

Post-Acute COVID-19 Syndrome Management

What You Need to Know

Reports of long-term effects of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection emerged early in the pandemic.¹ Fatigue, arthralgia, brain fog, and shortness of breath (SOB), are just some symptoms described by patients.

Based on 9 studies, the prevalence of post-acute syndrome, described as one or more symptoms, ranges from 32.6 to 87.4%.

- 32.6% from telephone surveys performed 2 months after acute disease in the U.S.
- 87.4% described by an Italian study, where patients were evaluated in person 2 months after the initial infection.^{3,4}
- Other studies out of France, UK, Spain, and China quote 66%, 74%, 50.9%, and 76% respectively.⁴⁻⁹

Systematic studies assessing prolonged effects of SARS-CoV-2 infections and appropriate clinical care are just emerging. Current care will largely depend on lessons learned from care of other disease processes that closely resemble problems described by post-acute coronavirus disease 2019 patients (also known as COVID-19 long-haulers).

Treatment of COVID-19 long-haulers should be approached in a multidisciplinary fashion.

Symptoms should not be minimized as life-threatening entities like pulmonary artery hypertension, severe lung fibrosis, and ventricular failure have been described. In the perioperative setting, practitioners should exemplify pragmatic approach and use of best practices from similar disease states to guide current perioperative care.

Definition of Post-Acute COVID-19 Syndrome (Long-haulers)

Persistence of symptoms or sequelae beyond 4 weeks from onset of acute symptoms.¹ There are two categories:

- **Subacute COVID-19** – symptoms lasting from 4-12 weeks
- **Chronic COVID-19 Syndrome** – symptoms beyond 12 weeks

Risk Factors for Developing Chronic Syndrome

- Patients who experienced severe disease
- Advanced age
- Obesity
- Diabetes
- Hypertension
- Chronic cardiac disease
- Chronic kidney disease
- Immunosuppression

Signs and Symptoms / Potential Complications

- **Nervous System**
 - Fatigue
 - Brain fog (cognitive dysfunction)
 - Anxiety/depression/PTSD
 - Sleep disturbances
 - Headaches
 - Disturbances in sense of smell and taste
- **Cardiovascular System**
 - Chest pain/palpitations
 - Connective tissue deposition in myocardium
 - Postural orthostatic tachycardia syndrome
 - Pulmonary artery hypertension
 - Right ventricular failure
- **Gastrointestinal System**
 - Diarrhea
 - Constipation
- **Renal system**
 - Chronic kidney disease
- **Respiratory System**
 - Shortness of breath
 - Cough
 - Persistent oxygen requirements
 - Pulmonary fibrosis
 - Damage requiring lung transplantation
- **Hematologic System**
 - Thromboembolism
- **Other**
 - Secondary bacterial, fungal, or other pathogen infections
 - Decline in quality of life
 - Muscular weakness
 - Joint pain
 - Hair loss

