

Exercise-Based Stroke Rehabilitation: Clinical Considerations Following the COVID-19 Pandemic

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Abstract

Background. The COVID-19 pandemic attributable to the severe acute respiratory syndrome virus (SARS-CoV-2) has had a significant and continuing impact across all areas of healthcare including stroke. Individuals post-stroke are at high risk for infection, disease severity, and mortality after COVID-19 infection. Exercise stroke rehabilitation programs remain critical for individuals recovering from stroke to mitigate risk factors and morbidity associated with the potential long-term consequences of COVID-19. There is currently no exercise rehabilitation guidance for people post-stroke with a history of COVID-19 infection. **Purpose.** To (1) review the multi-system pathophysiology of COVID-19 related to stroke and exercise; (2) discuss the multi-system benefits of exercise for individuals post-stroke with suspected or confirmed COVID-19 infection; and (3) provide clinical considerations related to COVID-19 for exercise during stroke rehabilitation. This article is intended for healthcare professionals involved in the implementation of exercise rehabilitation for individuals post-stroke who have suspected or confirmed COVID-19 infection and non-infected individuals who want to receive safe exercise rehabilitation. **Results.** Our clinical considerations integrate pre-COVID-19 stroke (n = 2) and COVID-19 exercise guidelines for non-stroke populations (athletic [n = 6], pulmonary [n = 1], cardiac [n = 2]), COVID-19 pathophysiology literature, considerations of stroke rehabilitation practices, and exercise physiology principles. A clinical decision-making tool for COVID-19 screening and eligibility for stroke exercise rehabilitation is provided, along with key subjective and physiological measures to guide exercise prescription. **Conclusion.** We propose that this framework promotes safe exercise programming within stroke rehabilitation for COVID-19 and future infectious disease outbreaks.

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Introduction

The COVID-19 pandemic is attributable to the severe acute respiratory syndrome virus (SARS-CoV-2) which was first reported in December 2019.¹ This evolving pandemic has resulted in more than 83 million confirmed cases globally and more than 1.8 million deaths.² Older age and the presence of risk factors and co-existing comorbidities like stroke or cardiovascular disease increase an individual's risk of infection, disease severity, and mortality after COVID-19.^{3,4}

While the acute and short-term complications of COVID-19 including respiratory,⁵ cardiovascular,^{3,6,7} hematologic,⁸ and neurological⁴ sequelae have been reported extensively, emerging data highlight that major multi-system complications may persist 6-months after infection^{2,9,10} (long haul or post-acute COVID-19 syndrome). Of concern for stroke recovery and rehabilitation, post-acute multimorbidity observed after COVID-19 potentially overlaps with similar multi-system effects of stroke.

Best practice guidelines strongly endorse interprofessional stroke rehabilitation programs for mitigating post-stroke health complications,¹¹ but in light of the COVID-19 pandemic, mitigating risk factors and morbidity associated with the short- and long-term consequences of COVID-19 is critical.^{12,13}

Exercise training is a recommended core component of stroke rehabilitation.^{14,15} The majority of literature in individuals with stroke focuses on aerobic exercise training, but resistance and neuromuscular training are also critical aspects of a comprehensive program. Exercise training can facilitate functional recovery (e.g., mobility and cognitive function),^{16,17} improved cardiorespiratory fitness,¹⁶ cardiovascular risk factors,¹⁸ muscular strength,¹⁹ and markers of neurorecovery.²⁰

Despite this substantial body of evidence, there are new challenges in the implementation of exercise training that are associated with the current COVID-19 pandemic,¹² and there is a lack of specific guidance for stroke rehabilitation service delivery. Indeed, the pandemic has led to significant changes in the delivery of all aspects of evidence-based stroke care,¹² where in-person and center-based activities are limited and physical distancing ensured to limit viral transmission.²¹ Specific to exercise following COVID-19 infection, guidelines and clinical decision making tools are available for return to play for athletes,²²⁻²⁵ cardiac rehabilitation,^{26,27} general rehabilitation,¹³ and acute stroke medical practices,²¹ but there is no guidance explicitly focused on exercise in the context of stroke rehabilitation.

Given the multi-system pathophysiology of COVID-19, stroke healthcare professionals are seeking guidance related to the safety and implementation of exercise rehabilitation for individuals post-stroke who may have suspected or confirmed COVID-19 infection and for ensuring a safe environment for

exercise for individuals who have not been previously infected. Therefore, the objectives of this manuscript are to (1) review the multi-system pathophysiology of COVID-19 related to stroke and exercise; (2) discuss the potential benefits of exercise for individuals post-stroke with suspected or confirmed COVID-19 infection; and (3) provide clinical considerations related to COVID-19 for exercise during stroke rehabilitation, including safety considerations, pre-participation screening, and prescription. The considerations discussed herein were developed by an international panel of clinical and biomedical research experts in stroke rehabilitation, exercise physiology, and neuroscience and are not intended to be absolute or definitive but rather to help inform clinical decision-making for the implementation of exercise within stroke rehabilitation settings and does not consider public-health regulations that may vary between different jurisdictions. The target patient audience is individuals post-stroke with suspected or confirmed COVID-19 infection. However, this information is also relevant for individuals post-stroke who have not been infected but who want to exercise in a safe environment.

This manuscript is divided into two sections:

1. *The Interaction of COVID-19, Stroke and Exercise* includes an overview of known transmission properties of SARS-CoV-2 and a review of common pathophysiological changes in stroke and COVID-19 infection as they relate to immune, pulmonary, cardiac and vascular, neurological, and musculoskeletal system function. A discussion of the potential benefits of exercise training in stroke for mitigating pathophysiological complications of COVID-19 is also included.
2. *Considerations for the Implementation of Exercise Stroke Rehabilitation During and After a Pandemic* provides considerations to inform clinical decision making for the implementation of exercise, from pre-participation screening and prescription and progression beyond current clinical practice guidelines^{14,15} in the context of COVID-19.

