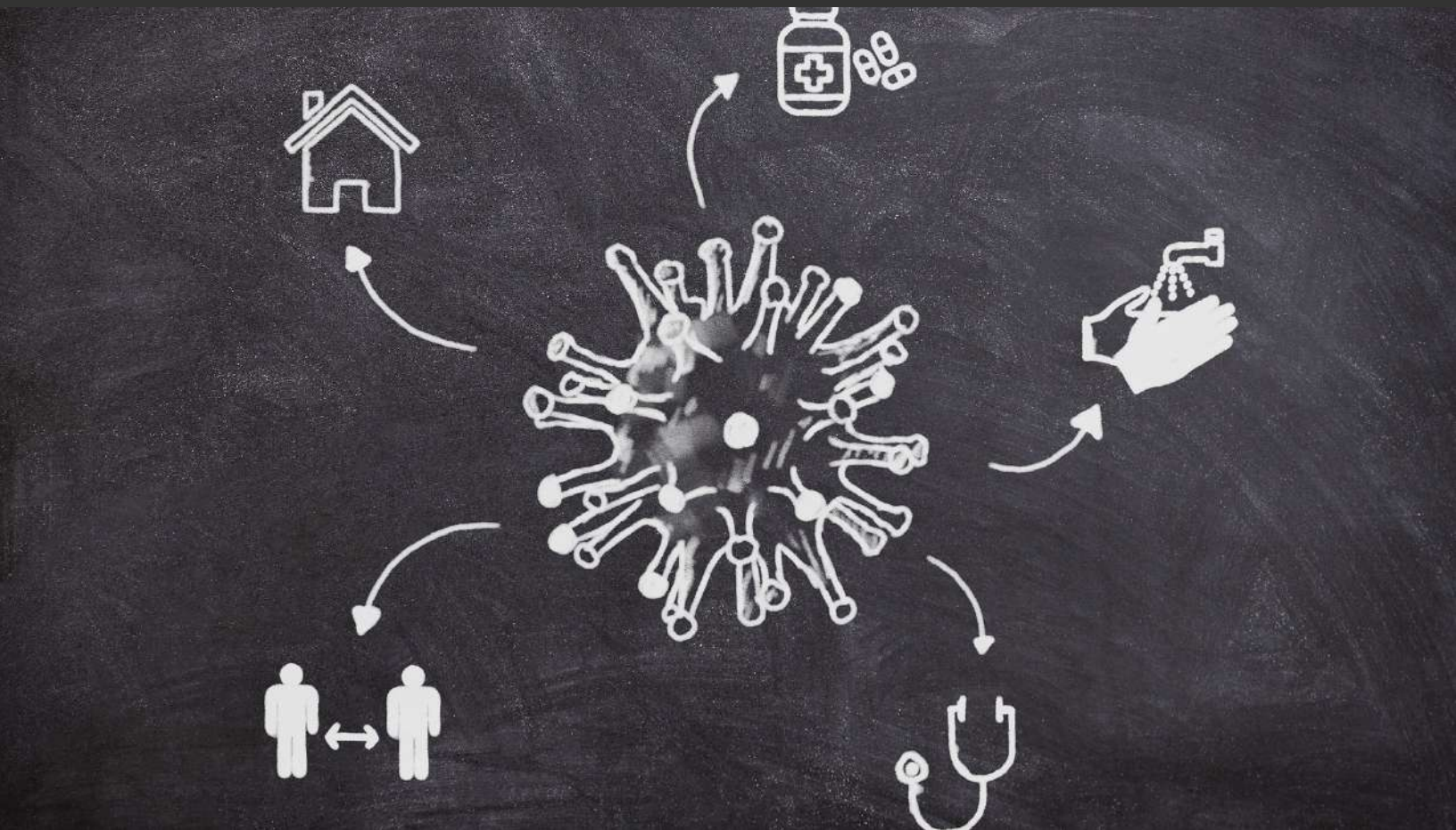
FLEX CEUs

Long Haulers - Physical Therapy Role in Post-COVID Rehabilitation



Introduction

Although the information about severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection continues to unfold, experts know more than they did in early 2020. Whether SARS-CoV-2 is asymptomatic or causes coronavirus disease 2019 (COVID-19), the infection is widely recognized as a multi-organ disease with diverse pathophysiological and clinical manifestations. Similar to other post-acute syndromes described in survivors of other viral epidemics, there have been increasing reports of prolonged symptoms after acute infection from COVID-19 has passed. Many survivors have identified themselves as long haulers and have contributed to the growing recognition of post-acute COVID-19, which is now formally known as Post-Acute Sequelae of SARS-CoV-2 infection (PASC). PASC is also referred to as Long COVID, Long Haulers, Long-term COVID-19, or LTC-19.

Section 1

Other viral infections, such as the SARS epidemic of 2003 and the Middle East respiratory syndrome (MERS) outbreak of 2012, have caused a similar constellation of lingering symptoms. While this reinforces the need to define, assess, and treat PASC, it also highlights concern for long-term dysfunction and disability.

Definition[2,5,12]

Long haulers, also known as PASC, is characterized by persistent symptoms and/or long-term complications beyond 4 weeks from the initial onset of symptoms.5 Symptoms can last weeks or months following an acute infection or may even appear weeks later. It has been documented in survivors of varying ages regardless of symptom severity.

While experts continue to determine the timeline of post-acute symptoms related to COVID-19, some studies suggest using a cut-off of 3-4 weeks from the onset of acute symptoms. This recommendation stems from the fact that SARS-CoV-2 has not been isolated after 3 weeks, thus suggesting that any persistent symptoms should not be considered part of an ongoing acute infection.

Based on recent literature, PASC is divided into two categories:

1. **Subacute COVID-19** which includes symptoms and abnormalities present from 4–12 weeks beyond acute COVID-19.

2. **Chronic or Post-COVID-19 Syndrome**, which includes symptoms persisting beyond 12 weeks of the onset of acute COVID-19. Furthermore, these symptoms are not attributable to alternative diagnoses.

Prevalence[1,4,5,10,11]

- On January 30th, 2021, the pandemic had already affected 102,107,858 people worldwide.[10] Researchers estimate about 10% of them will become long haulers.[11] Other sources estimate that 25–35% of COVID-19 survivors, regardless of infection severity, will experience PASC even after they no longer test positive for the virus or antibodies.
- A study conducted by the COVID-19 Longhauler Advocacy Project found that only about 3% of those with PASC have recovered, meaning they reported complete resolution of all symptoms and ailments related to their illness with COVID-19.
- However, it's important to realize that estimates of individuals infected with COVID-19 are likely to be significantly below representation since it is highly possible that many more individuals have been infected without formal COVID-19 testing and/or medical treatment. Recall that, early in the pandemic, many

hospital systems did not admit those with mild signs and symptoms. Those patients who were classified as having “mild” COVID-19 most likely never received care as the infection was expected to completely resolve. Unfortunately, these individuals with “mild” COVID-19 may be the ones who still experience persistent symptoms, even weeks following the onset of symptoms, and may make up a large cohort of those with PASC. This is supported by the fact that the median number of symptoms is still high three months after the onset of symptoms in hospitalized and non hospitalized patients.[4] Unfortunately, about 30% of individuals are still reporting symptoms nine months following infection.[1,5]

- About 20% of patients continue to exhibit significant reductions in lung capability along with posttraumatic stress at four months following viral recovery.[2] Although the upper and lower respiratory tracts are the main points of entry into the body, acute lung damage in the early phases of infection is likely to be followed by pulmonary fibrosis and chronic impairment of lung function, along with impaired quality of life. Increasing reports on the effect of SARS-CoV-2 infection on the central nervous system and the peripheral nervous system may also raise questions regarding long-term neurological sequelae.[3]

Risk factors for developing PASC[4,5,13]

- A new study suggests that those who experience more than five symptoms related to SARS-CoV-2 within the first week of infection may be more susceptible to developing PASC. The symptoms that were most predictive of PASC are fatigue, headache, hoarseness, myalgia, and dyspnea.