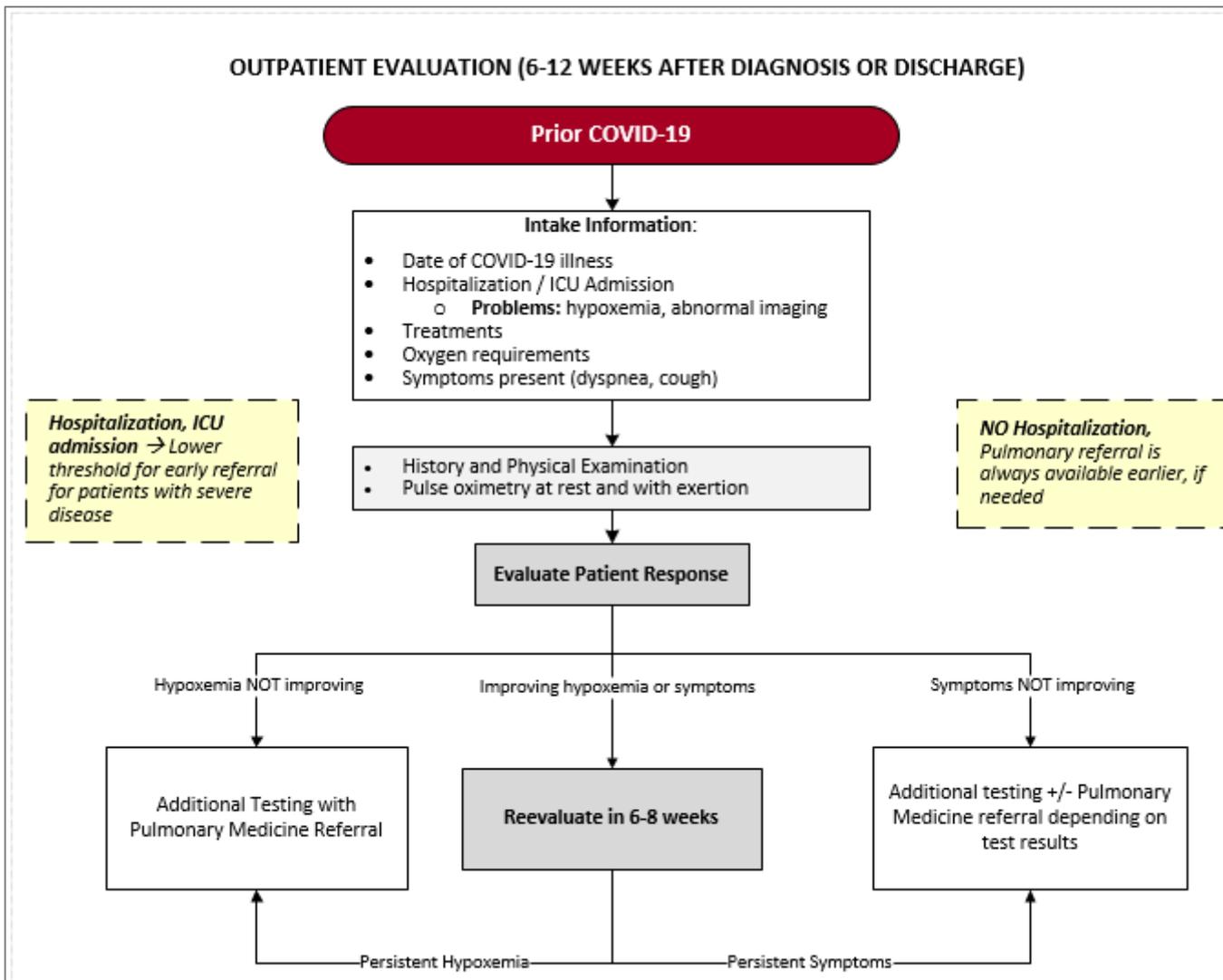
Considerations for the Perioperative Team

Multidisciplinary approach to care of these patients is of utmost importance. Patients with chronic symptoms should have their symptoms addressed pre-operatively. Evaluation on the day of surgery is strongly discouraged, except for urgent/emergent situations