Section 1) The Interaction of COVID-19, Stroke and Exercise

Transmission Properties of SARS-CoV-2

SARS-CoV-2 is a highly infectious respiratory disease that is transmitted via humans through respiratory droplets and aerosols that can affect multiple physiological systems (Figure 1 Part A).²⁸ In brief, the characteristic spike proteins of the virus binds to nasal epithelial cells via host functional receptors, particularly

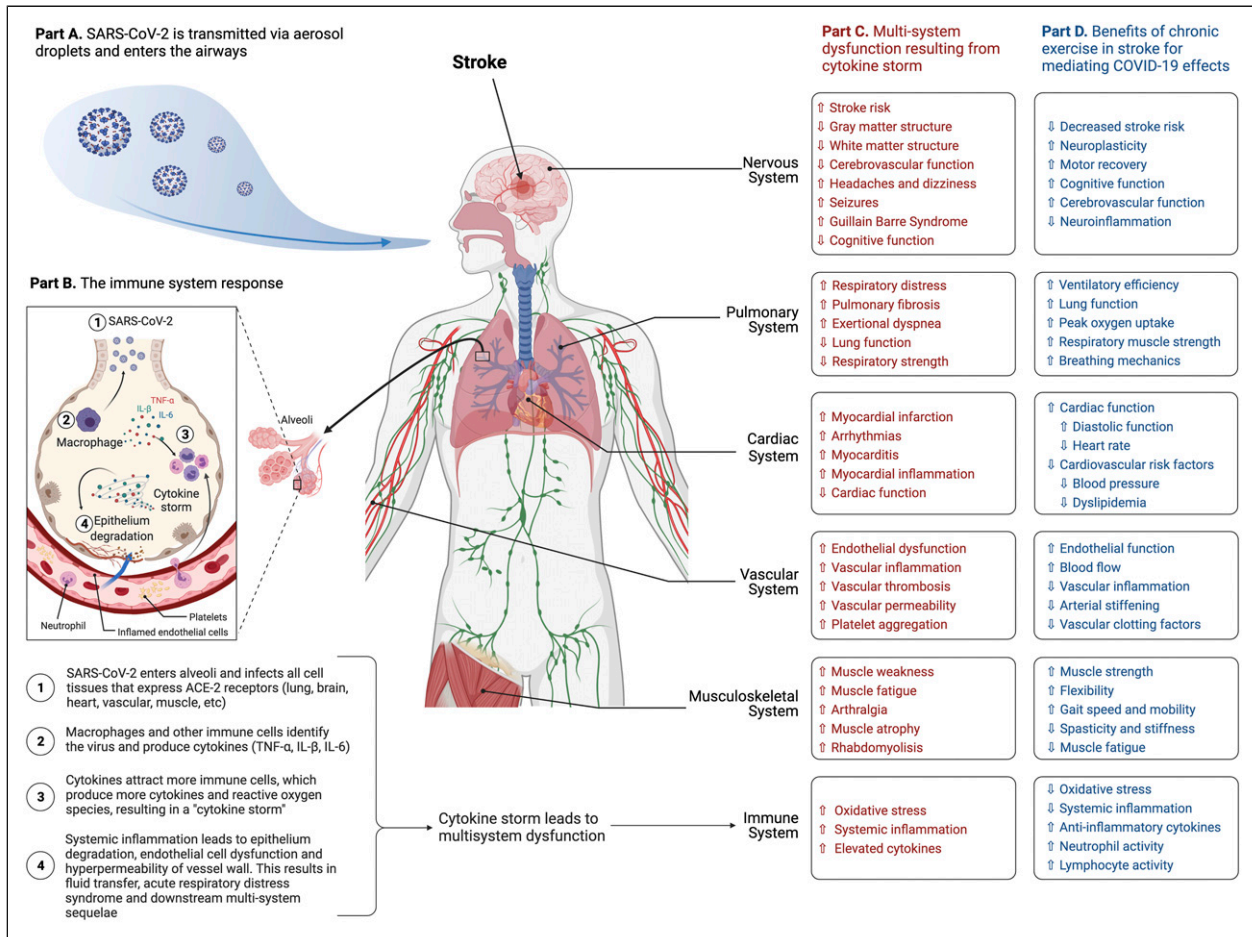


Figure 1. A Summary of (A) SARS-CoV-2 transmission, (B) the immediate immune system response, (C) associated multi-system pathophysiological complications of COVID-19 infection relevant to exercise, and (D) the known multi-system benefits of exercise in individuals with stroke. Created in [BioRender.com](https://www.biorender.com), used with permission.

angiotensin-converting-enzyme (ACE-2) receptors^{28,29} found in cell tissues throughout the body, including epithelial cells in the lungs, vascular endothelial and smooth muscle cells, and cardiomyocytes.²⁹ Binding to ACE-2 receptors mediates viral-epithelial cell membrane fusion and endocytosis, allowing the virus to enter host cells and begin replication and invasion of adjacent epithelial cells.²⁹

The Immune System

Infectious disease pathogens such as SARS-CoV-2 can act as a physiological catalyst for systematic inflammation contributing to cerebrovascular injury and increased risk of stroke.⁴ Pooled estimates suggest that 1.4% (95% CI: 1.0–1.9) of confirmed COVID-19 cases present with a new-onset cerebrovascular event, either as acute ischemic stroke or intracerebral hemorrhage.⁴

The immune system response to COVID-19 infection is depicted in [Figure 1](#) Part B. Acutely upon infection, a virus-induced release of cytokines and inflammatory markers

attract neutrophils, helper and cytotoxic T cells as an immune response, but in doing so, results in systemic tissue inflammation, injury, and decreased ACE-2 function.²⁸ ACE-2 dysfunction may also influence other mechanistic pathways, such as the renin-angiotensin system (RAS), which plays a crucial role in blood pressure regulation, fluid, and electrolyte balance, inflammation, and vascular hyperpermeability.²⁹

After the early stages of infection, the virus further propagates from the nasal epithelium to the upper and lower respiratory tract, leading to symptoms of acute upper respiratory tract infection and an induced "cytokine storm".^{29,30} The cytokine storm is characterized by an aberrant release of pro-inflammatory cytokines and chemokines (e.g., tumor necrosis factor- α [TNF- α]; Interleukin-1 β [IL-1 β]; and Interleukin-6 [IL-6]),²⁹ leading to systemic inflammation and multi-system dysfunction including respiratory,^{2,5} cardiovascular, hematological,^{6-8,31,32} neurological, and musculoskeletal sequelae ([Figure 1](#), Part C).³³⁻³⁵ The complex multi-system sequelae of COVID-19 share potential commonalities

