A Physiotherapy Framework to Managing Long COVID: A Clinical Approach

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Purpose: Individuals infected with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), the virus that causes coronavirus disease 2019 (COVID-19), can experience ongoing, often debilitating symptoms after the acute infection known as Long COVID (LC). LC has profound medical, social, and economic consequences worldwide. Prevalence estimates vary, but it is estimated that 10% to 35% of people infected with SARS-CoV-2 develop LC. The World Health Organization endorses physiotherapy as a vital component in LC symptom management and stabilization. Cardiorespiratory physiotherapists are often involved in the management of patients with LC phenotypes such as post-exertional malaise/post-exertional symptom exacerbation, post-COVID interstitial lung disease, dysautonomia, breathing pattern disorders, and chronic cough. However, specific guidance is lacking regarding physiotherapy assessment and safe intervention strategies. In this review, we describe the relevant pathophysiology of the condition, report common clinical phenotypes, and propose a clinical framework for physiotherapy assessment and safe intervention strategies. **(Cardiopulm Phys Ther J. 2025;36:19–29)** *Key Words: cardiorespiratory rehabilitation, post-exertional malaise, exercise*

INTRODUCTION

Long COVID (LC) is a term used to describe a chronic condition involving long-term sequelae after a SARS-CoV-2 infection and is present for at least 3 months as a continuous, relapsing, remitting, or progressive disease state that affects 1 or more organ systems.[1] This condition is also known as postacute sequelae of COVID-19 (PASC) and post-COVID-19 condition (PCC).[2] The prevalence of LC after an acute COVID-19 infection varies, with reports ranging between 3.3% and 58%,[3,4] and approximately 20% of sufferers report "severe" symptoms.[3]

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Physiotherapy has been suggested as a vital component in the management and treatment of symptoms experienced by people living with LC[5]; however, specific guidance has not been available on how to structure these treatments. Indeed, clarification on the underlying pathological process that physiotherapy aims to address remains poorly understood, with a focus to date on adapting existing treatments for people living with LC. With COVID-19 infections remaining high, physiotherapists need to provide safe rehabilitation,[6] expand their clinical skill set, and broaden their knowledge base to best serve the needs of people living with LC.

To provide safe rehabilitation, conditions such as exertional oxygen desaturation and other cardiac impairments should be investigated, identified, and/or ruled out before considering any rehabilitation of LC.[7,8] This is a crucial first step before applying any of the rehabilitative approaches that are outlined in the following framework. Furthermore, guidelines suggest the identification of other diagnosable conditions that are new or existing but

Clinical Pearls

- Physiotherapists should undergo training to familiarize themselves with the pathophysiology of LC as well as the mechanisms behind symptoms amenable to physiotherapy.
- The presence of exertional oxygen desaturation and cardiac impairment should be identified or excluded before considering any rehabilitation of LC.
- Rehabilitation should adapt to the identification of other medical diagnosable conditions that are new or existing but worsened by LC.
- Clinicians should understand the heterogenicity of LC and provide a thorough assessment to ensure appropriate patient phenotyping.
- Interventions such as pulmonary rehabilitation, breathing pattern retraining, and inspiratory muscle training are suitable in some patients with LC but not all.
- Physiotherapists have the potential to cause harm, and an understanding of dysautonomia and post-exertional malaise/post-exertional symptom exacerbation is essential to ensure safe, effective rehabilitation practices.

worsened by LC (e.g. Asthma, Sjogren, Migraine, Venous Thromboembolism), and if guidelines exist for these conditions, clinicians are urged to follow these.[1,9,10]

In this review, we discuss the relevant pathophysiological processes, describe current safe physiotherapy management of the symptoms reported by people living with LC, and propose a rehabilitative framework to approach the assessment, treatment, and management of LC symptoms.