- The severity of illness during acute COVID-19 infection, typically measured by admission to a critical care unit or the need for mechanical ventilation, has been significantly associated with the presence of persistent symptoms (such as dyspnea, fatigue/muscular weakness, and post-traumatic stress disorder), reduction in quality of life scores, abnormal pulmonary function, and observable changes on imaging in the post-acute COVID-19 settings. Furthermore, there have been relationships observed between pre-existing respiratory disease, higher body mass index, older age, and Black, Asian, and minority groups, and dyspnea at the 4–8 week follow-up mark. The likelihood of developing PASC rises with age, and anosmia is the most commonly reported symptom in the older generations.

- Some studies have shown there to be gender differences, with women being more likely to report fatigue and anxiety/depression at 6 months follow-up,

similar to statistics in SARS survivors. Additionally, previous studies in SARS survivors also match current data that show that 25–30% of COVID-19 survivors report new onset of secondary infections, such as bacterial or fungal infections. However, these secondary infections do not necessarily relate to PASC and its presentation.

- While other comorbidities, such as diabetes, obesity, chronic cardiovascular or kidney disease, cancer, and organ transplantation, are well-recognized determinants of increased severity and mortality related to acute COVID-19, their association with PASC outcomes in those who have recovered remains to be determined.

Signs and Symptoms of PASC[1,2,5,12]

Given the similarities between coronavirus disease 2019 (COVID-19) and diseases caused by other coronaviruses, post-acute and long-term sequelae that require specific treatment should be expected. Some of the most significant lingering effects include fatigue, worsened quality of life, dyspnea, cough, loss of taste or smell, joint pain, chest pain.[1,5]

Symptoms associated with PASC may persist weeks or even months after symptoms initially appear. According to the Centers for Disease Control and Prevention, these can include:

- Fatigue
- Dyspnea
- Cough
- Chest pain
- Difficulty with thinking and concentration (aka “brain fog”)
- Myalgias and arthralgias
- Headache
- Fever
- Heart palpitations
- Myocarditis

- Acute kidney injury
- Rash
- Smell and taste problems
- Memory problems
- Anxiety and depression
- Changes in mood
- Post-traumatic stress

System-specific symptoms are summarized below.

Pulmonary

- Dyspnea, decreased exercise capacity, and hypoxia
- Reduced diffusion capacity, restrictive pulmonary physiology, and fibrotic changes on imaging have been noted at follow-up of COVID-19 survivors

Cardiovascular

- Persistent symptoms may include palpitations, dyspnea, and chest pain
- Long-term sequelae may include increased cardiometabolic demand, myocardial fibrosis or scarring (detectable via cardiac MRI), arrhythmias, tachycardia, and autonomic dysfunction

Neurological

- Persistent abnormalities may include fatigue, myalgia, headache, dysautonomia, and cognitive impairment (sometimes referred to as “brain fog”)
- Anxiety, depression, sleep disturbances, and PTSD have been reported in 30–40% of COVID-19 survivors, similar to survivors of other coronaviruses.

Endocrine

- New or worsening control of existing diabetes mellitus, thyroid dysfunction, and changes to bone structure

Integumentary

- Hair loss

Recrudescence[17,18]

- Among COVID-19 survivors, 68% received a new diagnosis, and 38% visited a new specialist related to PASC symptoms. Preliminary data on the presentation of PASC and its related symptoms show a correlation to other chronic illnesses that have documented associations with Myalgic Encephalomyelitis/Chronic Fatigue Syndrome (ME/CFS), postural orthostatic tachycardia syndrome (POTS), other forms of Dysautonomia, and Mast Cell Activation Syndrome (MCAS). But while the emergence of such conditions is certainly a cause for concern, many have raised the question of the recurrence of symptoms associated with COVID-19.

- While additional research in this area is underway, there have been rare cases of suspected COVID-19 “recurrence” or “reactivation.” In this sense, recurrence, recrudescence, and reactivation refer to the reappearance of symptoms in survivors due to the persistence of the virus at immunologically separated sites within the body.

- The COCOREC (Collaborative study COvid RECurrences) study aimed at summarizing clinical and virological data of patients presenting a second confirmed COVID-19 episode, at least 21 days after the first onset, and after a symptom-free interval. Researchers presented 11 patients who experienced two separate symptomatic COVID-19 episodes, and they postulated that recurrence may be attributed to suboptimal control of the SARS-CoV-2 infection, thus allowing the second episode of viral replication. Age, immunity status, underlying lung disease, and the severity of the SARS-CoV2 infection are factors that may affect the body’s ability to control and eliminate the virus.

- According to the World Health Organization, there is no evidence that the patients who recovered from COVID-19 are immune from a second attack. Further studies are needed to determine if recrudescence is associated with relapse or reinfection of the virus that has not been completely eradicated from the body. Additionally, it is unclear if the administration of corticosteroids to patients with acute SARS-CoV-2 infection hinders the development of antibodies.

- Unfortunately, experts do not have answers to questions regarding whether individuals upon recovery are prone to repeat infection and how others develop immunity to the virus.
    - The development of immunity is a multistep process that takes place over one to two weeks. Immediately upon infection, the body activates a non-specific response in which macrophages, neutrophils, and dendritic cells delay the replication of the virus and subsequently may even prevent symptoms.
    - Next, the body creates antibodies that bind to the virus, known as immunoglobulins. T-cells are also generated to recognize and eliminate other cells infected with the virus. This process is called cellular immunity.
    - Together, these processes aim to eliminate the virus from the body and, if the response is strong enough, may prevent progression to severe illness or re-infection by the same virus. If this is the case, then antibodies are present in the bloodstream.
    - This finding is supported by several studies that show that people who have recovered from SARS-CoV-2 have antibodies to the virus.