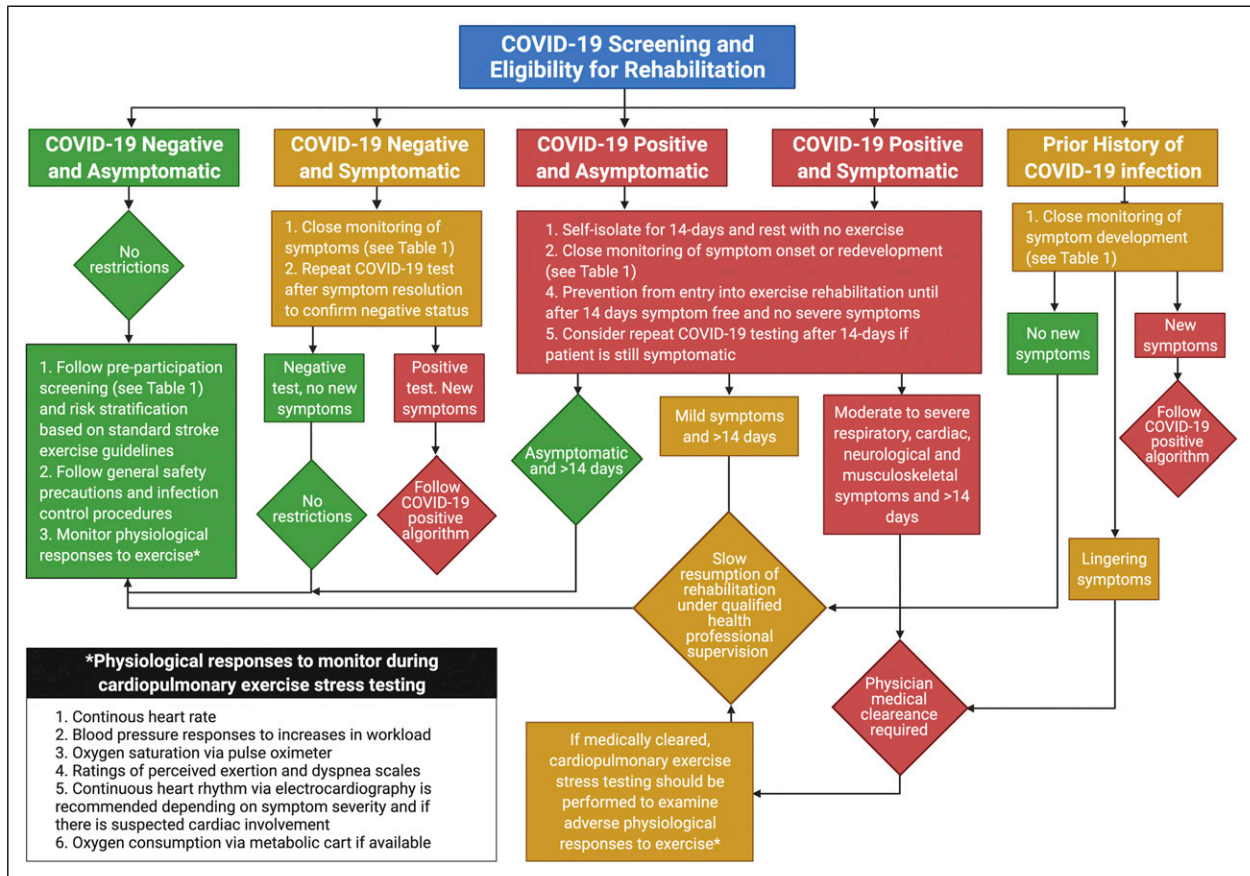


Figure 2. Example of a clinical decision-making flow chart for COVID-19 screening and eligibility for exercise rehabilitation for individuals with stroke. Created in BioRender.com, used with permission.

with the known pro-inflammatory and multimorbidity profile of stroke.

Regular exercise participation has known anti-inflammatory effects which may mitigate symptoms or protect against COVID-19 infection.³⁶ However, acute and long-term exercise is known to influence the immune system in a dose-dependent manner whereby high-intensity or very prolonged exercise may induce oxidative stress, the production of reactive oxygen species, the release of pro-inflammatory cytokines (e.g., TNF- α , IL-6), and reductions in the concentration of natural killer cells below preexercise levels.³⁷ Hence, the frequency, intensity, time, and type of exercise performed are important factors to consider during exercise prescription after COVID-19.³⁶ There is currently no data available regarding high-intensity exercise and the immune response in stroke, but data from non-stroke populations suggest that in the context of COVID-19 associated cytokine storm, participation in high-intensity or very prolonged exercise may act as an immunosuppressant and potentially increase risk of COVID-19 infection.³⁶

In contrast, moderate-intensity exercise can improve immune system function through the release of pro- (e.g., TNF- α) and anti-inflammatory (e.g., IL-10) cytokines, increased activity of neutrophils, and concentration of lymphocytes in

the vascular bed (e.g., CD4⁺ and CD8⁺ T cells).^{36,37} Upon exercise cessation, both inflammatory cytokines and lymphocyte concentration levels decline to normal pre-exercise levels.³⁷ This response is thought to be beneficial for lowering systemic inflammation and may reduce the intensity of symptoms associated with viral infection (Figure 1 Part D).^{36,37} Recent data suggest that participating in regular physical activity was strongly associated with a reduced risk for severe COVID-19 outcomes among infected adults without stroke.³⁸

Taken together, the initiation of relatively short bouts of exercise performed at low to moderate intensity is likely a safe and beneficial therapeutic strategy for improving multiple systems in individuals post-stroke who are deemed medically stable (e.g., typically in the early sub-acute phase)¹⁴ and who are ≥ 14 days symptom-free with suspected or confirmed post-COVID-19 infection (refer to Figure 2). Additionally, moderate-intensity exercise may provide protective effects against infection by strengthening the immune system for individuals who are not infected.