Nervous System	Consideration
Cognitive dysfunction	<ul style="list-style-type: none"> ▪ Avoid medications previously known to be associated with delirium, such as: <ul style="list-style-type: none"> ○ Benzodiazepines ○ Antihistamines, both H₁ and H₂ ○ High dose opioids ○ Scopolamine ○ Other medications with anticholinergic side effects ▪ Avoid intra-operative hypotension. Keep mean arterial pressure within 20% of pre-op values
PTSD	<ul style="list-style-type: none"> ▪ Consider avoiding ketamine administration
Anxiety	<ul style="list-style-type: none"> ▪ Premedication with agents other than benzodiazepines are encouraged. These include: <ul style="list-style-type: none"> ○ Low dose opioids ○ Alpha 2 agonists such as: guanfacine or dexmedetomidine
Cardiovascular System	Consideration
Medications	<ul style="list-style-type: none"> ▪ No change in ACE-I use is recommended. Follow institutional guidelines regarding pre-op administration ▪ Continue aspirin and beta-blockers per institutional guidelines
Chest pain, shortness of breath, exercise intolerance, and palpitations	<ul style="list-style-type: none"> ▪ These should be addressed pre-operatively in a multidisciplinary fashion. Day of surgery evaluation is discouraged unless urgent or emergent. In urgent/emergent situations consider: <ul style="list-style-type: none"> ○ ECG to evaluate arrhythmias ○ Echocardiography to evaluate biventricular function and pulmonary artery pressures
Intra-operative hypotension	<ul style="list-style-type: none"> ▪ Be cognizant of potential need for inotropic agents, especially in patients with right ventricular dysfunction who developed pulmonary fibrosis
Respiratory System	Consideration
Ongoing symptoms	<p>For continued symptoms of shortness of breath, persistent oxygen requirements, and exercise intolerance:</p> <ul style="list-style-type: none"> ▪ These should be address pre-operatively in a multidisciplinary fashion. Day of surgery evaluation is discouraged unless urgent or emergent.
Fibrosis	<ul style="list-style-type: none"> ▪ Consider pressure modes of ventilation ▪ Be cognizant of increased pulmonary artery hypertension and right ventricular dysfunction ▪ Follow lung protective ventilation guidelines (4-6 ml/kg) ▪ Promote good respiratory mechanics. Consider using Sugammadex for neuromuscular blocker reversal ▪ Avoid excessive administration of intravenous fluids. “Dry” lungs are happy lungs
Renal System	Consideration
Acute Kidney injury and chronic kidney disease	<ul style="list-style-type: none"> ▪ Ensure man arterial pressure within 20% of baseline ▪ Avoid excessive administration of intravenous fluids
Hematologic System	Consideration
Thromboembolic Disease	<ul style="list-style-type: none"> ▪ Patients with previously described clots should have a plan regarding bridge therapy for systemic anticoagulation ▪ Patients should receive perioperative chemical and mechanical prophylaxis ▪ Systemic anticoagulation should be restarted as soon as possible after surgery ▪ Aspirin should be continued
Other	<ul style="list-style-type: none"> ▪ Consider providing the least anesthetic possible ▪ Goal is to return patient to previous physical condition as soon as possible ▪ Ensure incentive spirometer in the PACU, early mobility on the floor, and proper consultations as needed

	Persistent Cough	Venous Thromboembolic Disease
Description	<ul style="list-style-type: none"> Post-infectious cough is common in patients after viral infection and may persist for 8 weeks or longer. Multiple pathogenic factors may be contributing, including transient with or without secretion drainage into the hypopharynx (upper airway cough syndrome), or aggravation of concomitant gastroesophageal reflux (GERD) resulting from increased abdominal pressure from coughing. The diagnosis of post-infectious cough is one of exclusion and may require a chest radiograph excluding lower respiratory tract involvement (pneumonia). 	<ul style="list-style-type: none"> Patients with covid-19 infection, especially those requiring hospitalization, may be at increased risk for venous thromboembolic disease. Many of these patients will be diagnosed with venous thromboembolic disease when hospitalized.
Testing	<ul style="list-style-type: none"> Chest radiograph 	<ul style="list-style-type: none"> Diagnosis of possible venous thromboembolic disease <ul style="list-style-type: none"> D-Dimer Venous ultrasonography Chest CT pulmonary angiography (CT PE study)
Treatments	<ul style="list-style-type: none"> Post-infectious cough is self-limited Inhaled short acting bronchodilators <ul style="list-style-type: none"> Inhaled ipratropium Inhaled short acting beta agonists Inhaled glucocorticoids if cough adversely affecting quality of life Oral glucocorticoids <ul style="list-style-type: none"> 30-40 mg prednisone tapered over 2-3 weeks (Low quality evidence) 	<ul style="list-style-type: none"> Upper airway cough syndrome <ul style="list-style-type: none"> Antihistamine-decongestant combinations Intranasal glucocorticoids Intranasal anticholinergics GERD <ul style="list-style-type: none"> H2-antihistamines Proton pump inhibitors <p><i>No role for antibiotics</i></p>
When to Refer	<ul style="list-style-type: none"> Abnormal chest radiograph Persistence of cough beyond 8 weeks for evaluation and management of chronic cough 	<ul style="list-style-type: none"> Not necessary for routine management of acute episodes Dyspnea that is not improving at the conclusion of treatment of the acute episode (3 months) for evaluation for chronic thromboembolic pulmonary hypertension