Section 1: Summary

- There have been increasing reports of prolonged symptoms after acute infection from COVID-19 has passed. This growing recognition of post-acute COVID-19 has led experts to formally recognize this constellation of symptoms as Post-Acute Sequelae of SARS-CoV-2 infection (PASC). PASC is also referred to as Long COVID, Long Haulers, Long-term COVID-19, or LTC-19.
- Long haulers, also known as PASC, is characterized by persistent symptoms and/or long-term complications beyond 4 weeks from the initial onset of symptoms. Symptoms can last weeks or months following an acute infection or may even appear weeks later. It has been documented in survivors of varying ages regardless of symptom severity.
- Researchers estimate about 10% of them will become long haulers. A new study suggests that those who experience more than five symptoms related to SARS-CoV-2 within the first week of infection may be more susceptible to developing

PASC. The symptoms that were most predictive of PASC are fatigue, headache, hoarseness, myalgia, and dyspnea.

- Symptoms associated with PASC may persist weeks or even months after symptoms initially appear. Some of the most significant lingering effects include fatigue, worsened quality of life, dyspnea, cough, loss of taste or smell, joint pain, chest pain.
- Unfortunately, experts do not have answers to questions regarding whether individuals upon recovery are prone to repeat infection and how others develop immunity to the virus.

Section 1: Key Words

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection - a viral respiratory illness caused by a coronavirus called SARS-associated coronavirus (SARS-CoV). SARS SARS-CoV-19 was first reported in China in late 2019.

Coronavirus disease 2019 (COVID-19) - a new disease caused by a novel coronavirus that has not previously been seen in humans.

Post-Acute Sequelae of SARS-CoV-2 infection (PASC) - also referred to as Long COVID, Long Haulers, Long-term COVID-19, or LTC-19. Refers to an array of persistent symptoms beyond the acute infection.

SARS - Severe acute respiratory syndrome (SARS) is a viral respiratory disease caused by a SARS-associated coronavirus.

Middle East respiratory syndrome (MERS) - a viral respiratory illness that is new to humans. It was first reported in Saudi Arabia in 2012 and has since spread to several other countries, including the United States. Most people infected with MERS-CoV developed severe respiratory illnesses, including fever, cough, and shortness of breath.

COVID-19 Longhauler Advocacy Project - a network of patient advocates, scientists, disease experts, and drug developers who have joined together to leverage their collective knowledge and resources to educate policymakers and accelerate research to transform our understanding of post-viral illness.

Myalgic Encephalomyelitis/Chronic Fatigue Syndrome (ME/CFS) - a disabling and complex illness with no known causes or cure.

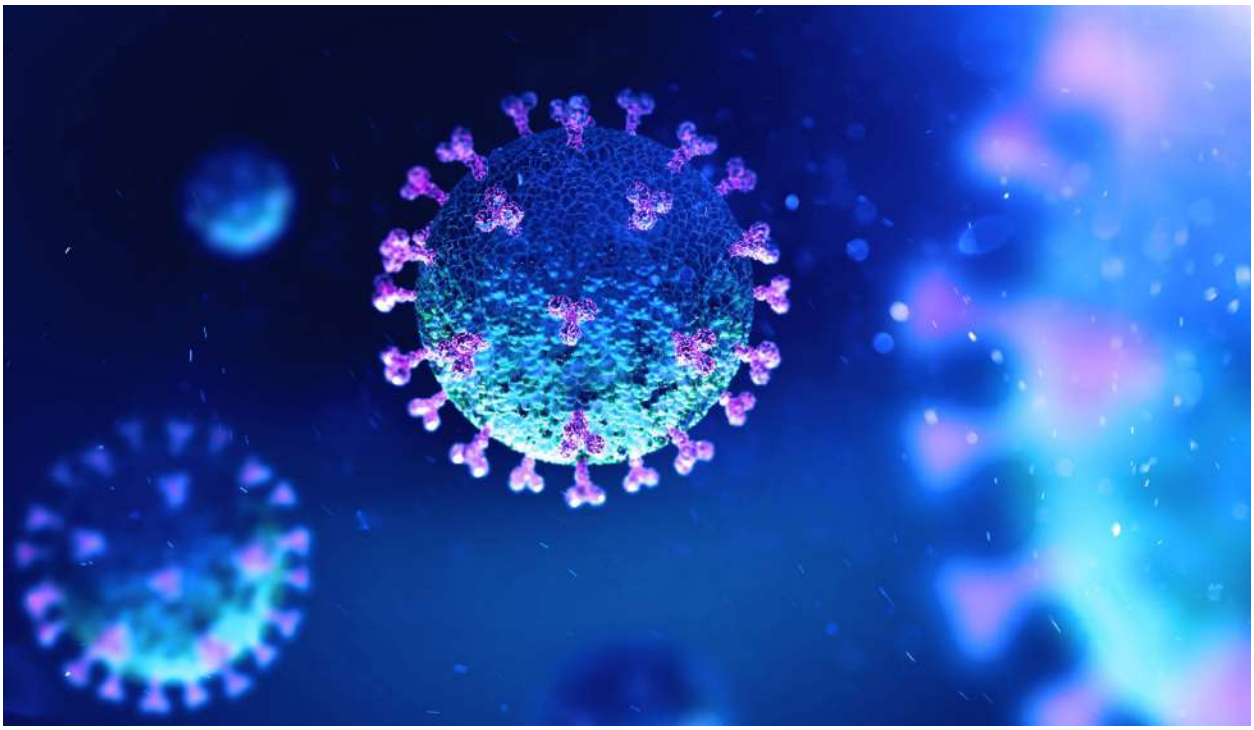
Postural orthostatic tachycardia syndrome (POTS) - a disorder of the autonomic nervous system.

Mast Cell Activation Syndrome (MCAS) - a condition in which the patient experiences repeated episodes of the symptoms of anaphylaxis.

Recrudescence - refers to the reappearance of symptoms in survivors due to the persistence of the virus at immunologically separated sites within the body.

Section 2

Pathophysiology[2,3,5]



Underlying pathophysiology mechanisms of acute infections secondary to COVID-19 have been identified and described in the literature. Generally, experts have agreed that the dominant infection mechanisms are systemic in nature and include:

- Direct viral toxicity
- Endothelial damage
- Microvascular injury
- Immune system dysregulation and stimulation of a hyperinflammatory state

- Hypercoagulability
- Maladaptation of the angiotensin-converting enzyme 2 (ACE2) pathway

Alternatively, there have been different proposed mechanisms contributing to the pathophysiological development of PACS. Such mechanisms include:

- Virus-specific pathophysiologic changes
- Immunologic abnormalities and inflammatory damage in response to the acute infection
- Prolonged sequelae of post-critical illness

It was initially postulated that SARS-CoV-2 was unable to traverse through the blood-brain barrier (BBB), but this has since been proven otherwise.