The Pulmonary System

Stroke can have direct or indirect effects on the respiratory system. Individuals with stroke may present with diminished

lung volumes and capacities, impaired breathing mechanics, asymmetric ventilation, and decreased inspiratory and expiratory muscle strength.^{39,40} Hemiparesis from stroke contributes to diminished respiratory muscle strength that is less than half of non-stroke counterparts,⁴¹ leading to respiratory insufficiency, reduced exercise capacity, dyspnea, and further physical inactivity.⁴⁰ Pulmonary and diaphragmatic complications, including ineffective cough, dysphagia, can increase the risk for respiratory illness and viral infection.⁴²

Pulmonary symptoms are one of the hallmark signs of COVID-19. The viral invasion of type-2 alveolar epithelial cells and pulmonary capillary endothelial cells results in both acute and post-acute pulmonary complications, including exertional dyspnea, pneumonia, and acute respiratory distress syndrome.^{28,30} Up to 85% of individuals with COVID-19 show bilateral lung pathology, including ground-glass opacities, interstitial thickening, pulmonary fibrosis, and consolidation.²⁸ Pulmonary function is diminished beyond the acute stages of COVID-19 infection, manifesting as decreased carbon monoxide diffusion capacity, diminished lung volumes and capacities, and weakened respiratory muscles.^{2,5} Long-term data indicate that individuals with more severe acute illness can also have persistently impaired pulmonary diffusion capacities, reduced residual volume, abnormal chest imaging manifestations, and reduced 6-Minute Walk-Test distance at 6-month follow-up.² Thus, impaired capillary-alveolar gas exchange, damaged lung tissue, and weakened respiratory muscles in the acute phases of infection are likely to result in impaired breathing mechanics and pulmonary diffusion capacities in the long term. Improving pulmonary function and lung tissue is a rehabilitation priority post-COVID-19.¹³

Compared to the strong body evidence of benefits of exercise on the cardiovascular system in stroke,¹⁵ the effect of exercise on respiratory structure and function is less extensive.⁴⁰ Aerobic exercise is likely to enhance pulmonary function,⁴⁰ thereby improving the efficiency of respiration and peripheral muscle oxygen extraction. Furthermore, inspiratory muscle training and expansion exercises improve pulmonary function and trunk control in individuals with hemiparetic stroke.⁴³ Recent, albeit limited data, suggests that exercise training and cardiopulmonary rehabilitation is feasible and potentially efficacious for improving pulmonary function among individuals following COVID-19 infection.⁴⁴ Guidelines for conducting diagnostic laboratory exercise stress testing with metabolic gas exchange and pulmonary function testing during COVID-19 are now available.⁴⁵

The Cardiac and Vascular Systems

Impaired cardiovascular function is not only a primary risk factor but also a cause and consequence of stroke. Cardiovascular complications, including myocardial infarction, systolic and diastolic cardiac dysfunction, electrocardiogram abnormalities and arrhythmias,⁴⁶ are common following

stroke.⁴⁷ The prevalence of cardiovascular risk factors (e.g., hypertension) are also high in individuals with stroke, accelerating atherosclerotic processes, vascular dysfunction, and arterial stiffening.⁴⁸

Cardiovascular complications are common in the short- and long-term after COVID-19 infection, including arrhythmias, myocardial injury, myocarditis, and stroke.^{6,7,31,32} Moreover, individuals with pre-morbid cardiovascular comorbidities are at greater risk of severe infection and mortality from COVID-19.³¹ An increase in troponin levels, disproportionate systemic inflammatory response, impaired function of ACE-2 receptors and the RAS are potential mechanisms underlying cardiovascular dysfunction associated with COVID-19.^{3,49} Long-term cardiovascular effects of COVID-19, including myocardial abnormalities and inflammation have also been reported.³² Changes in cardiac function and structure, including reduced ventricular ejection fraction and higher left ventricular volume, have been observed to persist up to 92 days following COVID-19 infection.³²

Up to 88% of individuals with COVID-19 infection also experience microvascular and thrombotic complications.^{49,50} Of particular concern for all and those recovering from a stroke are new cerebrovascular events precipitated by COVID-19-induced immune response and pathology, including platelet aggregation, coagulation dysfunction, and thromboembolism.^{8,50} Cerebral hypoperfusion appears to persist for at least 3 months following COVID-19 infection.⁵¹ Abnormal blood clotting alterations⁴⁹ and changes in cerebral blood flow are associated with inflammation and cytokine storm.⁵¹ Peripheral, central and cerebrovascular changes may precipitate the occurrence of ischemic stroke or transient ischemic attack, which has been reported in approximately 1–3% of patients with COVID-19.^{4,33,52}

Aerobic exercise has been extensively investigated in stroke rehabilitation,¹⁶ and is effective for improving cardiorespiratory fitness,¹⁶ reducing cardiovascular risk factors,¹⁸ and enhancing peripheral, central cardiovascular, and cerebrovascular function.^{18,53} A recent study, which included patients with stroke, demonstrated that individuals with greater cardiorespiratory fitness had a lower risk of hospitalization due to COVID-19, suggesting a protective effect of cardiorespiratory fitness.⁵⁴ Thus, access to exercise training in stroke rehabilitation settings remains ever-important for individuals with stroke who have experienced COVID-19. Guidelines for the safe restoration of cardiac rehabilitation^{26,27} have been published in anticipation of the surge in rehabilitation needs following COVID-19. However, while some strategies could be translated to individuals with stroke with cardiovascular comorbidity, specific exercise guidelines for stroke rehabilitation are still lacking.

The Nervous System

The extent and nature of neurological sequelae after stroke depends on the type, size, and location of the brain lesion(s)

and includes speech, language, and sensory deficits,⁵⁵ and functional impairments (e.g., weakness, spasticity, and cognitive).^{55,56} Post-stroke fatigue⁵⁷ and the potential for seizures and epileptic events⁵⁸ are common and can impact functional recovery and exercise participation after stroke.