PATHOPHYSIOLOGY OF LONG COVID

The underlying pathophysiology of LC is complex and involves multiple interconnected mechanisms.[2] Evidence suggests that persistent viral reservoirs remain active within the body and contribute to ongoing immune activation and chronic inflammation.[11,12] Viral RNA and proteins have been detected in various tissues months after initial infection, suggesting a potential source of sustained immune response and tissue damage.[11,12]

Mitochondrial bioenergetic impairment in LC is present, and reduced fatty acid oxidation and carbohydrate metabolism contribute to persistent fatigue and functional decline.[13-17] SARS-CoV-2 infection disrupts mitochondrial function through inflammation and oxidative stress, impairing ATP production, and this dysfunction particularly affects the mitochondria's ability to metabolize fatty acids and glucose efficiently, exacerbating energy deficits.[5,18-21] The resulting metabolic imbalance is linked to post-exertional malaise (PEM)/post-exertional symptom exacerbations (PESE), muscle weakness, muscle biopsy changes, and exercise intolerance.

Systemic immune dysregulation is also common.[16,21] People living with LC often present with elevated levels of proinflammatory cytokines and autoantibodies, indicating chronic inflammation and potential autoimmunity. This dysregulated immune response may lead to multiorgan involvement, affecting the respiratory, cardiovascular, and nervous systems.[11,22,23]

Finally, microvascular and endothelial dysfunction is implicated in the pathogenesis of LC.[11,24] SARS-CoV-2's ability to infect endothelial cells can result in vascular inflammation and the formation of microthrombi, which may impair blood flow and contribute to symptoms such as fatigue, chest pain, and cognitive dysfunction.[11,24]

SYMPTOMS OF LONG COVID

People living with LC demonstrate a variety of symptoms ranging from mild to debilitating. The most commonly reported symptoms include fatigue and PEM/PESE, dyspnea, cognitive impairment and brain fog, chest pain, chronic cough, muscle pain, headaches, gastrointestinal disturbances, anxiety, and depression.[11,25] These symptoms may be associated with a range of significant COVID-19 sequelae, including cardiac muscle damage[26] and pulmonary embolism.[27] Therefore, all patients must have an appropriate level of investigation to allow for accurate management.[1,8]

LONG COVID PATHOPHYSIOLOGICAL MECHANISMS RELEVANT TO CARDIORESPIRATORY PHYSIOTHERAPY

For this review, we have chosen to describe further mechanisms relevant to the scope of the outpatient cardiorespiratory physiotherapist. LC is known to encompass many other conditions and may include new diagnoses. We refer readers to Greenhalgh et al.,[2] World Health Organization,[7] World Physio,[8] and NASEM[1] documents for further LC-specific reading.

Muscle and Mitochondrial Dysfunction

Muscle biopsies in people living with LC reveal histological abnormalities, including muscle fiber atrophy, focal necrosis, and mitochondrial dysfunction.[13] These muscle changes are associated with sarcopenia, characterized by progressive loss of muscle mass and function.[28] Mitochondrial bioenergetic impairment in LC has been found in multiple research studies with reduced fatty acid oxidation and carbohydrate metabolism.[13-17] Alterations in muscle metabolism and sarcopenia may contribute to persistent symptoms like exercise intolerance, PEM/PESE, general weakness, and functional limitations in LC.[13] Due to these research findings, physiotherapy exercise prescription may have to be extensively modified and may be contraindicated in rehabilitation (see section on PEM/PESE below).

Post-COVID Interstitial Lung Disease (ILD). Post-COVID ILD refers to the development of fibrosis of the lung parenchyma, particularly in those with severe COVID-19 infections, resulting in impaired lung function.[28,29] Post-viral ILD has been well-studied from earlier SARS pandemics and most commonly involves the development of interstitial scar tissue in the lungs due to severe inflammation and injury from the virus.[30,31] This cohort may have required hospitalization for COVID-19 pneumonia with or without the need for mechanical ventilation.[30-32] Oxygen desaturation may be present in these patients, and they can benefit from supervised pulmonary rehabilitation programs with improvements in exercise capacity, respiratory symptoms, fatigue, and cognition.[33]