	Hypoxemia	Dyspnea	Persistent Radiographic Abnormalities
Description	<ul style="list-style-type: none"> Lower respiratory tract involvement of covid-19 infection resulting in pneumonia can lead to hypoxemia that results in either a new prescription for supplemental oxygen or an increased flow of supplemental oxygen from baseline in patients with pre-existing chronic respiratory failure. Most of these patients will have a history of hospitalization for covid-19 infection. While improvement in hypoxemic may occur slowly over a period of 3-4 months after diagnosis or discharge, hypoxemia that is not improving is concerning for post-viral organizing pneumonia or post-inflammatory pulmonary fibrosis. 	<ul style="list-style-type: none"> The differential diagnosis of dyspnea in the post-covid infection setting is wide and includes the pulmonary considerations of infectious pneumonia, organizing pneumonia, post-inflammatory pulmonary fibrosis, and venous thromboembolic disease and the non-pulmonary conditions of post-viral syndrome, anemia, thyroid disease, and cardiac disease, in addition to all of the non-covid related conditions that can cause and contribute to dyspnea. 	<ul style="list-style-type: none"> Persistent radiographic abnormalities in patients who were hospitalized with covid-19 are common and may persist for at least 3-6 months or longer after diagnosis and discharge. If dyspnea and hypoxemia are improving, conservative management with clinical follow up is appropriate.
Testing	<ul style="list-style-type: none"> Pulse oximetry evaluation at rest and with exertion at 2-3 months after diagnosis or discharge Chest radiograph High resolution chest CT Full pulmonary function studies (spirometry, lung volumes, DLCO) 6 minute walk at time of referral (see below) 	<ul style="list-style-type: none"> Pulse oximetry at rest and with exertion Chest radiograph Full pulmonary function studies, including spirometry, lung volumes, DLCO, 6 minute walk Labs: CBC with differential, chem7, LFTs, BNP, TSH with reflex D-dimer, lower extremity venous ultrasonography, Chest CT pulmonary angiography (CT PE study) ECG +/- transthoracic echocardiogram 	<ul style="list-style-type: none"> Chest radiograph if symptoms or hypoxemia, if present, are not improving In patients who are clinically improving, the necessity of repeating thoracic imaging to document resolution of the radiographic abnormalities is controversial.)
When to Refer	<ul style="list-style-type: none"> Hypoxemia that is worsening Hypoxemia that is not improving at 2-3 month evaluation Hypoxemia that has not resolved or returned to baseline at 3-4 month evaluation 	<ul style="list-style-type: none"> In patients without a history of covid-19 related hospitalization: <ul style="list-style-type: none"> Abnormal pulmonary tests (chest radiograph or pulmonary function studies) Unrevealing dyspnea evaluation (“unexplained dyspnea”) 2-3 months after the diagnosis In patients with a history of covid-19 related hospitalization Not improving or unresolved hypoxemia 	<ul style="list-style-type: none"> Persistent radiographic abnormalities in patients whose symptoms or hypoxemia are either failing to improve or in whom clinical improvement has stalled.