Emerging data demonstrate that COVID-19 can infect the nervous system directly (e.g., binding and entry mediated by ACE-2 receptors)⁵⁹ or indirectly through systemic events (e.g., hypoxia, hypercoagulation).⁶⁰ Centrally, changes to white matter microstructure and gray matter atrophy have been observed 3-months following COVID-19 infection,⁵¹ which may be associated with systemic inflammation, peripheral organ system dysfunction, and cerebrovascular changes.⁶¹

Olfactory and gustatory disorders, headaches, and dizziness are amongst the most commonly described neurological symptoms, although the exact etiology is unclear.³⁴ Anosmia and ageusia are also reported frequently, and early detectable neurological manifestations of COVID-19 infection (prevalence 36% (95% CI: 21–50) and 39% (95% CI: 24–53), respectively).^{52,62} Other serious consequences of direct COVID-19 infection have been described, such as Guillain-Barre Syndrome.³³

Persistent symptoms such as fatigue, difficulty concentrating, and memory problems, amongst other symptoms, collectively termed as ‘brain fog’ have also been described.⁶³ Cognitive deficits in executive functioning and working memory, have been reported in those who have recovered from COVID-19 infection,⁶⁴ underscoring the potential chronic effects of COVID-19 infection or “long-covid.” Persistent cognitive deficits may be associated with hospitalization due to sequelae related to COVID-19,^{64,65} such as acute respiratory distress syndrome, which has been associated with cognitive impairment.⁶⁶

Notably, there is a potential overlap in neurological complications of stroke and those of COVID-19. Individuals with COVID-19 commonly report fatigue (prevalence 65%, 95% CI: 60–71)⁶⁷ and headaches (prevalence: 15%, 95% CI: 10–19),⁶² sequelae commonly found post-stroke. Though less prevalent, ataxia (prevalence: .3%, 95% CI: 0.1–0.7) and seizures have also been reported (prevalence: .9%, 95% CI: 0.5–1).⁶²

Exercise is an effective method to promote neurological recovery after stroke. Moderate- and high-intensity aerobic exercise may stimulate brain plasticity mechanisms that underlie motor function recovery after stroke.²⁰ Higher cardiorespiratory fitness and physical activity participation has been associated with preservation of gray and white matter structures in older individuals,^{68,69} and engagement in exercise can improve cognitive function post-stroke.¹⁷ In light of the known neurological complications associated with stroke and COVID-19, exercise could be an important aspect of rehabilitation services for stroke patients with COVID-19.

The Musculoskeletal System

Musculoskeletal complications from stroke can include muscle weakness and spasticity. Skeletal muscle adaptations due to metabolic disorders and sedentary behaviors can lead to the onset and progression of stroke-related sarcopenia,⁷⁰ characterized by skeletal muscle atrophy and changes in motor function that can lead to poor mobility, physical inactivity, and further motor impairments.⁷¹ Recent pooled estimates suggest that musculoskeletal deficits and stroke-related sarcopenia impact up to 42% of stroke survivors.⁷¹

COVID-19 may also manifest in complications in the musculoskeletal system. Muscle weakness and myalgia^{34,72} have been reported in 36% of cases,⁷³ of which have been attributed to cytokine storm and systemic inflammation.⁷⁴ Myositis and arthralgia⁷⁵ have been described in the early and later stages of infection, and cases of reactive arthritis⁷⁶ have been described as symptoms of acute infection. Rhabdomyolysis, a downstream complication of myositis, has also been described in an observational study of 140 infected patients (17% incidence rate).⁷⁷ Sarcopenia⁷⁸ and cachexia⁷⁹ are common long-term musculoskeletal complications of COVID-19.

In individuals with SARS-CoV-1, combined moderate-intensity aerobic and resistance exercise training programs improved skeletal muscle strength and reduced fatigue⁸⁰; analogous benefits may be possible following COVID-19 infection.³⁵ In stroke, resistance exercise training targeting ~50–80% of 1-repetition maximum has been shown to improve muscle strength and endurance,^{16,19} important factors for mobility, gait and other activities of daily living. The benefits of exercise on musculoskeletal outcomes are less evidenced in the specific context of COVID-19.

Section 2) Considerations for the Implementation of Exercise Stroke Rehabilitation During and After a Pandemic

Evidence-based scientific statements¹⁵ and best practice recommendations¹⁴ for exercise after stroke have been previously published. In this section, we outline additional clinical considerations for the implementation of exercise in the context of COVID-19. We acknowledge that the COVID-19 situation and volume of potential patients requiring care varies significantly from region to region; thus, the following considerations are not meant to be absolute or definitive recommendations but must be considered in the context of current local institutional, public health, and governmental guidelines.

Safety Considerations for the Implementation of Exercise During COVID-19

It is critical for healthcare professionals to follow their respective governmental and institutional guidelines regarding

Table 1. Safety Considerations for Implementation of Exercise During COVID-19.

1. Testing for COVID-19 infection as a screen before participation in stroke rehabilitation.
2. Minimizing interaction between patient groups, for example, separating inpatient and outpatient rehabilitation exercise areas to reduce the risk of viral transmission.
3. Administering a COVID-19 Pre-Participation Screening Questionnaire online or by telephone at least 24-hours before each rehabilitation appointment (see sample in [Table 2](#)). Such a questionnaire can assess for possible exposure, changes in status, or development of new symptoms and to guide clinicians on how to proceed with exercise.
4. Adopting high standards of hand hygiene and proper use of personal protective equipment (e.g., face shield, surgical face mask, surgical gown, and gloves) for both clinicians and individuals poststroke.¹³
 - While patients may be reticent about wearing surgical face masks during exercise, the use of face masks is tolerated and can be worn safely and do not impair respiratory function and breathing during moderate or high-intensity cardiovascular exercise.⁸⁷
 - Clinicians are encouraged to monitor signs and symptoms of impaired gas exchange (e.g., sudden headache, feeling disoriented or dizzy, or abnormal shortness of breath for a given workload) during exercise to prevent any potential adverse effects derived from the use of personal protective equipment.
5. Minimizing the number of individuals present in the training space in accordance with standard safety protocols (e.g., maximum of 2 instructors to 1 participant).
6. Maintain adequate airflow and ventilation and distancing between exercise equipment (at least 2 m) to mitigate the potential for aerosol and droplet transmission.
 - If necessary, may consider the installation of infrastructure such as clear plastic sheet barriers around stationary exercise equipment.
7. Use of antibacterial and antiviral filters with standard mouthpieces when acquiring metabolic measurements during exercise stress testing.⁴⁵
8. Cleaning all exercise stress testing equipment, safety monitoring equipment (e.g., electrocardiogram, stethoscope, blood pressure monitor, and pulse oximeter), and components of the metabolic cart (e.g., flow-mass meters)⁴⁵ following local infection control practice standards and per manufacturer's instructions after each use.
9. Incorporating virtual exercise rehabilitation activities for individuals with stroke who do not require close monitoring and can exercise independently (e.g., low cardiovascular risk and medically stable)

safety precautions. To ensure a safe environment for exercise and reduce the risk of COVID-19 transmission during in-person program activities, healthcare professionals should consider implementing the safety considerations presented in [Table 1](#) and the COVID-19 pre-screening and eligibility for exercise rehabilitation questionnaire in [Table 2](#).