Diaphragm Dysfunction. Diaphragm dysfunction and diaphragm thinning are present in posthospitalized LC cases, which indicates a weakening of the diaphragm muscle.[34-36] The diaphragm, the most important muscle in tidal breathing, can suffer from muscle atrophy due to extended periods of disuse (i.e. mechanical ventilation), illness, inflammation, and reduced physical activity.[37] The diaphragm is innervated by the phrenic nerves, and reduced conduction or damage to this nerve has been found after mild and severe COVID-19 infection.[35] Diaphragm wasting is often detected through imaging techniques such as ultrasound or MRI, which reveal a thinner, less functional diaphragm muscle.[37] Inspiratory muscle training (IMT) has been shown to improve diaphragm strength and function in people living with LC who have previously been hospitalized.[38]

Breathing Pattern Disorders (BPDs). Breathing pattern disorder (BPD) in LC is characterized by larger than normal breathing or excessive respiratory rate that leads to excessive expiration of carbon dioxide (CO_2).[39-41] Hypocapnia or low CO_2 can magnify or cause various symptoms, including dizziness, tingling in the extremities, chest pain, and shortness of breath.[42] BPD in LC may be driven by damage to the carotid bodies, autonomic dysfunction, persistent respiratory issues, and, at times, anxiety.[18,39-41,43] Managing BPD involves breathing retraining to restore normal physiologic breathing patterns and stabilize CO_2 levels.[44]

Dysautonomia and Vagus Nerve Dysfunction

Dysautonomia, specifically postural orthostatic tachycardia syndrome (POTS), has been increasingly recognized in people living with LC.[45] Furthermore, vagus nerve dysfunction and injury resulting from a COVID-19 infection have been implicated in LC dysautonomia and POTS[46] and involves persistent infection and inflammation affecting the vagus nerve, which can lead to autonomic dysfunction, and symptoms like dysphonia, dysphagia, dizziness, tachycardia, fatigue, brain fog, and altered voice quality.[47] Diagnosis may involve ultrasound imaging and nerve conduction studies for the vagus nerve, while POTS can be diagnosed by the active stand test (AST) or tilt table testing (TTT).[48,49] Treatment options include fluid management, anti-inflammatory medications,[50] physiotherapy, and breathing retraining.[51,52]

CLINICAL FRAMEWORK AND PHENOTYPING FOR PHYSIOTHERAPY MANAGEMENT

With the changing shape of physiotherapy rehabilitation for people living with LC, treatment safety, phenotyping, and individualization are key.[6]

As stated above, before applying treatment to people living with LC, we endorse guidelines that suggest an approach to determine the safety of intervention, including screening and investigations for exertional desaturation, myocarditis, cardiac myocardial damage, pulmonary embolism, and PEM/PESE.[1,8] Furthermore, adapting the rehabilitation approach is needed if other diagnosable conditions are new post-LC or existing but worsened by LC (e.g. venous thromboembolism). Clinicians are urged to review guidelines (both local and international) for the management of these conditions, and guidelines may differ from country to country.[1,9,10]

We present the evidence for 5 common LC traits amenable to physiotherapy assessment and interventions: PEM/PESE, post-COVID ILD, dysautonomia, BPD, and chronic cough. For these 5 traits, we have provided an overview of assessment and treatment using the current literature and expert clinical opinion (see Table 1). Our group also proposes safety profiles for common physiotherapy treatments in Table 2. While each trait has its own uniquely identifying signs, symptoms, assessment, and management, we acknowledge in clinical practice that these phenotypes are frequently seen in combination with PEM/PESE and can exist with other conditions. Therefore, identification and screening for PEM/PESE should be considered, both before and during the management and treatment of other phenotypes.[1,8]

Post-exertional Malaise (PEM)/Post-exertional Symptom Exacerbation (PESE) and Post-exertional Neuroimmune Exhaustion (PENE)

