international review of thoracic diseases.* 2011;81(2):124-128.
- 23. ZuWallack R, Crouch R. American Association of Cardiovascular and Pulmonary Rehabilitation Guidelines for Pulmonary Rehabilitation Programs. 4 ed. Champaign, IL: Human Kinetics; 2011.
- 24. Thompson W, Gordon E, Pescatello L. *ACSM's Guidelines for Exercise Testing and Prescription.* 8th ed: Lippincott Williams and Wilkins; 2010.
- 25. Garvey C, Fullwood MD, Rigler J. Pulmonary rehabilitation exercise prescription in chronic obstructive lung disease: US survey and review of guidelines and clinical practices. *Journal of cardiopulmonary rehabilitation and prevention*. 2013;33(5):314-322.
- 26. Khusid MA, Vythilingam M. The Emerging Role of Mindfulness Meditation as Effective Self-Management Strategy, Part 1: Clinical Implications for Depression, Post-Traumatic Stress Disorder, and Anxiety. *Mil Med.* 2016;181(9):961-968.
- 27. Bradley H, Esformes J. Breathing pattern disorders and functional movement. *Int J Sports Phys Ther.* 2014;9(1):28-39.
- 28. Cavaggioni L, Ongaro L, Zannin E, Iaia FM, Alberti G. Effects of different core exercises on respiratory parameters and abdominal strength. *J Phys Ther Sci.* 2015;27(10):3249-3253.
- 29. Cahalin LP, Braga M, Matsuo Y, Hernandez ED. Efficacy of Diaphragmatic Breathing in Persons With Chronic Obstructive Pulmonary Disease: A Review of the Literature. *Journal of Cardiopulmonary Rehabilitation and Prevention*. 2002;22(1):7-21.
- 30. Mayer K, Boustany H, Cassity E, et al. ICU recovery clinic attendance, attrition and patient outcomes: the impact of severity of illness, gender and rurality. *Critical Care Explorations*. 2020;In Press.
- 31. Vindegaard N, Benros ME. COVID-19 pandemic and mental health consequences: Systematic review of the current evidence. *Brain Behav Immun.* 2020;89:531-542.
- 32. Baig AM, Khaleeq A, Ali U, Syeda H. Evidence of the COVID-19 Virus Targeting the CNS: Tissue Distribution, Host-Virus Interaction, and Proposed Neurotropic Mechanisms. *ACS Chem Neurosci.* 2020;11(7):995-998.
- 33. Pons-Escoda A, Naval-Baudín P, Majós C, et al. Neurologic Involvement in COVID-19: Cause or Coincidence? A Neuroimaging Perspective. *American Journal of Neuroradiology*. 2020;41(8):1365-1369.

- 34. Poncet-Megemont L, Paris P, Tronchere A, et al. High Prevalence of Headaches During Covid-19 Infection: A Retrospective Cohort Study. *Headache: The Journal of Head and Face Pain*.n/a(n/a).
- 35. Lau HM, Ng GY, Jones AY, Lee EW, Siu EH, Hui DS. A randomised controlled trial of the effectiveness of an exercise training program in patients recovering from severe acute respiratory syndrome. *The Australian journal of physiotherapy*. 2005;51(4):213-219.
- 36. Jason LA, Evans M, So S, Scott J, Brown A. Problems in defining post-exertional malaise. *J Prev Interv Community*. 2015;43(1):20-31.
- 37. José A, Dal Corso S. Inpatient rehabilitation improves functional capacity, peripheral muscle strength and quality of life in patients with community-acquired pneumonia: a randomised trial. *Journal of physiotherapy*. 2016;62(2):96-102.
- 38. Pfefferbaum B, North CS. Mental Health and the Covid-19 Pandemic. *New England Journal of Medicine*. 2020;383(6):510-512.

				-					
Tablai	Dhualaal		d Compitive		Magazina	Defers on		hy fai a a l'	Dahahilitatian
i anie:	POVSICAL	Emononal an	<u>a t.oonmve</u>	CHIICOMES.	MEASILIE	Belore an	η απέι Ρ	nvsicat	Renaniliation
I GANCE.	i iiyoloul,			Catoonico	mououro	Doioro un		i i y oloui	1 Chabintation
			0						

	Initial Physical	Post 8-Weeks of	Reference		
Assessment	Therapy Examination	Physical Therapy	Values		
Muscle strength	Examination	meatment			
Medical Research Council-sum score (60)	55/60 ^a	59/60	$48 + 6^{b}$		
Handgrin kilograms	24 (R) 36 (L)	33 (R) 34 (L)	10 5 [0-21 5]		
Muscle power (lower-extremity	2 T (T(), 00 (L)		10.0 [0 2 1.0]		
unilateral leg press)					
2-lb resistance (Watts)	14.3	17.7	$9.9 \pm 3.5^{\circ}$		
10% of body weight resistance (Watts)	88	134	63.7 ± 31		
Timed-Up and Go Test (TUG)					
TUG (seconds)	9.0	7.3	9.6 ± 1.4^{d}		
TUG + Cognitive task (seconds	12.8	9.0	10.8 ± 2.1		
Percent difference in cognitive task (%)	-34%	-21%	-8.9%		
Short Performance Physical Battery					
4-meter gait speed (m/s)	1.25	1.17	0.88 ± 0.3^{e}		
5 times sit-to-stand (seconds)	12.6	9.5	11.9 ± 5.1		
Balance composite score (4)	4	4	3.6 ± 0.8		
Total (12)	11	12	9.2 ± 2		
6-minute walk test			<i>,</i>		
Distance (meters)	312	511	640 [†]		
MRC-dyspnea scale	2	1	0-5		
Montreal Cognitive Assessment					
Total (30)	27	28	<23 MCl ^g		
Delayed Recall (5)	2	3			
Impact of Events Scale-Revised					
Total	36	46	> 33 provisional		
Mean response	1.6	2.1	PTSD ⁿ		
Intrusion mean	1.6	1.9			
Avoidance mean	0.75	1.25			
Hyperarousal mean	2.8	3.5			
Health-related Quality of Life					
Eq-5D-5L (VAS, 0-100)	50	40	65 ± 16′		
Eq-5D-5L (mean)	2.6	2.8			