Focused History and Physical:

- Stress, Anxiety, Depressive symptoms
- Negative life effects, Abuse
- Previous gastrointestinal infections

- Post-COVID, patients may have increased perception of pain due to psychological distress and/or inflammatory cell recruitment/activation.
- Psychological stress exacerbates GI symptoms and psychosocial disturbances amplify illness experience and adversely affects health status.

Chronic Abdominal Pain

Functional GI Disorders

Chronic Bloating & Distention

Description

- Chronic abdominal pain is pain that is present for more than three months. It may be present all the time or it may come and go.

- Functional gastrointestinal disorders (FGID), also known as disorders of gut-brain interaction, including irritable bowel syndrome (IBS) and functional dyspepsia.
- FGIDs are not psychiatric disorders, although stress and psychological difficulties can make FGID symptoms worse.

Testing

- CBC and differential CRP levels
- Coeliac disease screening
- Screening for *G. lamblia*

- FGIDs are disorders of function (how the GI tract works), not structural or biochemical abnormalities.
- As a result, x-rays, blood tests and endoscopies can show essentially normal results.

- **If warning signs present:** Labs, endoscopy, imaging
- **Constipation:** Digital rectal exam (DRE), High resolution anorectal manometry (HRAM)
- **Diarrhea:** Check serologies
- **If symptoms persist:** Hydrogen breath tests (HBT)

Treatments

General Measures

- Supportive environment
- Validation of symptoms
- Patient education
- Agree and set realistic goals

Diet and Nutrition

- Avoid dairy for the time being
- Probiotics
- High fiber diet / diet supplements

Diet and Nutrition Related Symptoms

- Institute specific dietary changes
- **If symptoms persist:** Consider empiric therapy with an antibiotic, probiotics, or antispasmodic
- **If symptoms still persist:** treat for an abnormal viscerosomatic reflex or visceral hypersensitivity

Psychological / Behavioral

- Cognitive behavioral therapy
- Hypnotherapy

Psychological / Behavioral

- Beware of eating disorders (CNS, ANS, ENS dysfunction)
- Gut-directed hypnotherapy
- Cognitive behavioral therapy
- Mindfulness-based stress reduction

Pharmacological

- Tricyclic anti-depressants
- Serotonin noradrenergic reuptake inhibitors
- **Step-up therapy:** Gabapentin or Pregabalin

Pharmacological

- Central Neuromodulators

- **Constipation:** Treat empirically or consider referral for biofeedback
- **Diarrhea:** Treat empirically

- There is increasing evidence to support that COVID-19 can cause long-term neuropsychiatric problems, including new symptoms and exacerbation of chronic conditions.
- Comprehensive evaluation is key, including screening and assessment of cognition, sleep, substance use, and functional performance.

- Impact on life varies; some are able to work while others go on disability
- No clear correlation with severity of COVID infection, age, or comorbidities

Symptoms

- Brain Fog, Headache, or Fatigue
- Issues with short-term memory, concentration, word-finding/speech difficulty
- Sleep difficulties

- Adjustment disorder, depression, anxiety, PTSD
- Substance Use Disorders
- Paresthesia
- Dysautonomia

Assessment & Testing

- **Complete History and Physical**
- **Sleep Evaluation**
- **Medical Work up**
 - MRI brain with contrast(if significant cognitive impact or stroke symptoms)
 - EMG/Nerve Conduction Studies (if Paresthesias)
 - EEG (if altered conscious, seizures)
 - Lumbar Puncture (if severe cognitive deterioration)
 - Autonomic Function/Tilt table (if Dysautonomia)

- Screening Tools**
- Patient Health Questionnaire (PHQ-9)
 - Generalized Anxiety Disorder Questionnaire (GAD-7)
 - Montreal-Cognitive Assessment (MOCA) or Self-Administered Gerocognitive Examination (SAGE)
 - PTSD Symptom Scale
 - Insomnia Severity Index
 - Alcohol Use Disorder Identification Test Drug Abuse Screening Test (AUDIT/DAST)

- Blood work**
- CMP, CBC, TSH,
 - Vitamin B12, Vitamin D
 - Hemoglobin A1C (neuropathy)
 - HIV, RPR, Thiamine, Folate (severe cognitive deterioration)

Treatments

- **Supportive care through active listening is key**
- Restoration of sleep / wake cycle
- Optimize nutrition / hydration
- Be aware of any supplement usage
- Encourage physical activity / exercise
- Monitor for substance use / abuse

- Psychotherapy support groups
- Rehabilitation services
- Pharmacologic management should be focused on control and improvement of predominant symptoms and maximize function but caution should be given to polypharmacy and disruption of sleep.