PEM/PESE/PENE is frequently reported in people living with LC.[23,53,54] PEM/PESE/PENE is characterized by a significant worsening of symptoms following physical, mental, or cognitive exertion that can last for days or even weeks and can be episodic.[19,55] It is important to note that PEM/PESE/PENE is not a symptom in and of itself but describes what is often a cluster of symptoms that worsen after engaging in activities that could be previously tolerated.[8] PEM/PESE/PENE is perhaps the most important clinical symptom to be aware of when treating people living with LC, as it can alter the use of exercise as a treatment, or in the case of moderate to severe PEM/PESE/PENE, exercise therapy is contraindicated.[8,56]

PEM/PESE is also a hallmark characteristic of another infection-associated illness, myalgic encephalomyelitis

TABLE 1

Clinical Reasoning Approach and Physiotherapy Phenotypes in Long COVID

1. Identify Contraindications to Rehabilitation
Assessment for Exertional Oxygen Desaturation and Other Cardiac Impairments Should Be Completed and Ruled Out Before Considering Any Rehabilitation of LC. Referral to Relevant Cardiology Specialist or Respiratory Physician as Needed
2. Management of Other Associated Conditions Using Guidelines Where Available
3. Once Cleared by Relevant Investigations, Screen for PEM/PESE and Consider the following Phenotypes

Trait	PEM/PESE	Post-COVID ILD	Dysautonomia	Breathing Pattern Disorder	Chronic Cough
Populations onset	Female >Male Nonhospitalized Postacute	Post-ICU, Hospitalized Male >Female Obesity Diabetes Acute	Female >Male Nonhospitalized Postacute	Female >Male Nonhospitalized Postacute	Female >Male Hospitalized (intubated and nonintubated) Nonhospitalized Acute Postacute
Symptoms	Worsening symptoms after minimal exertion Extreme fatigue brain fog	Exertional breathlessness Impaired endurance	Symptoms with postural changes Fatigue Brain fog	Inability to get a satisfying breath Breathlessness disproportionate to physiology	Persistent cough
Signs	Elevated resting heart rate Exertional intolerance (e.g. physical, cognitive, environmental)	Decreased SpO_2 with exertion Exertional breathlessness	Elevated HR in standing Inappropriate HR response to activity/exercise (chronotropic intolerance)	Upper chest breathing Frequent sighing Erratic breathing	Persistent cough Urge to cough Throat sensations
Assessments	DePaul symptom questionnaire PEM/PESE activity questionnaire (PAQ) FUNCAP27 FUNCAP55	Lung function tests and 6MWT Short physical performance battery Maximum inspiratory pressure Cardiopulmonary exercise testing	Tilt table test Nasa lean test Active stand test Malmo POTS Compass 31	BPAT Nijmegen Questionnaire Capnography Diaphragm ultrasound Maximal inspiratory pressure	Leicester Cough Questionnaire (LCQ) Cough-specific Quality of Life Questionnaire (CQLQ) Hull Airway Reflux Questionnaire (HARQ) Cough Severity (using modified BORG or VAS)
Treatments	Energy management and pacing Symptom or HR titrated physical activity Education Avoidance of flare-ups Breathing pattern retraining	Pulmonary rehabilitation Inspiratory muscle training	Recumbent exercise CHOPs Physical counter-maneuvers Compression Breathing pattern retraining	Breathing pattern retraining in all positions Inspiratory muscle training	Refer to specialist cough clinic Referral to SLT or physiotherapists with experience in cough control therapy Breathing pattern retraining Education
Comorbidity Modifications	Dysautonomia—caution with supine exercise and PEM/PESE EDS—joint protection strategies		EDS—joint protection strategies		

6MWT, 6-Minute Walk test; BPAT, breathing pattern assessment tool; CHOPs, Children's Hospital of Philadelphia exercise protocol; EDS, Ehlers–Danlos syndrome; HR, heart rate; ICU, intensive care unit; PEM, post-exertional malaise; PESE, post-exertional symptom exacerbation; POTS, postural orthostatic tachycardia syndrome; SLT, speech-language therapy.