Pre-Participation Screening and Eligibility for Exercise Stroke Rehabilitation

Return to physical activity and exercise is vital for stroke recovery, but appropriate and safe participation requires adequate pre-participation screening and eligibility assessment for exercise stroke rehabilitation,^{14,15,81} especially in the context of post-COVID-19 rehabilitation. Only qualified healthcare professionals should assess safety and suitability for graded exercise stress testing with or without electrocardiography (ECG) and metabolic gas exchange, and training for individuals post-stroke,¹⁴ including those who may have a suspected or confirmed COVID-19 infection. To assist with clinical decision-making, we have developed an evidence-based COVID-19 decision-making flow chart for pre-participation screening and eligibility for exercise in stroke rehabilitation ([Figure 2](#)). This flow-chart can also assist with clinical decision-making about whether further medical assessment and/or exercise stress testing with ECG and metabolic gas exchange is required before engaging in exercise. This flow chart incorporates the COVID-19 Pre-Screening Exercise Questionnaire outlined in [Table 2](#).

For all decision points, general safety precautions and infection control procedures should remain in place.

Dual Diagnosis: Acute Stroke and COVID-19 Infection. In the event of acute “dual diagnosis” of stroke and COVID-19 (such as acute stroke resulting from COVID-19, or acute stroke and acquired infection during hospital stay), clinicians should follow local institutional guidelines regarding COVID-19 safety precautions and acute stroke medical practices until the patient is deemed medically stable to participate in exercise.²¹ This aligns with previously published stroke exercise guidelines that recommend that formal exercise rehabilitation may be considered once the individual is medically stable.^{14,15}

Individuals Post-Stroke who are COVID-19 Negative and Asymptomatic. Individuals post-stroke who are COVID-19 negative and asymptomatic ([Table 2](#), Part B) should undergo routine standardized pre-participation screening and individualized assessment and risk stratification as per published guidelines.^{14,15}

Individuals Post-Stroke who are COVID-19 Negative and Symptomatic. If an individual is COVID-19 negative but is symptomatic ([Table 2](#), Part B and C), they should refrain from participating in formal exercise rehabilitation until symptom-free and undergo repeat COVID-19 testing to confirm negative status. Once symptoms are resolved and confirmed negative status, participants should undergo pre-participation

Table 2. COVID-19 Pre-Screening and Eligibility for Exercise Rehabilitation Questionnaire.

Part A: COVID-19 Vaccination Status		
1. Has the patient been vaccinated for COVID-19? If YES, please indicate the date(s) of vaccination. Dose 1: _____ Dose 2 (if applicable): _____	YES	NO
Part B: General COVID-19 Screening		
1. Does the patient have a pending COVID-19 test? If YES, please indicate date of test: _____	YES	NO
2. Has the patient had a confirmed case of COVID-19? If YES, please indicate date of last COVID-19 test: _____ Type of test (PCR, antigen, other): _____	YES	NO
3. Has the patient had close contact with a confirmed case of COVID-19? If YES, please indicate date of exposure: _____	YES	NO
4. Is the confirmed case of COVID-19 symptomatic?	YES	NO
5. Has the patient traveled abroad or has been in contact with someone who has traveled abroad in the last 14 days?	YES	NO
6. Does the patient have any new COVID-19 symptoms?	YES	NO
<ul style="list-style-type: none"> • If the patient answers NO to all questions in Part B, they are presumed to be COVID-19 negative and asymptomatic and can proceed with exercise rehabilitation and pre-participation screening. • If the patient answers YES to any of the above questions in Part B, they must proceed to Part C of this questionnaire. 		
Part C: COVID-19 Medical History and Symptom(s) Checklist		
1. If the patient has a previous case of COVID-19, did they require oxygen, and were they put on a ventilator?	YES	NO
2. If the patient has a previous case of COVID-19, were they diagnosed with any other respiratory, cardiac, neurological, or musculoskeletal complications? If YES, please list diagnoses: _____	YES	NO
3. Does the patient report any of the general COVID-19 symptoms?		
• Temperature equal to or over 38°C	YES	NO
• Fever	YES	NO
• Chills	YES	NO
• General fatigue and weakness	YES	NO
• Gastrointestinal symptoms (abdominal pain, diarrhea, and vomiting)	YES	NO
• Feeling very unwell	YES	NO
• Date of symptom onset: _____		
• Duration of symptoms: _____		
4. Does the patient report any of the following respiratory symptoms?		
• New or worsening cough	YES	NO
• Shortness of breath or difficulty breathing at rest	YES	NO
• Shortness of breath or difficulty breathing with exertion	YES	NO
• Date of symptom onset: _____		
• Duration of symptoms: _____		
5. Does the patient report any of the following cardiovascular symptoms? ²⁵		
• Fainting or loss of consciousness	YES	NO
• Chest pain or sensation of chest pressure	YES	NO
• Experience rapid fluctuations in heart rate	YES	NO
• Palpitations, including skipped, racing, or dropped heartbeats	YES	NO
• A reduction in self-reported fitness	YES	NO
• Date of symptom onset: _____		
• Duration of symptoms: _____		

(continued)

Table 2. (continued)

6. Does the patient report any of the following neurological symptoms? ^{34,52}			
• New loss of smell or taste		YES	NO
• Headache		YES	NO
• Dizziness		YES	NO
• Changes in mental status/confusion		YES	NO
• Neuralgia (stabbing and burning sensations)		YES	NO
• Worsening seizures or epilepsy if present		YES	NO
• Myoclonus (sudden muscle spasms)		YES	NO
• Vision disturbances		YES	NO
• Date of symptom onset: _____			
• Duration of symptoms: _____			
7. Does the patient report any of the following musculoskeletal symptoms? ³⁵			
• Muscle, body aches, and pains		YES	NO
• Bone and joint pain		YES	NO
• Date of symptom onset: _____			
• Duration of symptoms: _____			
• If the patient answers NO to all questions in Part C , they are asymptomatic and can proceed with exercise rehabilitation and preparticipation screening.			
• If the participant answers YES to any of the questions in Part C , participants should be referred for additional COVID-19 testing and seek medical clearance prior to rehabilitation and pre-participation screening.			