When to Refer

- Refer to PT / OT for weakness, fatigue, inability to complete activities of daily living
- Refer to speech therapy for difficulty with cognitive functions, speech limitations

- Refer to Neurology with abnormal screen results or persistence of symptoms beyond 8 weeks for evaluation and management
- Refer to Psychiatry with abnormal screen results or persistence of symptoms beyond 8 weeks for evaluation and management
- Refer to Neuropsychology or Rehab psychology depending on availability for persistent cognitive deficits

- **Complete History and Physical**
- Rule out inflammatory processes
- Functional assessment: use your PT / OT partners
- Be mindful of weakness and deconditioning other than limbs (e.g. swallowing)
- Electrodiagnostic testing for symptoms not improving to differentiate between focal vs. more diffuse process

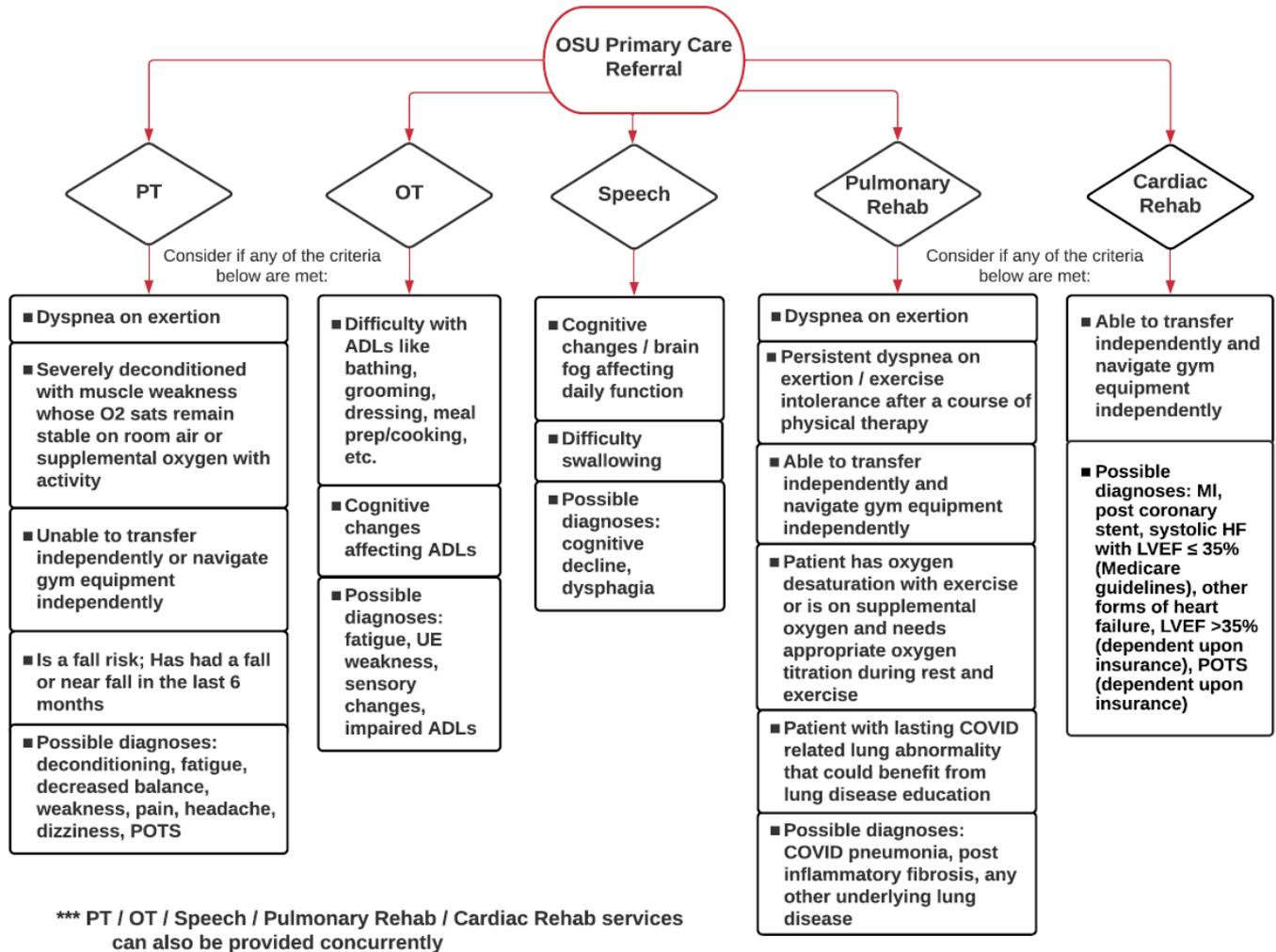
- When to Refer**
- Unable to function in everyday life
 - Uses an assist device related to COVID
 - Risk for falls