TABLE 2

Treatment Safety for Common Treatments in Long COVID

Treatment	PEM / PESE	Post-COVID ILD	Dysautonomia	Breathing Pattern Disorder	Chronic Cough
Exercise	Risk of HARM	Graded Exercise Program	Recumbent Exercise Program	Monitor for adverse events	Monitor for adverse events
Breathing Retraining	Monitor for adverse events	Safe	Safe	Safe	Safe
Inspiratory Muscle Training	Monitor for adverse events	Safe	Monitor for adverse events	Safe	Unknown risk profile

Green, Recommended with thorough patient assessment; Yellow, Precaution—adaptation likely required; Red, Likely contraindication or unknown risk of harm; PEM/PESE, post-exertional malaise/post-exertional symptom exacerbation; ILD, interstitial lung disease.

(ME).[19,53,55] In defining ME, the International Consensus Criteria lists PEM/PESE as features of post-exertional neuroimmune exhaustion (PENE), which more specifically refers to the breakdown in the energy production system and dysregulation of the nervous, immune, and endocrine systems.[57] Throughout history, nomenclature has fluctuated between PEM, PESE, and PENE, although all refer to an abnormal physiological response to what can be considered normal or minimal activities of daily living.[8,57] For the context of this paper, as many people living with LC identify with the terms PESE and PEM, these will be the terms primarily referred to.

It is important to recognize that people living with ME have historically been both under and inappropriately treated by many health care professionals, and physiotherapists are encouraged to upskill and learn from past mistakes as we engage in rehabilitation processes with LC.[23,55,56]

Noting again that PEM/PESE is not 1 symptom, it has some key features that help in identifying its presence, including delayed onset, increased disproportionate fatigue, worsening of symptoms, extended recovery duration, and activity intolerance (see Table 3).

PEM/PESE involves alterations to mitochondrial energy production and metabolism, immune system dysregulation, and autonomic nervous system dysfunction.[13-17,57,58] Evidence suggests that PEM/PESE is related to disturbances in cellular energy production and inappropriate metabolic waste accumulation.[13,16] After exertion, there is a dysregulated immune response, leading to inflammation and fatigue.[13,16,55,59] Furthermore, the autonomic nervous system might be dysfunctional in individuals with PEM/PESE (see section below on Dysautonomia).[50]

From a rehabilitation perspective, given the high incidence of PEM/PESE in people with LC,[50] health professionals must practice principles of safe rehabilitation for this population.[6,8] Safe rehabilitation refers to the process of recovering from an injury, illness, or surgery in a manner that minimizes risk and maximizes the chances of a full recovery. To that end, the focus should be on appropriate screening measures to rule out red flags, such as cardiac impairment, exertional oxygen desaturation, autonomic dysfunction, and, of course, PEM/PESE, before engaging in treatment.[6,8,13,56] A framework for assessing and managing PEM/PESE in 3 levels (severe, moderate, and no PEM/PESE) has been proposed,[56] but further research is required before this approach can be adopted on a large scale. Noting the episodic and often-unpredictable nature of PEM/PESE, health professionals are encouraged to constantly monitor individual's responses to assessments and treatment interventions, using evidence-based assessments throughout the rehabilitation process (i.e. DePaul Symptom Questionnaire, the PEM/PESE Activity Questionnaire, and functional capacity questionnaires FUNCAP55 and FUNCAP27).[8,60-62] While collaborative approaches to pacing, planning, prioritization, and positioning will continue to be important for patients with PEM/PESE, research is needed to provide optimal safe management and treatment.[6,13,55,56]

Post-COVID ILD

Patients with post-COVID ILD present with a primary symptom of exertional breathlessness as well as measurable impairments to lung function, CT scans, and oxygen desaturation.[29] This presentation is, in many ways, akin to other interstitial lung diseases in which treatment pathways are well established, particularly regarding the benefit of pulmonary rehabilitation (PR).[63]

PR is a well-described complex intervention centered around graded exercise, education, and behavior change.[64] The benefits of PR are multifaceted, with