- New findings demonstrate that SARS-CoV-2 can, in fact, alter the BBB and thereby enter the brain. This finding would support the appearance of neurological symptoms and sequelae, microthrombi, and the occurrence of encephalitis associated with COVID-19.
- In addition, SARS-CoV-2 may enter the brain through synaptic transfer, optic and olfactory nerve pathways, and vascular cells in the BBB. Regardless of the method of invasion, when it finally reaches its destination, the infection rapidly replicates to cause swelling, functional impairment, and/or cell death.
- Early changes to the neurological system following acute SARS-CoV-2 may be explained by the way in which the infection passes through the BBB. However, this also presents an argument for an underlying mechanism of long-term neurological sequelae. Rapid viral replication, cell damage, and activation of the immune system and inflammatory mediators, including cytokines, are the likely causes of the acute symptoms of COVID-19 and may provide reasonable explanations for the long-term sequelae of SARS-CoV-2 infection.
- The increase in inflammatory mediators termed ‘cytokine storm’ may explain the presence of multi-organ damage and long-term effects of SARS-CoV-2 on the central nervous system. Cytokine storming occurs when a large number of pro-inflammatory cytokines are released, thus causing increases in vascular permeability, excessive and abnormal coagulation, and multiple-organ failure. These cytokines may also play a role in increasing the permeability of the virus

into the central nervous system through vascularity and the BBB. Lastly, the cytokine storm may also have a profound effect on the formation of microthrombi which may explain the incidence of cerebral vascular accidents in those with COVID-19.

Long-term respiratory implications of COVID-19 are unknown. However, researchers have established a commonality between COVID-19 survivors, which is lung damage.

- Despite the fact that COVID-19, and therefore PASC, causes systemic impairments, there are documented histopathological findings that may be the underlying cause of long-term functional sequelae in this population. Findings include diffuse destruction of the alveolar epithelium, capillary damage, and pulmonary consolidation.

- Consequently, alterations in the lung's diffusion capacity with respect to carbon monoxide are affected in patients with COVID-19, similar to survivors of SARS and MERS. Both of those illnesses have been associated with lung impairments lasting months to years.

- These abnormal histological findings correlate with impairments in exercise capacity. Research on individuals recovering from secondary pneumonia following SARS has been found to have lower scores on the 6-minute walking test and 36-item Short Form General Health Survey than the general population.

- Furthermore, respiratory dysfunction observed in those with acute SARS-CoV-2 infection reflects inflammatory damage to all three locations of the respiratory system including the trachea, the bronchi, and the alveolar sacs. The inflammation stemming from the 'cytokine storm,' discussed above, is often followed by long-term fibrotic changes and may potentially contribute to functional deficits seen in patients with PASC.

Moreover, clinicians should realize that pathophysiological damage sustained during acute infection of SARS-CoV-2 may be associated with adverse psychological outcomes. Given the sequelae of damage to the central nervous system by SARS-CoV-2, there is concern regarding its long-term effects on cognitive function in those with PASC. Furthermore, it is possible that there is an underlying connection and relationship between SARS-CoV-2 infection, Alzheimer's Disease, and other neurodegenerative diseases which stands to be proven in the research. The theory behind this is the fact that inflammatory responses and loss of neuronal volume are common structural

changes that are commonly seen in neurodegenerative diseases. It is plausible that the SARS-CoV-2 infection accelerates such processes.

Response to vaccines[16]

- SARS-CoV-2 vaccines are presumed to be the best method to achieve immunity and, therefore, end the pandemic. However, the appearance of PASC has introduced new concerns regarding the impact the COVID-19 vaccines might have on patients with PASC.
- A recent study examined the effects of the COVID-19 vaccine on PASC symptoms. Patients who were previously hospitalized with COVID-19 were administered the Pfizer or AstraZeneca vaccines and followed for one month.
    - The rates of lingering symptoms were high as 82% reported increased amounts of fatigue (61%), dyspnea (50%), and insomnia (38%).
    - Pertinent findings were as follows:
        - Some degree of improvement in PASC symptoms was observed in the vaccinated group as compared to unvaccinated controls.

    - An increase in symptom resolution was documented among the vaccinated (23.2%) as compared to unvaccinated individuals (15.4%).
    - When comparing the pre and post-vaccination periods, there was no effect on worsening of mental well-being or quality of life.
    - Results of the study did not differ based upon the brand of vaccine that was administered.
  - This small study confirmed that patients with PASC can safely receive the COVID-19 vaccine. However, additional data that confirms or refutes this monumental study is critical.
- The Centers for Disease Control and Prevention state that people who have had COVID-19 can still receive the COVID-19 vaccine, regardless of whether or not they have symptoms. Experts suggest waiting at least 10 days following the resolution of symptoms before receiving the vaccine.

Ongoing research[14,15]

- As of February 23, 2021, the National Institute for Health announced a newly-formed initiative, the NIH PASC Initiative, to learn more about the lasting effects of SARS-CoV-2 and how it contributes to widespread and prolonged symptoms commonly reported by individuals with PASC. A secondary aim of this initiative is to develop methods of assessing, diagnosing, and treating PASC.
- Long COVID Alliance was developed by the COVID-19 Longhauler Advocacy Project. Its sole mission is to assist patients and physicians work together to mitigate signs and symptoms associated with PASC.
- The Global Long COVID Data Consortium is collecting data from those with and without PASC to create a cohort of data. In doing so, researchers hope to study susceptibility to long-term effects, the emergence of symptoms and symptom clusters, commonalities between PASC and other post-viral illnesses, and potential treatments.
- Researchers at Stanford University, Stony Brook University, and Johns Hopkins Bloomberg School of Public Health are gathering information on patient experiences with acute and long-term COVID-19 symptoms in order to identify effective treatment strategies for PASC.

- The Patient-Led Research Collaborative examined the experiences of patients suffering from COVID-19 with prolonged symptoms. They found that the main difference between people who tested positive and people who tested negative was not necessarily the symptoms they experienced (as most symptoms were similar), but the timing of their testing. Researchers also emphasized that, because so many individuals did not undergo testing, results are not an accurate portrayal of the larger subset and comprehensive conclusions could not be drawn from the existing data. A new study looking at antibody testing results and neurological and cardiovascular symptoms, as well as the impact on mental health, is currently enrolling new participants.
- Researchers from the Pulmonary Wellness Foundation and the University of Dayton are recruiting patients for a clinical trial of a rehabilitation program for those suffering from PASC. Eligible participants will undergo an orthostatic tolerance test, pre-and post-treatment exercise tolerance tests, and 24 treatment sessions that will involve aerobic exercise, supplemental oxygen, or both.

Section 2: Summary

- Experts have agreed that the dominant infection mechanisms are systemic in nature and include direct viral toxicity, Endothelial damage, microvascular injury, immune system dysregulation, hypercoagulability, and maladaptation of the angiotensin-converting enzyme 2 (ACE2) pathway.
- New findings demonstrate that SARS-CoV-2 can, in fact, alter the BBB and thereby enter the brain. This finding would support the appearance of neurological symptoms and sequelae, microthrombi, and the occurrence of encephalitis associated with COVID-19.
- Given the sequelae of damage to the central nervous system by SARS-CoV-2, there is concern regarding its long-term effects on cognitive function in those with PASC but new research is needed to prove the exact relationship.
- The Centers for Disease Control and Prevention state that people who have had COVID-19 can still receive the COVID-19 vaccine, regardless of whether or not they have symptoms. Experts suggest waiting at least 10 days following the resolution of symptoms before receiving the vaccine.
- As of February 23, 2021, the National Institute for Health announced a newly-formed initiative, the NIH PASC Initiative, to learn more about the lasting effects

of SARS-CoV-2 and how it contributes to widespread and prolonged symptoms commonly reported by individuals with PASC. In addition to the NIH PASC Initiative, various other researchers across the country are putting forth efforts to discover more about the origins, risk factors, effects, and treatments for PASC.