Table headings are color coded to coincide with the clinical decision making flow-chart in [Figure 2](#).

screening prior to commencing exercise rehabilitation ([Figure 2](#)).^{14,15}

Individuals Post-Stroke who are COVID-19 Positive and Asymptomatic. Individuals post-stroke who are COVID-19 positive and asymptomatic should self-isolate for 14 days and not participate in structured exercise rehabilitation. Standard stroke medical practices and rehabilitation should still be maintained. Clinicians are encouraged to frequently assess COVID-19 status and monitor the onset and redevelopment of new symptoms ([Table 2](#), Part B and C). After 14-days and symptom free, participants should then undergo standardized pre-participation screening prior to commencing exercise rehabilitation ([Figure 2](#)).^{14,15} Depending on institutional guidelines, repeat COVID-19 testing may be required to confirm negative status before exercise rehabilitation enrollment.

Individuals Post-Stroke who are COVID-19 Positive and Symptomatic. Individuals post-stroke who are COVID-19 positive and symptomatic should self-isolate for 14 days and not participate in formal exercise rehabilitation until symptom free. Standard stroke medical practices and rehabilitation should still be maintained. Clinicians are encouraged to frequently assess COVID-19 status and monitor the onset and redevelopment of new symptoms ([Table 2](#), Part B and C).

If a patient previously reported mild symptoms and is no longer positive for COVID-19 infection after 14-days, then a slow resumption of low-intensity exercise rehabilitation under qualified healthcare professional supervision (e.g., physiotherapist, nurse, and physician) should be instituted.

Standard pre-participation and risk stratification should also be followed.^{14,15}

Patients who experienced moderate to severe symptoms (e.g., requiring oxygen supplementation, hypoxic on room, and cardiac symptoms) and who are greater than 14-days after infection should have medical clearance before participating in exercise rehabilitation. Depending on institutional guidelines, participants may be required to undergo a repeat COVID-19 test to confirm negative status. Once medically cleared for formal exercise rehabilitation, participants should undergo pre-participation screening and exercise stress testing with ECG and metabolic gas exchange to examine any abnormal physiological exercise responses or exercise-induced symptoms ([Figure 2](#)).^{14,15}

Individuals Post-Stroke with History of COVID-19 Infection. For individuals' post-stroke with a prior history of COVID-19 but who are currently symptom-free, close monitoring of symptom redevelopment is recommended. If no new symptoms are present on the COVID-19 Pre-Participation Screening Questionnaire, individuals may then undergo standard pre-participation screening^{14,15} and slowly commence exercise rehabilitation under the supervision of a medical health professional (e.g., physiotherapist, nurse, and physician).

For individuals presenting with persistent post-acute multi-system sequelae as identified by the COVID-19 Pre-Participation Screening Questionnaire ([Table 2](#), Part C), medical clearance is required before participating in exercise rehabilitation. Once medically cleared, these participants should undergo pre-participation screening^{14,15} and exercise stress testing with ECG and metabolic gas exchange to examine any abnormal physiological responses to exercise.

If an individual post-stroke with a previous COVID-19 infection develops new symptoms, these individuals should be re-tested for suspected COVID-19 infection, self-isolate for 14 days, and refrain from exercise rehabilitation until symptom-free. After being symptom free for more than 14 days, participants should undergo a repeat COVID-19 test to confirm negative status. Clinician decision-making should be informed by pathways outlined in [Figure 2](#).

Considerations for Exercise Stress Testing

The “gold-standard” exercise stress test with ECG and metabolic gas exchange is recommended and routinely employed in clinical practice for individuals post-stroke¹⁴ and post COVID-19.^{82,83} These tests provide clinicians with clinically relevant information, including but not limited to the capacity of individuals with stroke to physiologically adapt in response to graded aerobic exercise (e.g., blood pressure)⁴⁰ and baseline measures of cardiorespiratory fitness and ventilatory efficiency. For individuals post-stroke and recovered from COVID-19 with potentially underlying or unknown cardiopulmonary pathologies, exercise stress testing with ECG and metabolic gas exchange can provide key diagnostic and pathologic information, including clinically suspected myocarditis,²⁵ exercise-associated oxygen desaturation, hypoxemia, intolerance, and exertional dyspnea.⁸⁴ Clinicians can also utilize outcomes of exercise stress tests to develop individualized dosing parameters and appropriate aerobic exercise prescription (e.g., the calculation of heart rate reserve or ratings of perceived exertion achieved on an exercise stress test is often used to establish the target exercise training intensity) for individuals with stroke.¹⁴ For muscular strength and resistance exercise training, clinicians can utilize 1-repetition maximum testing to objectively establish target training loads (e.g., 50%–80% of 1-repetition maximum) for free-weights, elastic resistance bands.¹⁵

However, given the potentially large volume of patients and that not all practice settings (e.g., inpatient vs outpatient) will have access to specialized exercise stress testing facilities and equipment (e.g., ECG, metabolic cart, and recumbent stepper) or qualified personnel to conduct objective aerobic exercise pre-participation screening,⁸¹ a symptom-limited test or submaximal exercise stress test where clinically feasible may be included as a part of pre-participation exercise screening after stroke.¹⁴ While clinicians may decide to rely solely on subjective reports and clinical observation for exercise prescription,⁸¹ this is not recommended as it can result in overlooked diagnostic or pathologic information (e.g., that might be only observed via ECG or metabolic gas exchange) and inaccurate and inappropriate dosing especially among individuals with previous COVID-19 infection.