Symptoms

- Inability to function in everyday life
- Decreased endurance (fatigue)
- Myalgias
- Arthralgias
- Arthritis pain
- Muscle wasting / weakness
- Deconditioning / Dyspnea on exertion
- Muscle weakness
- Headaches
- Decreased balance / fall risk
- Brain fog / cognitive issues
- Joint pain
- Difficulty swallowing
- Vertigo / dizziness
- Anxiety / depression / PTSD

Well established connections with other post-viral inflammatory autoimmune diseases:

- Parvovirus B19
- Chikungunya
- HIV
- HSV
- Hepatitis A, B, C, etc.



References

- Wang F, et al. (2020) *Med Sci Monit*, 26e928996
- Zhang Z, et al. (2020) *Sci Rep* 10:19649
- Lopez-Leon S, et al; medRxiv.2021 Jan 30:2021.01.27.21250617
- The Writing Committee for the COMEBAC Study Group. Four-Month Clinical Status of a Cohort of Patients After Hospitalization for COVID-19. *JAMA*. 2021;325(15):1525–1534. doi:10.1001/jama.2021.3331
- Gawande, A: The Heroism of Incremental Care. *Annals of Medicine*, 1/5/2017
- Carfi A, Bernabei R, Landi F, for the Gemelli Against COVID-19 Post-Acute Care Study Group. Persistent Symptoms in Patients After Acute COVID-19. *JAMA*. 2020;324(6):603–605. doi:10.1001/jama.2020.12603
- Korterink, J., Devanarayana, N., Rajindrajith, S. et al. Childhood functional abdominal pain: mechanisms and management. *Nat Rev Gastroenterol Hepatol* 12, 159–171 (2015). <https://doi.org/10.1038/nrgastro.2015.21>
- Zhu Y, Wang Z, Zhou Y, et al. (2020) Summary of respiratory rehabilitation and physical therapy guidelines for patients with COVID-19 based on recommendations of World Confederation for Physical Therapy and National Association of Physical Therapy. *J Phys Ther Sci*. 32(8):545-549.
- Tansey CM, Louie M, Loeb M, et al. One-Year Outcomes and Health Care Utilization in Survivors of Severe Acute Respiratory Syndrome. *Arch Intern Med*. 2007;167(12):1312–1320. doi:10.1001/archinte.167.12.1312
- Chaolin Huang*, Lixue Huang*, Yeming Wang*, Xia Li*, Lili Ren*, Xiaoying Gu*, Liang Kang*, Li Guo*, Min Liu*, Xing Zhou, Jianfeng Luo, Zhenghui Huang, Shengjin Tu, Yue Zhao, Li Chen, Decui Xu, Yanping Li, Caihong Li, Lu Peng, Yong Li, Wuxiang Xie, Dan Cui, Lianhan Shang, Guohui Fan, Jiuyang Xu, Geng Wang, Ying Wang, Jingchuan Zhong, Chen Wang, Jianwei Wang†, Dingyu Zhang†, Bin Cao. 6-month consequences of COVID-19 in patients discharged from hospital: a cohort study. *The Lancet*. 2021
- Graham EL, et al; Persistent neurologic symptoms and cognitive dysfunction in non-hospitalized COVID-19 “long haulers.” *Annals of Clinical and Translational Neurology*. 2021