Section 2: Key Words

Pathophysiology - the study of abnormalities in the body

Blood-brain barrier - a barrier between the brain's vascular system and the cells and other components that make up brain tissue

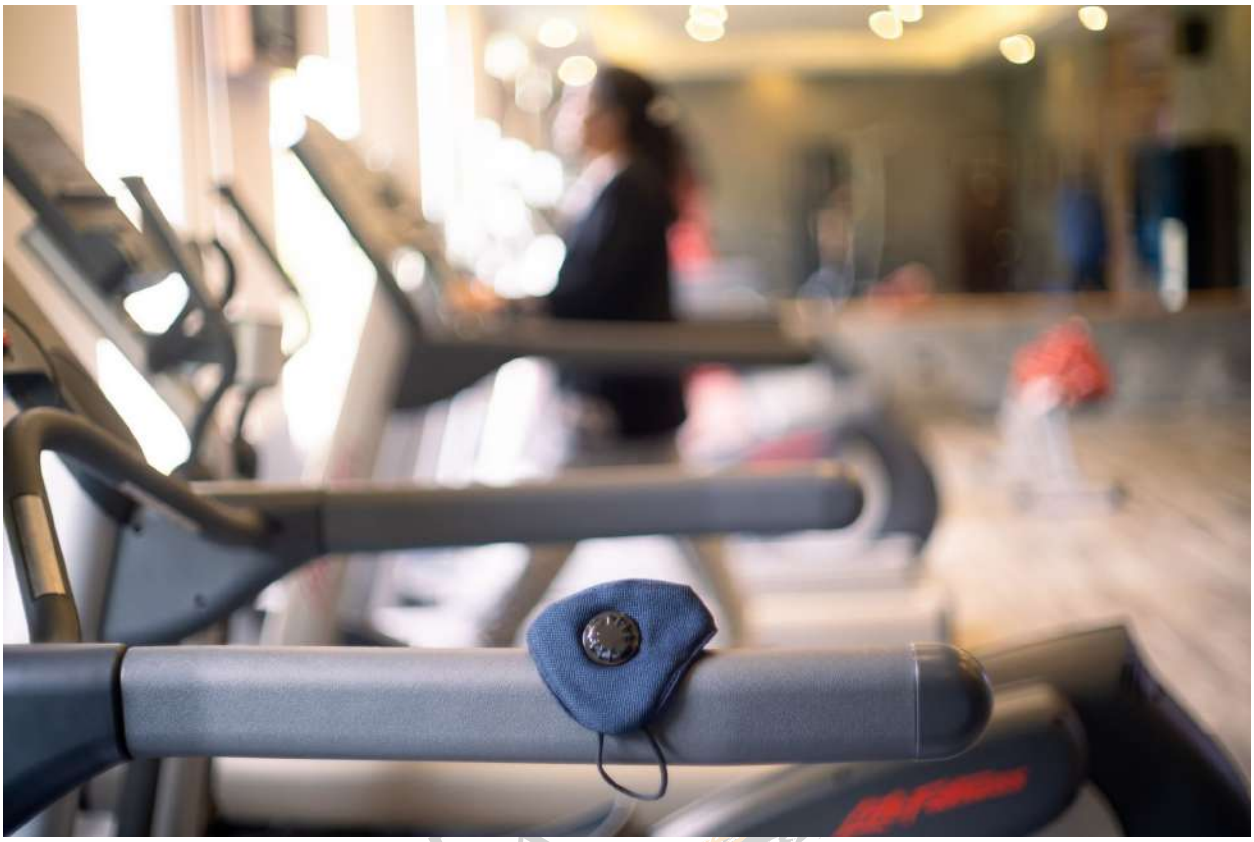
Encephalitis - Inflammation of the brain

Cytokine storm - autoimmune disorders characterized by constitutional symptoms

NIH PASC Initiative - new NIH initiative to identify the causes and ultimately the means of prevention and treatment of individuals who have been sickened by COVID-19 but do not recover fully over a period of a few weeks

Section 3

Evaluating and treating patients with confirmed or suspected PASC requires an organized approach with a comprehensive rehabilitation team. It is likely that these patients will require services from physical therapy, occupational therapy, speech-language pathology, psychology, and physiatry. Additionally, it is critical that the rehabilitation team collaborates with the acute medical care team to ensure that the patients' needs are met.



Implications for Rehabilitation Specialists[2,6,7]

- Rehabilitation of PASC should be viewed with a holistic approach to evaluation, assessment, and treatment. Due to its expansive presentation, clinicians should utilize a biopsychosocial model that monitors changes and the effects of interventions across the continuum of care.
- The complexity and variability of the damage caused by COVID-19, combined with pre-existing chronic conditions, signifies that there is not a single approach to patients who present with PASC. Furthermore, there are known cardiovascular, respiratory, neurological, renal, gastrointestinal, and psychological effects that are likely to delay recovery in any rehabilitation setting.
    - The enormous amounts of stress placed on the body from fighting the virus can prompt a chronic stress response with the subsequent release of adrenaline and epinephrine. Such consequences have drastic effects on the heart and renal systems and will affect the patient's ability to exercise.
    - Apart from its well-known effects, the virus can affect the central and peripheral nervous systems and circulation. Therefore, it is plausible to

assume that patients may develop persisting dysfunction of almost any organ system and exhibit almost any symptom and sign following COVID-19.

- While data on PASC continues to be collected, there have been studies to illustrate the degree to which physical function is impaired following COVID-19. Studies using the Short Physical Performance Battery have found individuals to have limitations in mobility and functional performance. Those who underwent a 2-minute walk test demonstrated shorter walking distances and reported that their tolerance to exercise (endurance) had worsened after COVID-19. Clinicians should be aware that patients who attend physical therapy with a history of COVID-19 are susceptible to impairments in body function and structure, activity limitations, and participation restrictions that may be undetected, especially if the patient is referred to therapy for non-COVID related deficits.

Treatment approaches to PASC[7-10,19-21]

- As with other health conditions, clinicians should direct the treatment and plan of care around the patient's priorities, needs, and goals while covering all domains of the biopsychosocial model. Those with PASC should be followed closely especially in the initial three to six months upon returning to exercise programs.
- A prospective surveillance model (COVID19-PSM) has been proposed for patients with PASC as it may enable clinicians to identify early signs of impairment, predict severity of dysfunction, and allow for early intervention when feasible. Similar prospective surveillance models have been successful in patients undergoing cancer rehabilitation.
    - The proposed COVID19-PSM is divided into three sections: **rapid screening**, **general assessment**, and **specific assessments** for each system that is affected. Specific assessments are then tailored to address three areas as observed in Figure 2.1: Cardiorespiratory, Neuromuscular, and Mental Health.