TABLE 3

Clinical Features of PEM/PESE/PENE

Delayed onset of symptoms	Symptoms appear several hours or even days after exertion. This delay can make it challenging to connect the exertion with the subsequent symptoms
Increased fatigue	The level of fatigue is highly disproportionate to the activity undertaken. Even routine or mild activities can lead to severe exhaustion that significantly impairs daily functioning
Worsening of any/all symptoms	Beyond fatigue, PESE can exacerbate other symptoms of long COVID, such as cognitive difficulties (often referred to as "brain fog"), muscle and joint pain, headaches, and sleep disturbances
Duration	Recovery from PESE can take an extended period, often requiring more rest and a longer time to return to baseline levels of functioning. In some cases, the recovery period may be lengthy and can significantly affect a person's quality of life
Activity intolerance	There is often a reduced tolerance for both physical and cognitive activities. Previously manageable tasks might become overwhelming or unmanageable, including basic activities of daily living

improvements in physiology (increased muscular strength, endurance, and reduced cardiovascular demand), psychology (increased confidence with exercise, reduced depression and anxiety), and self-management (improved locus of control).[65] While initially designed for COPD, PR has been validated in a range of respiratory pathologies, including interstitial lung diseases, providing improvements in functional exercise capacity, dyspnea, and quality of life.[63,66]

Given the interstitial nature of severe COVID-19 infections, it was natural that PR was explored in this cohort. Early studies provided promising results, with most patients demonstrating improvements in physical function and exercise capacity.[33,67,68] However, a small subcohort experienced a regression in fatigue symptoms, which was not fully understood at this time.[33,67,68] It is important to highlight that many of these early studies had a high proportion of patients (up to 87%) requiring hospital admission during their acute COVID-19 illness, suggesting a high pulmonary burden and increased potential for illness-related sarcopenia.[33,67,68]

As the pandemic progressed, there was emerging evidence of a large cohort of patients presenting with symptoms akin to ME, of which PEM/PESE was a significant factor.[56] Graded exercise therapy and, thus, by nature, PR became scrutinized and was soon listed as a precaution for people living with LC who demonstrated PEM/PESE.[6] Recently, PR studies have focused on inspiratory muscle training (IMT),[69,70] a proven therapy in interstitial lung disease.[71] In LC, IMT has demonstrated improvements in pulmonary function, dyspnea, physical capacity, and quality of life.[63,72] As with PR and graded exercise, caution should be taken when using IMT with patients with PEM/PESE and dysautonomia. Furthermore, physiotherapists are encouraged to continue to screen and monitor for PEM/PESE throughout the PR program to ensure LC patient safety. PR remains valuable in patients with post-COVID ILD when used with appropriate screening. However, physiotherapists are encouraged to take a cautious approach, particularly if patients have overlapping LC conditions (e.g. post-COVID ILD and PEM/PESE, or post-COVID ILD and dysautonomia).[44]

Dysautonomia

Dysautonomia, and specifically postural orthostatic tachycardia syndrome (POTS), has been increasingly recognized in patients with COVID-19 in the postinfectious stage or LC.[50] Dysautonomia refers to a broad category of disorders characterized by malfunctioning of the autonomic nervous system (ANS), which regulates involuntary physiological functions such as heart rate, blood pressure, digestion, respiratory rate, urination, sexual arousal, and temperature control.[73,74] The ANS is divided into the sympathetic and parasympathetic nervous systems, which work together to maintain homeostasis. In individuals with dysautonomia, this balance is disrupted, leading to a wide range of symptoms varying in severity.[73,75,76]

POTS, specifically, refers to the development of orthostatic symptoms associated with an increase in heart rate greater than or equal to 30 beats per minute (from normal resting heart rate) but not associated with orthostatic hypotension.[50] The gold standard diagnostic tool is the head-up tilt table test; however, if equipment is unavailable, heart rate and blood pressure may be observed during a 10-minute active stand test.[48] The onset of POTS may be precluded by immunological factors such as infection, vaccination, trauma, pregnancy, surgery, or psychosocial stress.[75] The syndrome affects younger (15–45 years of age), predominately female individuals.[75] The etiology of POTS is thought to involve a combination of central and peripheral autonomic dysfunction, hypovolemia, hyperadrenergic states, breathing pattern disorder, and possibly autoimmune factors.[20,75-77]