^a MRC-ss scoring 4/5 bilateral shoulder abduction, 4/5 hip flexion, 4/5 left dorsiflexion, and remaining muscles 5/5¹¹

^b Muscle strength (MRC-ss and Handgrip) measured in 60 patients surviving mechanical ventilation (age 69 [49-77])¹¹

^c Muscle power measured in patient's post-ICU for ARF (age 55 ± 17 years old)¹²

^{*d*}Timed-up and go test plus cognitive component measured in ten healthy older adults (age 76.4 \pm 7)¹⁴

^e SPPB performed in 985 older adults (64.4 ± 2.8)¹³

^f Predicted 6MWD based on height, weight, age and female sex¹⁹

^gMild cognitive impairment for MOCA¹⁵

^h IES-R measures distress and >33 represents provisional diagnosis of post-traumatic stress disorder¹⁶

ⁱEQ-5D (VAS), 0 = poor quality of life up to 100 best quality of life¹⁷; reference value in ICU survivors measured 1-month post discharge²⁹

Figure Captions

Trajectory (day): 0 3 25 35	56	62															120	153
		Physical Rehabilitation Treatment																
	Ű	Session	# 1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	9
COVID-19 positive on PCR		Time (mins)	40	45	45	50	50	60	70	80	45	55	80	55	50	45	45	
1 st Provider Appt (ID)		METS (mean)	2.0	2.4	2.4	2.8	3.0	3.1	3.5	3.5	3.2	3.9	3.8	4.4	3.7	4.2	3.5	
W Holter Monitor		METS (peak)	2.4	3.4	3.4	6.0	4.2	6.0	4.3	8.2	3.5	4.6	6.0	6.6	5.5	6.5	4.0	
COVID-19 negative PCR		mRPE (peak)	5	4	5	5	6	5	4	6	4	6	5	6	5	5	4	
Physical Therapy Evaluation		HR (peak)	78	78	94	91	109	107	92	131	92	130	91	164	87	141	102	
Neurologic Appt / MRI		SpO ₂ (lowest)	96	88	95	94	97	94	95	98	96	97	95	94	94	94	96	
Warm-up activities			λ	λ	λ	λ	λ	λ	λ	λ	λ	λ	λ	À	λ	λ	λ	
Seated Recumbent Stepper				4	Y	4	4	4	M	4	4	4	4	4	4		4	
Seated UBE			ķ	1	5	4	51	4	1	4	-1	-1	4	4	-1	1	1	
Treadmill walk			~		-	-		_	Ξ,	_	$\overline{}$	_					-	
Strength Training				ጞ	庎	%₀	ľ	x	1	Ŕ	ĸ	∕‰	ጞ	x	庎	∕‰	Ŕ	
Breathing & core stability exercises				汸		Ť	庆	- Tin	ጞ			Ť	÷.	庎		汸		
ancing						d.										~		
K Cool-down						Х		Х	ፖ			ፖ	Х					

Figure 1: Patient's course of infection and recovery displayed as a timeline (black line at top of image) and the physical rehabilitation treatment per each session with physiological variables. The figure depicts the timeline for illness with specific focus on the physical therapy treatment management. The physiological responses to treatment are represented in the MET levels, oxygen saturations (SpO₂) and heart rate. The treatment program utilized a varied approach with focus on aerobic training, strength training, and diaphragmatic breathing techniques. The physical therapist used clinical judgement and autonomy to select each intervention, and thus some interventions were not incorporated in every session. Appt = appointment; ECHO = echocardiogram; HR = heart rate; METS = metabolic equivalents; MRI = magnetic resonance imaging; mRPE = modified rating of perceived exertion scale; PCR = Polymerase chain reaction; SpO2 = blood oxygen saturations. UBE = upper extremity bicycle ergometer.



Figure 2: Patient's self-reported engagement in activity during eight-week physical rehabilitation program

The patient completed a walking program (orange) and home exercise plan (HEP, blue). The HEP was structured from resistance training exercises and breathing techniques performed in the clinic. The general focus included exercises involving major muscle groups such as standing hip exercises (4-way exercises) and standing upper extremity exercises (mid-rows and overhead shoulder press) with resistance band, as well as functional movements (squats, lunges, and repetitive sit-to-stand training). In addition, the patient was informed to gradually increase participation in instrumental activities of daily living and leisure activities at mild to moderate intensities. The patient reported participating in laundry, light-cleaning and grooming her dog early in her program that progressed to gardening, mowing, and cycling in weeks 4-6 and swimming in weeks 7 and 8. Time participating in activities gradually increased except in weeks 5 and 7 which may associate with increases reports of malaise, headaches, and fatigue due to over-exertion in the prior weeks.