Figure 2.1 Specific Assessments for the Cardiorespiratory, Neuromuscular, and Mental Health dysfunction

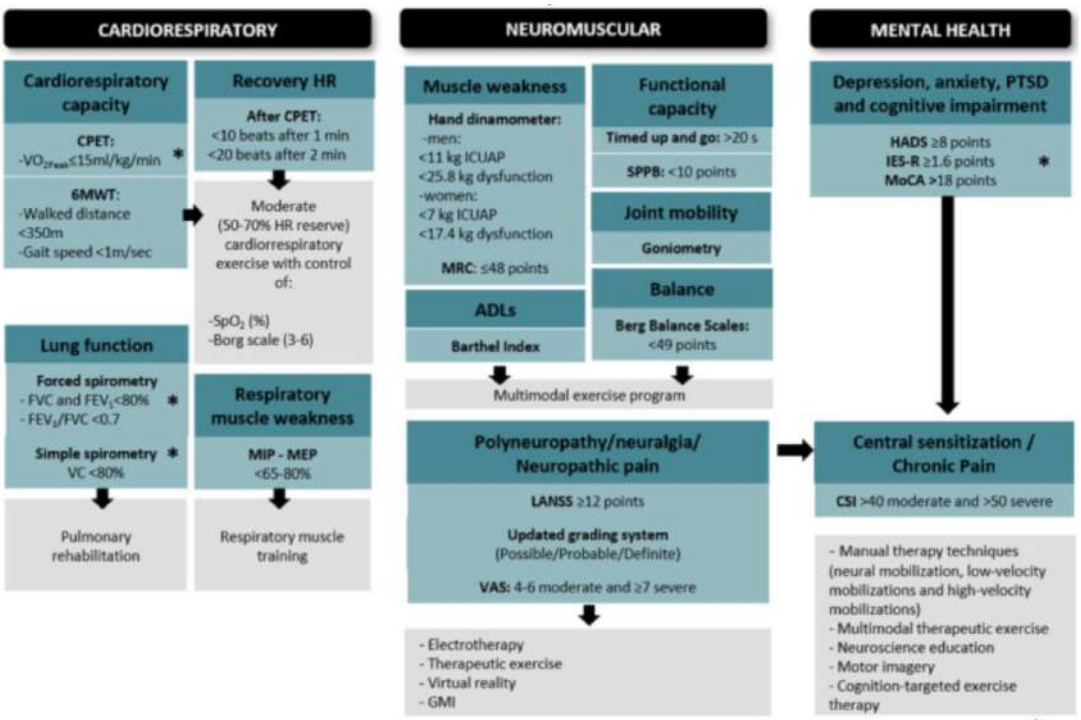


Image adapted from *Postigo-Martin, P., Cantarero-Villanueva, I., Lista-Paz, A., Castro-Martín, E., Arroyo-Morales, M., & Seco-Calvo, J. (2021). A COVID-19 Rehabilitation Prospective Surveillance Model for Use by Physiotherapists. Journal of clinical medicine, 10(8), 1691. https://doi.org/10.3390/jcm10081691*

- Under the COVID19-PSM, patients who present with suspected cardiorespiratory dysfunction should undergo appropriate outcome measures including a 6-minute walk test, spirometry, or cardiopulmonary exercise testing. In the event that pulmonary rehabilitation, supervised aerobic exercise, or respiratory muscle training is not effective in addressing the patient's impairments, then patients should be referred to a specialist.

- Due to the potential for neurological dysfunction after COVID-19, tests and measures and outcome measures that examine muscle weakness, functional performance, range of motion, static and dynamic balance, neuropathy, and pain should be performed. These complications affect the patients' general functional capacity, making it difficult for them to perform activities of daily living or to return to work.

A comment regarding neuropathic pain: It is unclear how prolonged pain, whether it's related to peripheral neuropathies or central sensitization, originates in post-viral syndromes. However, efforts should be taken to avoid progression to chronic pain patterns by incorporating manual therapy, therapeutic exercise, motor imagery, and/or cognitive behavioral therapy into the patient's plan of care.

- Lastly, it is abundantly clear that COVID-19 survivors, especially those who required critical care or mechanical ventilation, are at risk of developing long-term psychological distress and disorders such as depression, anxiety, and post-traumatic stress disorder. These conditions are known to compromise the immune system and may further prolong recovery. The COVID19-PSM includes mental health assessments and suggests that patients identified as suffering from mental health problems should be referred to an appropriate specialist.

- Guidelines for returning to physical activity after COVID-19

    - For individuals recovering from a mild COVID-19 infection, the National Strength and Conditioning Association and Collegiate Strength and Conditioning Coaches Association Joint committee recommend a gradual return to activity. The committee suggests incorporating the 50/30/20/10 Rule that can be administered over a 4-week period.

        - The 50/30/20/10 Rule suggests that training volume is reduced by at least 50% of the normal exercise load for the first week. Then, volume is decreased by 30%, 20%, and 10% in the following three weeks as long as the patient is able to tolerate the training program.

        - Clinicians are encouraged to make modifications to the training volume and load if an individual requires a gradual return to activity over a period of months as opposed to weeks.

    - English and Scottish Institute of Sport suggests that individuals should be able to perform activities of daily living and ambulate at least 500 meters on level surfaces without excessive fatigue or dyspnea prior to resuming physical activity. Experts caution that clinicians should consider the patient's baseline and modify recommendations accordingly. Those who were previously unable to ambulate 500 meters should not be kept from initiating physical activity at a level that is appropriate for them.

- For other cases, clinicians should initiate light-intensity activity for at least two weeks before progressing to more moderate forms of activity. Then, patients may progress to activities like intervals of brisk walking, stairs negotiation, jogging, swimming, or cycling separated by recovery periods. Finally, patients may begin performing complex exercises that incorporate coordination, strength, and balance. Activities such as running with direction changes, side-steps, shuffles, and circuit training should be incorporated, especially if the individual is active or athletic. Once patients feel as if they have returned to their baseline levels of activity, then they may be appropriate for discharge from physical therapy. Experts suggest a minimum of seven days at each phase.
    - The Borg Rating of Perceived Exertion (RPE) scale can be used as a method to gauge exercise intensity and effort. The RPE scale is also helpful in allowing clinicians to select appropriate activities as the patients progress through graded physical activity.
    - Light intensity exercise is equivalent to RPE less than 11, and patients should be able to hold a full conversation without difficulty at this level. Activities that are considered to be light intensity include household and light garden tasks, gentle walking, and balance or yoga exercises. Breathing, stretching, and light strengthening activities can also be incorporated into the patient's activity plan.
    - Exercise intensity should be gradually increased by 10-15 minutes at the same RPE when tolerated. Clinicians should monitor exercise recovery for at least one hour after exercise. Abnormalities in breathing rhythm or dyspnea, heart rate, fatigue, lethargy, or exercise tolerance may indicate that the individual is not ready to progress and should return to a lower intensity level or seek additional medical attention.
- The Post-Acute COVID-19 Exercise and Rehabilitation (PACER) Project is an initiative led by the APTA Academy of Cardiovascular & Pulmonary Physical Therapy.
    - According to the expert panel of the PACER project, it is common to see patients with tachycardia, hypoxemia, orthostatic hypotension, shallow

breathing, and fatigue following COVID-19. When reintroducing strength training in this population, follow the Specific Adaptation to Imposed Demand (SAID) principle, which states that the body adapts specifically to imposed demands that are placed upon it. Other considerations for strength training include compound over isolated movements, types of muscle contractions, and patient-regulated exercise prescription.