Rehabilitation management of patients with POTS often begins with thorough patient education regarding disease pathophysiology, avoidance of orthostatic triggers, and nonpharmacological symptom-stabilization measures.[75,76] One such measure familiar to physiotherapists is the implementation of recumbent and graded aerobic exercise to address physical and cardiovascular deconditioning. However, graded exercise should be approached with caution in individuals with suspected post-COVID dysautonomia or POTS. These patients may demonstrate symptoms of PEM/PESE observed in conditions such as ME/CFS and some connective tissue disorders (i.e. Ehlers–Danlos).[53] As previously stated, physical activity, including graded exercise, can elicit PEM/PESE symptoms or crashes, resulting in severe physical fatigue, cognitive dysfunction, flu-like symptoms, palpitations, chest pain, dizziness, headache, and breathlessness disproportionate to activity level.[55,57,78] Therefore, it is crucial for patient safety that physiotherapists conduct a thorough patient interview and utilize evidence-based screening tools described in the previous section to identify PEM/PESE and hypermobile conditions before initiating any return-to-movement or graded exercise programs.[55]

Other evidence-based nonpharmacological interventions should be implemented based on individual patient presentation and in consultation with the referring physician or provider.[75,76] Physiotherapists may also offer guidance in patient-specific strategies to avoid prolonged recumbency and immobilization, instruction in gradual positional changes, especially in the morning or after meals, and instruction in physical counter-maneuvers (leg crossing, heel-raises, weight shifting, squatting, and muscle tensing) to manage acute and chronic symptoms.[75,76] In addition to blood volume management, safe exercise strategies, and positional adaptations, respiratory physiotherapy may be indicated to address breathing pattern dysfunction in patients with POTS.[20,51] Physiotherapy-led breathing retraining in these patients can improve breathing patterns and symptom burden quantified by the Nijmegen questionnaire and Brompton Breathing Pattern Assessment Tool (BPAT).[51,79]

Breathing Pattern Disorders (BPD)

BPD is a term, interchangeable with dysfunctional breathing,[80] that describes a maladaptive change in breathing pattern that results in both respiratory and nonrespiratory symptoms, which can occur in the absence of or in excess of organic causes.[42] BPD has been measured more than 200 days after COVID-19 infection using cardiopulmonary exercise testing,[81] and hypocapnia and hyperventilation have also been described in people living with LC.[39-41] As with all cases of BPD, other causes of unexplained dyspnea must be investigated or ruled out before physiotherapy treatment progresses beyond basic breathing retaining exercises.[2]

Broadly, the pathophysiology of BPDs can be broken down into biomechanical causes, such as diaphragm dysfunction and apical breathing; biochemical changes, including hypocapnia and hyperventilation; and biopsychological causes, such as upregulation of the sympathetic nervous system and anxiety.[18,39-41] BPDs are known to overlap with a wide variety of conditions, such as asthma,[82,83] diaphragm thinning,[84] and POTS.[20,51,79] Apical dominant breathing and excessive sighing are common signs of BPD and are amenable to treatment with breathing exercises.[82,83] BPD retraining to stabilize CO2 levels and restore normal physiologic breathing patterns is indicated for people living with LC.[2,44,85]

Physiotherapy assessment of BPD involves a variety of tools and measures to determine contributing factors.[44] This is due to the lack of a gold standard diagnostic method.[42] Objective measures can include the BPAT,[86] Nijmegen Questionnaire (NQ),[87,88] capnography,[89] and maximal inspiratory pressure.[90]

The BPAT is a useful part of the breathlessness assessment for people living with LC.[85,91] It has a high sensitivity (89.5%) and moderate specificity (78.3%) for diagnosing breathing pattern disorders in LC.[85,91] Patients with positive BPAT scores ($\geq$4) demonstrated significantly higher levels of breathlessness compared to those with negative scores.[86]

Capnography can provide insight into the physiological consequences of BPDs. Despite normal respiratory

rates, many people living with LC exhibit low end-tidal carbon dioxide ($ETCO_2$) levels.[92]