- Outpatient Screening and Management of Depression in Adults. (OSUWMC intranet site): <https://onesource.osumc.edu/sites/ebm/Documents/Guidelines/DepressionOutpt.pdf>
- Nalbandian, A., Sehgal, K., Gupta, A. et al. Post-acute COVID-19 syndrome. *Nat Med* (2021).
- Chopra, V., Flanders, S. A. & O’Malley, M. Sixty-day outcomes among patients hospitalized with COVID-19. *Ann. Intern. Med.* <https://doi.org/10.7326/M20-5661> (2020).
- Carfi, A., Bernabei, R., Landi, F. & Gemelli Against COVID-19 Post-Acute Care Study Group. Persistent symptoms in patients after acute COVID-19. *J. Am. Med. Assoc.* 324, 603–605 (2020).
- Carvalho-Schneider, C. et al. Follow-up of adults with noncritical COVID-19 two months after symptom onset. *Clin. Microbiol. Infect.* 27, 258–263 (2021).
- Arnold, D. T. et al. Patient outcomes after hospitalisation with COVID-19 and implications for follow-up: results from a prospective UK cohort. *Thorax* <https://doi.org/10.1136/thoraxjnl-2020-216086> (2020).
- Moreno-Pérez, O. et al. Post-acute COVID-19 syndrome. Incidence and risk factors: a Mediterranean cohort study. *J. Infect.* <https://doi.org/10.1016/j.jinf.2021.01.004> (2021).
- Huang, C. et al. 6-month consequences of COVID-19 in patients discharged from hospital: a cohort study. *Lancet* 397, 220–232 (2021).
- Garrigues, E. et al. Post-discharge persistent symptoms and health-related quality of life after hospitalization for COVID-19. *J. Infect.* 81, e4–e6 (2020).
- Halpin, S. J. et al. Postdischarge symptoms and rehabilitation needs in survivors of COVID-19 infection: a cross-sectional evaluation. *J. Med. Virol.* 93, 1013–1022 (2021).

Guideline Authors

- | | |
|----------------------------|---------------------|
| • Derrick Herman, MD | • ReNea Owens, PT |
| • Jeffrey Horowitz, MD | • Carson Felkel, MD |
| • James Tita, MD | • Doug Scharre, MD |
| • Edward Levine, MD | • Kevin Johns, MD |
| • Stephen Feagins, MD | • David Kasick, MD |
| • Emmanuel Ofori, MD | • Matt Owens, MD |
| • Alexa Meara, MD | • Susan Hawk, LPC, |
| • John DeWitt, PT, DPT, AT | LMSW |
| • Marci Gerken, PT, MPT | |
| • Matt Owens, MD | |

Guideline Approved

[Approval Date] First Edition.

Disclaimer: Clinical practice guidelines and algorithms at The Ohio State University Wexner Medical Center (OSUWMC) are standards that are intended to provide general guidance to clinicians. Patient choice and clinician judgment must remain central to the selection of diagnostic tests and therapy. OSUWMC’s guidelines and algorithms are reviewed periodically for consistency with new evidence; however, new developments may not be represented.