Thus, the need for monitoring cardiac rhythm via ECG should be based on an individual’s medical history,⁸⁴ COVID-19 history, and presence of persistent post-acute symptoms. Exertional dyspnea, hypoxemia, cardiac arrhythmias,

and aberrant blood pressure responses are hallmark characteristics following stroke and COVID-19 infection. Therefore, cardiorespiratory responses, including heart rate and rhythm, blood pressure, oxygen saturation, oxygen uptake, and ratings of perceived exertion and dyspnea scales⁸⁴ should be monitored continuously throughout the exercise stress test for individuals with previous COVID-19 infection who experienced moderate to severe or post-acute symptoms ([Figure 2](#)). Other submaximal exercise stress testing protocols without ECG or gas exchange are clinically feasible,⁸⁵ valid and reliable alternatives to maximal exercise stress testing⁸⁶ and may be most appropriate for mild cases without significant comorbidities and if exercise rehabilitation programs target only low to moderate intensity.¹⁴

Nonetheless, in accordance with current stroke exercise recommendations^{14,15} clinicians are required to objectively monitor (1) heart rate via heart rate monitor or manual palpation, (2) blood pressure via manual sphygmomanometer or automated blood pressure monitoring, (3) oxygen saturation via pulse oximeter, (4) ratings of perceived exertion, and (5) dyspnea scale throughout the test, with values being recorded during last 30 seconds of each stage of exercise.⁸⁴

Per standard exercise stress testing guidelines, all exercise stress tests with or without ECG and metabolic gas exchange should be conducted by trained and qualified health care professionals with direct access to physician support, external defibrillator, and antiviral/bacterial filters and mouthpiece for exercise stress testing.¹⁴ Relative and absolute exercise testing termination criteria as per the American College for Sports Medicine guidelines should be followed,⁸⁴ with particular attention to signs and symptoms such as moderate-to-severe angina, changes in oxygen saturation (e.g., $SpO_2 \leq 80\%$), blood pressure (e.g., drop in systolic blood pressure of >10 mmHg, despite an increase in workload in conjunction with ischemia, or exaggerated blood pressure response), dyspnea, and if necessary due to suspected abnormal cardiovascular involvement from COVID-19, the presence of cardiac arrhythmias via ECG. Exercise stress testing logistics, including PPE requirements for patients and medical personnel, pre-test considerations and post-test decontamination are presented in [Table 1](#) and additional details are published elsewhere.⁸²

Exercise Prescription and Progression for Individuals With Previous COVID-19 Infection

There is currently a lack of high-quality empirical evidence for exercise rehabilitation in post-COVID-19 populations. In line with previous expert-consensus COVID-19 exercise recommendations^{13,22,23} and considering the potential immunoprotective benefits of low-to-moderate intensity exercise for COVID-19,³⁶ clinicians should encourage a gradual increase of exercise training volume (e.g., starting at 50% of frequency, intensity, and time) 2 weeks after acute symptom

resolution for individuals with moderate-to-severe COVID-19 infection. For mild and asymptomatic cases, a gradual increase of exercise training volume and prescription should be based on objective exercise stress testing, clinical judgment and symptom severity (Figure 2).¹³ In all cases, objective exercise stress testing will enable clinicians to tailor exercise prescriptions based on an individual's physiological response to aerobic exercise (e.g., percentage of heart-rate reserve, maximal heart rate, and/or ratings of perceived exertion achieved during an exercise stress test) and a percentage of 1-repetition maximum for resistance exercise prescription.^{14,15} Nonetheless, continued monitoring of exercise-induced symptoms and COVID-19 symptom reproduction is essential during exercise progression and should be encouraged in all practice settings.

Vaccination Status

As patients and staff in the exercise rehabilitation facility undergo vaccination, institutional procedures and governmental policies may continue to recommend infection control measures to remain in place. We encourage stroke rehabilitation professionals to document patient's vaccination status and date(s) of vaccination upon entry into rehabilitation (Table 2, Part A).

In-Person vs Virtual Exercise Rehabilitation for Stroke

As outlined for cardiac rehabilitation settings,²⁶ there are valid concerns regarding the transition to and implementation of virtual exercise stroke rehabilitation, including limited data on effectiveness, lack of access to equipment and resources, and challenges with virtual risk-stratification and safety monitoring. For individuals who are deemed higher risk (e.g., previous COVID-19 positive test), exercise rehabilitation with direct in-person supervision is encouraged to allow access to safety monitoring (e.g., ECG and blood pressure monitoring) and emergency response (external defibrillator and emergency personnel). For individuals with stroke who have no previous COVID-19 history or are deemed medically stable and low risk after pre-participation screening, exercise prescription for remote and home-based exercise programs can be effective and implemented safely as per published guidelines.¹⁴ The use of remote non-invasive oxygen saturation pulse oximeters and heart rate monitors could be used to monitor exercise responses and mitigate any potential safety concerns during virtual exercise rehabilitation.

Concluding Statements

The COVID-19 pandemic continues to evolve and affect millions of individuals globally. With the growing recognition of variants and post-acute persistent complications from COVID-19,^{9,10} rehabilitation services remain a critical priority as a core health strategy to reduce the burden of COVID-19,

including among people with stroke. Therefore, specific exercise-based stroke rehabilitation recommendations to optimize recovery from stroke and COVID-19 are greatly needed.

Research conducted before COVID-19 identified several barriers to aerobic exercise implementation in stroke rehabilitation settings, including therapists' lack of knowledge and skills with pre-participation screening and exercise prescription.⁸¹ These implementation challenges have been heightened in the current pandemic and will arguably continue beyond the pandemic, given the multi-system pathophysiological changes and high prevalence of multimorbidity among individuals with stroke.

We supported the clinical considerations presented using pre-COVID expert consensus stroke exercise recommendations^{14,15} and relevant information from cardiac, pulmonary and general rehabilitation and return-to-play for athletic populations.^{13,22-27,45} Based on the current literature and depending on patient volume, available resources, exercise stress testing with ECG and metabolic gas exchange should be conducted for individuals post-stroke with moderate to severe symptoms or post-acute symptoms from COVID-19 infection. Objective testing gives clinicians the ability to identify the potential risk for exercise-associated oxygen desaturation, hypoxemia, intolerance, and exertional dyspnea during rehabilitation. Testing should examine the response to exercise, including heart rate and rhythm, blood pressure, oxygen saturation, oxygen uptake, and ratings of perceived exertion and dyspnea. In mild cases without significant comorbidities and if exercise rehabilitation programs target only low to moderate intensity, other objective exercise stress tests without ECG and metabolic gas exchange, including submaximal exercise stress testing, are valid and feasible alternatives to assist with the development of individualized dosing parameters and appropriate exercise prescription.

In conclusion, we present COVID-19 specific considerations to inform clinical decision-making to restore exercise implementation in stroke rehabilitation settings. These considerations incorporate the best available evidence in exercise physiology and clinical judgment in stroke rehabilitation to guide the implementation of safe exercise prescription and participation for individuals with stroke.

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