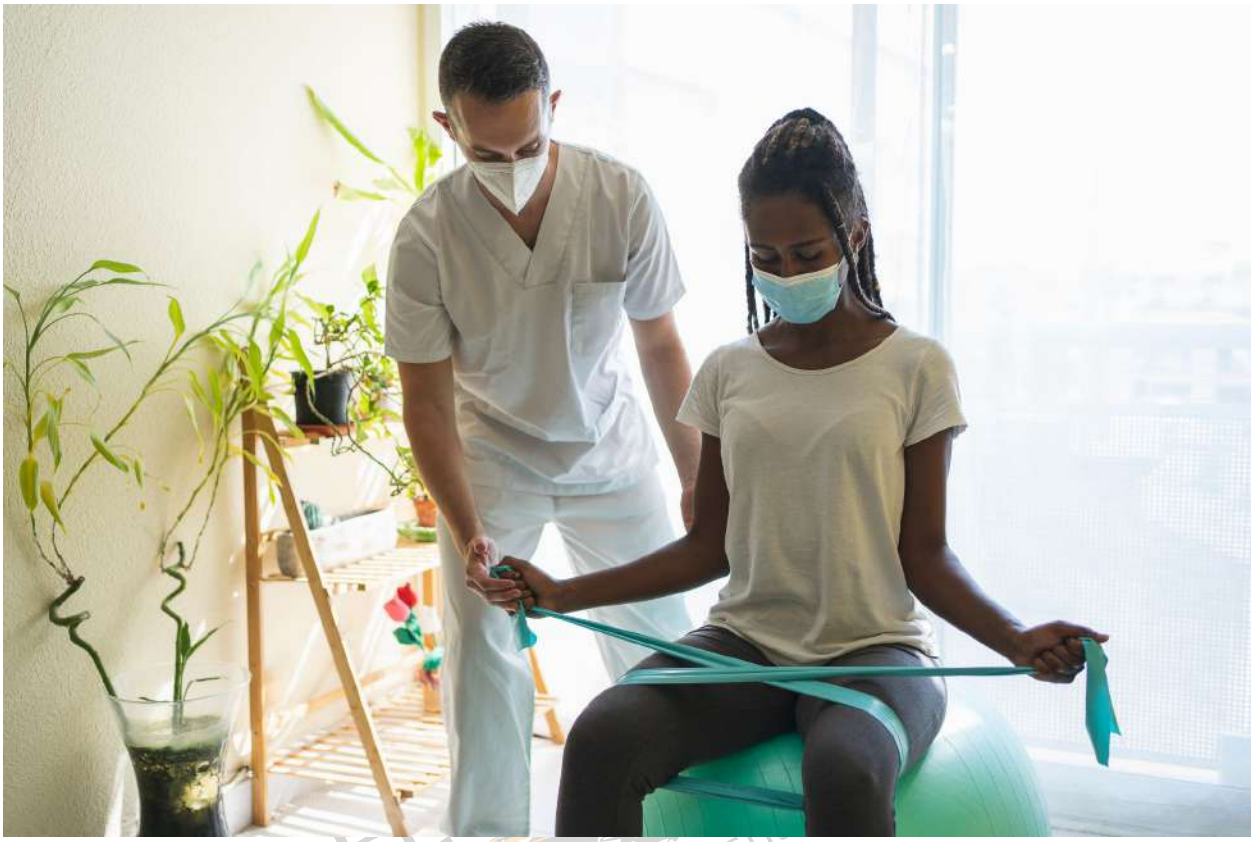
    - Patient-regulated exercise prescription is separated into two categories: Reps in Reserve (RIR) and Rate of Perceived Exertion (RPE). The aim of either practice is to have the patient work to a moderate level of activity based upon his or her subjective perception of effort.

    - Monitoring patients during strength training is critical to ensure patient safety. Methods for monitoring include observation, taking vital signs, measuring pulse oximetry, and asking the patient about RPE.

    - Be aware that mask-wearing may affect exercise performance and effective communication during treatment sessions. Studies have shown that mask-wearing can cause higher ratings of perceived exertion, increased dyspnea, and feelings of claustrophobia while wearing a face mask during exercise. Researchers also found that masks affected physical and mental outcomes at low, moderate, and high-intensity exercise.

- Other highlights from the PACER project include incorporating combined outcome measures that directly correlate with function to measure patients' functional capacity. These include the Timed Up and Go, Short Performance Physical Battery, Senior Fitness Test, and the COVID-19 Core Outcome Measures.

Realistic goals and expectations for patients with PASC[7-10,19,20]



- The following recommendations are adapted from the COVID-19 Core Outcome Measures: Clinical Application Algorithm.
    - Complete a thorough chart review and systems review when evaluating patients with a history of COVID-19 infection. Screen for cardiovascular disease, a history of heart failure, and ongoing hypoxia. Use the Wells Clinical Prediction Rule for venothrombosis embolism and the Ankle Brachial Index when applicable.
    - Utilize guidelines from the American College of Sports Medicine for exercise testing and physical activity. Clarify any vital sign parameters with the medical team and be sure to follow them during any type of physical activity. Monitor reports of dyspnea and rate of perceived exertion during all treatment sessions.
    - Complete a 6-Minute Walk Test and gait speed measurements on all patients.

    - Consider the impact of social isolation, patients' emotional state, loss of functional ability, critical care survivorship, and changes in work or life situations on the patient's mental health. Administer the Hospital Anxiety and Depression Screen and screening for possible mental health disorders.
    - Consider the impact of impaired sensory systems and coordination. If there are deficits in the patient's ability to perform dual tasks, use the Timed Up and Go Cognitive Test. For upper extremity neurological deficits, administer the Finger Tapping Test and the Goal Attainment Scale, and use the Neuro Core Outcomes Set for lower extremity neurological or balance deficits. If patients present with stroke-like symptoms, utilize outcome measures described in the StrokeEDGE.
    - It is recommended to perform remeasurements every 30 days and every three, six, and 12 months following a COVID-19 diagnosis.
- Clinicians should prioritize strengthening and cardiorespiratory activity in patients who are diagnosed with PASC. These activities are beneficial for patients' overall fitness but also a range of other impairments such as fatigue, stress and anxiety, depression, and weakness.
    - Cardiovascular impairments should be treated with moderate-intensity exercise, with careful monitoring of pulse oximetry. Exercise is contraindicated if oxygen saturation values decrease by <90% or a decrease by more than 4% from baseline.
    - Monitoring objective fitness data is helpful to determine exercise capacity and tolerance in patients with PASC. Clinicians should measure recovery heart rate which reflects the reactivation of the parasympathetic system after physical exercise. Data suggests that physical exercise capacity and performance are abnormal if the difference between baseline heart rate and maximal heart rate achieved during physical exercise is less than 10 or 20 beats after one and two minutes, respectively.
- The Specific Adaptation to Imposed Demand (SAID) principle is particularly relevant to patients with neurological and musculoskeletal damage associated with PASC. Although little is known about the extent of neuromuscular and musculoskeletal damage, experts recommend a variety of tests and measures, as well as outcome measures, to quantify impairments and dysfunction.