Maximal inspiratory pressure is a useful measure of respiratory muscle dysfunction in people living with LC.[93] Respiratory muscle weakness, more than 5 months after diagnosis, may explain persistent dyspnea experienced by people living with LC who demonstrate poor exercise tolerance.[93]

Treatment should include education, muscle relaxation exercises of the upper chest and accessory muscles, paced breathing exercises, and coordination of breathing with tasks such as walking and talking.[2,44] Inspiratory muscle training has been studied in people living with LC,[69,70] and if applied in a manner that does not exacerbate BPD or PEM/PESE, it should also be useful in the rehabilitation process.[56]

Chronic Cough

Chronic cough is one of the most common presenting symptoms of COVID-19 and can persist for weeks or months following a SARS-CoV-2 infection.[94] Chronic cough is defined as "a cough that lasts for eight weeks or longer" and is a disabling disorder for many patients, often leading to stigmatization and social isolation.[95] The severity depends on the duration, intensity, and association with concomitant symptoms.[95,96] Cough is a reflex that occurs through the activation of peripheral sensory nerves into the vagus nerve, which provides input to the brainstem; SARS-CoV-2 may infect these vagal sensory nerves, leading to neuroinflammation and neuroimmune interactions and amplification of the afferent signals to the brain stem as mechanisms of cough hypersensitivity.[94,97]

Unlike cough that persists after the common cold, chronic cough in LC is often accompanied by other systemic manifestations, which likely indicates a multifactorial pathophysiology.[2] The accompanying presence of dyspnea, pain, fatigue, and cough may point to a derangement of the central nervous system.[94,98] Furthermore, chronic cough is postulated to exist on a spectrum of laryngeal dysfunction that includes other disorders such as exercise inducible laryngeal obstruction (EILO), vocal cord dysfunction, and muscle tension dysphonia.[99,100]

Contributing causes of chronic cough, such as sinus disease, gastroesophageal reflux disease, lung disease or airway inflammation, ACE inhibitor therapy, or vocal cord pathology, should be investigated in people living with LC.[2,94]

Optimal management of LC chronic cough remains unclear, although guidelines for current approaches to chronic cough serve as a reference.[94] Physiotherapy and speech-language therapy can contribute as nonpharmacological interventions, including nasal and laryngeal hygiene practices, cough suppression, hydration, general education, and breathing exercises.[101,102]

FUTURE DIRECTIONS

There is a great deal of work to be done to face the ongoing challenges of LC, from disease prevention to caring for those already affected. The scientific community continues to investigate possible mechanisms of action that may lead to the development of diagnostic testing and novel therapeutics to guide treatment.[96] In the interim, it is imperative to refine our investigations of nonpharmacological treatment and/or established treatment strategies, including physiotherapy, in caring for people living with LC. Investigation of physiotherapists' current level of knowledge surrounding LC symptom identification and management may provide insight into educational strategies necessary to address the knowledge gap. Further study of the safety and efficacy of specific physiotherapy interventions among all discussed phenotypes would be useful in creating clinical practice guidelines for general use. Investigation into the efficacy of existing screening tools and outcome measures is needed to determine if such tools and measures are appropriate for people living with LC. This information may assist future investigators in developing new instruments for screening, symptom intensity, frequency, and quality of life. Finally, future studies should explore the utility of available technology, such as wearable devices, to identify physiological trends among the phenotypes and provide biofeedback as a pacing strategy.

CONCLUSION

The heterogeneity of LC symptom presentation presents some challenges to cardiorespiratory physiotherapy care. The application of safe assessment and management strategies based on the underlying pathophysiology is essential to stabilize often debilitating symptoms affecting an individual's ability to meaningfully engage in daily life. In outlining clinical phenotypes, we hope to provide an evidence-based, patient-centric clinical framework that encourages physiotherapists to make informed decisions regarding screening, assessment, and individualized intervention strategies. In doing so, physiotherapy intervention strategies remain safe, informed, and personalized in hopes of encouraging symptom stabilization and episodic relief.

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