- Clinicians should not underestimate the role of patient and caregiver education which can cover many areas including expectations for rehabilitation, safety, how to facilitate social integration, disease management, and techniques for energy conservation. Additionally, all patients should be reminded about good sleep, nutrition, and hydration practices.

- Intense activity should be avoided in those experiencing myalgia or muscle fatigue. From a musculoskeletal perspective, return to exercise in patients with PASC should be symptom-guided.

- All clinicians need to consistently screen for mental health disorders in patients with PASC. The presence of such conditions should not preclude individuals from physical activity, but rather allow for additional referrals when needed. Psychological sequelae of PASC may include mood dysfunction, poor sleep, loss of appetite, and low motivation. In those individuals, physical activity should be encouraged as it has a positive impact on mood and mental wellbeing and has a role in the prevention and treatment of mental health conditions.

Section 3: Summary

- Evaluating and treating patients with confirmed or suspected PASC requires an organized approach with a comprehensive rehabilitation team. Clinicians should utilize a biopsychosocial model that monitors changes and the effects of interventions across the continuum of care.

- Clinicians should be aware that patients who attend physical therapy with a history of COVID-19 are susceptible to impairments in body function and structure, activity limitations, and participation restrictions that may be undetected, especially if the patient is referred to therapy for non-COVID related deficits.

- A prospective surveillance model (COVID19-PSM) has been proposed for patients with PASC as it may enable clinicians to identify early signs of impairment, predict severity of dysfunction, and allow for early intervention when feasible. Clinicians should also screen all patients for signs of mental health disorders, especially those who require critical care or mechanical ventilation in the hospital.

- Physical activity guidelines may be helpful for clinicians who are working with patients with PASC. Each guideline has a different structure, but clinicians are urged to utilize a gradual return to physical activity with careful monitoring by

taking vital signs, measuring pulse oximetry, and asking the patient about perceived levels of exertion.

Section 3: Key Words

Short Physical Performance Battery - a series of tests used to evaluate lower extremity function and mobility in older individuals.

2-minute walk test - a performance-based measure that quantifies an individual's endurance while walking for two minutes

COVID19-PSM - a prospective treatment model for treating patients with COVID-19 infections

50/30/20/10 Rule - a method that uses reductions in training volume over a period of four weeks

Borg Rating of Perceived Exertion (RPE) scale - a method of quantifying a patient's perception of effort

Post-Acute COVID-19 Exercise and Rehabilitation (PACER) Project - an initiative led by the APTA Academy of Cardiovascular & Pulmonary Physical Therapy

Patient-regulated exercise prescription - specific plan of fitness-related activities that are designed for a specified purpose and progressed according to the patient's tolerance

Reps in Reserve (RIR) - a training method that describes how many repetitions are completed in one set

Wells Clinical Prediction Rule - a clinical practice guideline to determine the presence of a deep venous thrombosis

Ankle Brachial Index - a quick, non-invasive way to check for peripheral artery disease (PAD)

6-Minute Walk Test - a performance-based measure that quantifies an individual's endurance while walking for six minutes

Hospital Anxiety and Depression Screen - a screening measure used to determine depressive-like symptoms

Neuro Core Outcomes Set - a group of physical outcome measures appropriate for a variety of neurological health conditions

StrokeEDGE - recommendations for a variety of outcome measures to be utilized in the stroke population across the continuum of care

Specific Adaptation to Imposed Demand (SAID) principle - a theory of specificity that states adaptations in the body will occur when the body is placed under some form of stress

Section 4: Case study and Discussion

Adrianne is a 45-year-old who is referred to outpatient physical therapy by the primary care provider after being hospitalized for four days with COVID-19. She did not require critical care or ventilator support and was sent to outpatient physical therapy upon returning home with family. Past medical history includes postpartum depression and Type 2 diabetes. Adrianne does not have a history of heart problems, nor did she report cardiac-related issues during hospitalization.

Upon arriving at her physical therapy evaluation, Adrienne is assisted into the clinic by her daughter. She is using a portable supplemental oxygen device with a nasal cannula and moves slowly, leaning on her daughter for support.

Adrianne endorses difficulty walking for long distances, climbing stairs, and performing household tasks. She suffers from high levels of fatigue, lightheadedness upon standing, and low levels of motivation. Prior to being hospitalized for COVID-19, Adrianne was independent for all tasks and mobility and worked as an IT manager. She has not been able to return to work due to her lingering symptoms.

1. How does Adrianne's past medical history affect her diagnosis and prognosis?
2. Using her length of stay in the hospital and COVID-19 disease severity, is Adrianne considered to be at risk for developing PASC?
3. State 2-3 reasons why Adrienne may require supplemental oxygen at rest.
4. Provide three recommendations to decrease the risk or severity of lightheadedness related to orthostatic hypotension.

Responses

1. How does Adrianne's past medical history affect her diagnosis and prognosis?
    a. The complexity of the damage caused by COVID-19, combined with pre-existing chronic conditions, is likely to delay recovery in any rehabilitation

setting. It is highly likely that Adrianne's presentation may progress into PASC depending upon her response to treatments. Furthermore, Adrianne's history of depression may affect her willingness to participate in therapies thus confounding the risk of developing PASC.

2. Using her length of stay in the hospital and COVID-19 disease severity, is Adrianne considered to be at risk for developing PASC?

    a. At this time, experts are unsure as to why some individuals develop PASC. Increased disease severity, defined by a critical care stay and use of mechanical ventilation, has been significantly associated with the presence of persistent symptoms in post-acute settings. Since Adrianne did not require mechanical ventilation or critical care and was referred to therapy earlier than 28 days post-infection, she does not appear to be at a heightened risk for developing PASC according to these markers.

3. State 2-3 reasons why Adrienne may require supplemental oxygen at rest.

    a. Pulmonary pathology

    b. May have experienced pulmonary hypertension during hospitalization, causing shortness of breath

    c. Restrictive breathing pattern due to weak inspiratory muscles

4. Provide three recommendations to decrease the risk or severity of lightheadedness related to orthostatic hypotension.

    a. Encourage hydration, especially upon waking

    b. Increase time spent in upright positions as opposed to lying in bed

    c. Encourage slow position changes to allow the cardiovascular system to adapt

Conclusion

Post-Acute Sequelae of SARS-CoV-2 infection (PASC), also referred to as Long COVID, Long Haulers, Long-term COVID-19, or LTC-19 is a serious concern in some individuals following severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). As the infection continues to unfold, experts know very little about PASC, its risk factors, or prognosis. While it is clear that clinicians should be targeting the physical limitations and

restrictions that present alongside PASC, more research is desperately needed to address many questions about the long-term implications and disability that may arise from COVID-19.

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