# 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. Fatigue, arthralgia, brain fog, and shortness of breath (SOB), are just some symptoms described by patients.

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. The most commonly reported symptoms include fatigue, shortness of breath, cough, joint pain and chest pain. Other long-term symptoms include brain fog, depression, muscle aches, headaches, intermittent fever and heart palpitations.

Symptoms should not be minimized. The more serious, but less common, symptoms affect different organs in the body (e.g., inflammation of the heart muscle, lung function and kidney abnormalities, skin rashes, hair loss and neurologic issues, such as smell and taste problems, insomnia and memory issues).

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

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

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

## Signs and Symptoms / Potential Complications

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

# Gastrointestinal



- **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.<br>▪ FGIDs are not psychiatric disorders, although stress and psychological difficulties can make FGID symptoms worse. | |
| **Testing** | ▪ CBC and differential CRP levels<br>▪ Coeliac disease screening<br>▪ Screening for *G. lamblia* | ▪ FGIDs are disorders of function (how the GI tract works), not structural or biochemical abnormalities.<br>▪ As a result, x-rays, blood tests and endoscopies can show essentially normal results. | ▪ **If warning signs present:** Labs, endoscopy, imaging<br>▪ **Constipation:** Digital rectal exam (DRE), High resolution anorectal manometry (HRAM)<br>▪ **Diarrhea:** Check serologies<br>▪ **If symptoms persist:** Hydrogen breath tests (HBT) |
| **Treatments** | **General Measures**<br>▪ Supportive environment<br>▪ Validation of symptoms<br>▪ Patient education<br>▪ Agree and set realistic goals<br><br>**Psychological / Behavioral**<br>▪ Cognitive behavioral therapy<br>▪ Hypnotherapy<br><br>**Pharmacological**<br>▪ Tricyclic anti-depressants<br>▪ Serotonin noradrenergic reuptake inhibitors<br>▪ **Step-up therapy:** Gabapentin or Pregabalin | **Diet and Nutrition**<br>▪ Avoid daily for the time being<br>▪ Probiotics<br>▪ High fiber diet / diet supplements<br><br>**Psychological / Behavioral**<br>▪ Beware of eating disorders (CNS, ANS, ENS dysfunction)<br>▪ Gut-directed hypnotherapy<br>▪ Cognitive behavioral therapy<br>▪ Mindfulness-based stress reduction<br><br>**Pharmacological**<br>▪ Central Neuromodulators | **Diet and Nutrition Related Symptoms**<br>▪ Institute specific dietary changes<br>▪ **If symptoms persist:** Consider empiric therapy with an antibiotic, probiotics, or antispasmodic<br>▪ **If symptoms still persist:** treat for an abnormal viscero-somatic reflex or visceral hypersensitivity<br><br>▪ **Constipation:** Treat empirically or consider referral for biofeedback<br>▪ **Diarrhea:** Treat empirically |

**Alarm features:**
- Weight loss, bleeding and anemia would require additional testing / referral (eConsult)

# Musculoskeletal



- **Complete History and Physical (patient safe to exercise from cardiac perspective)**
- 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

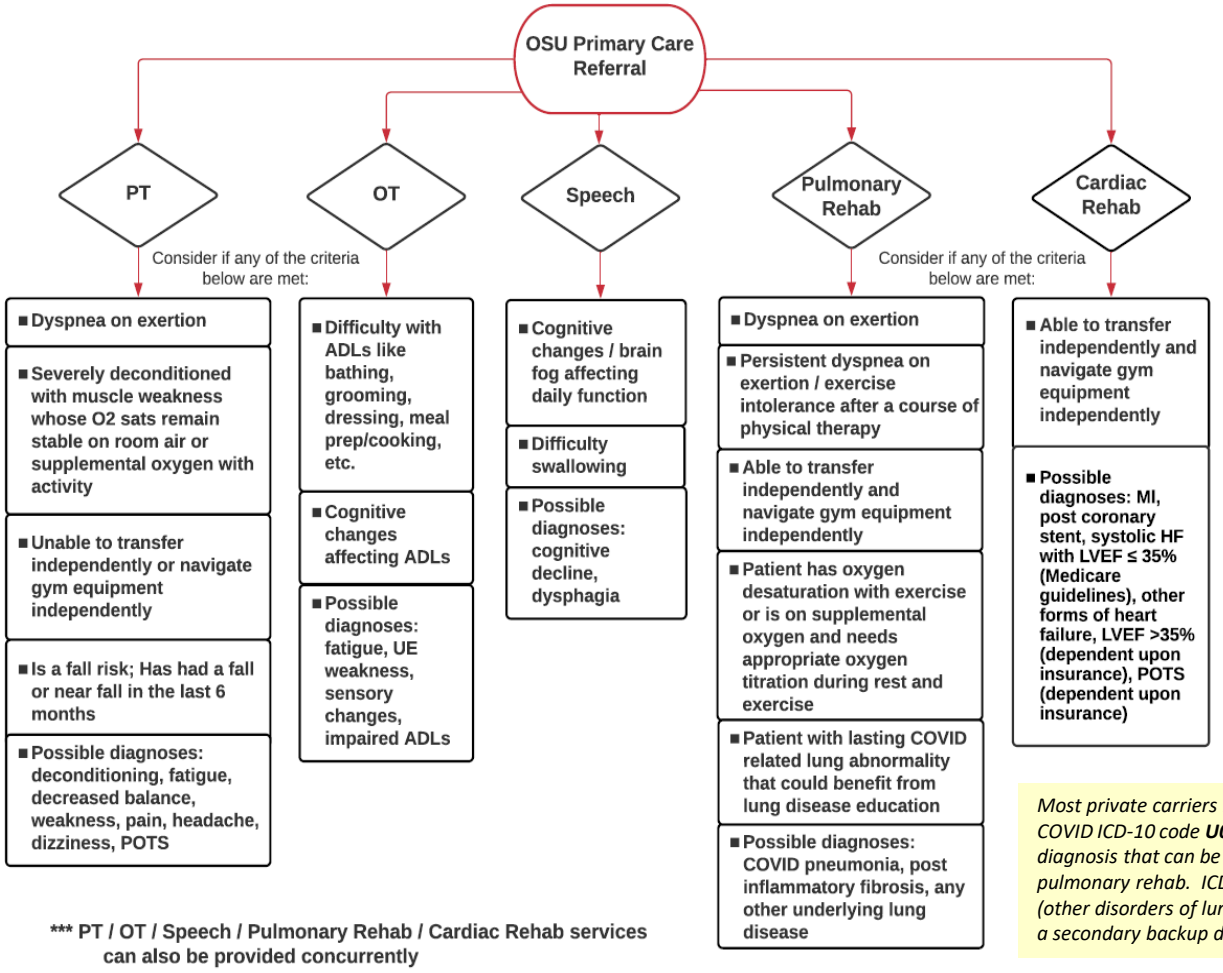
- Unable to function in everyday life
- Uses an assistive device related to COVID-19
- Risk for falls
- Consider referral to **rheumatology** if objective evidence on exam of inflammatory arthritis, concerns for myositis ( i.e., elevated CK and weakness on exam, or abnormal EMG) or other signs of systemic autoimmune diseases

## 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.




*Most private carriers have accepted the COVID ICD-10 code **U07.1** as a diagnosis that can be used for pulmonary rehab. ICD-10 code **J98.4** (other disorders of lung) may be used as a secondary backup diagnosis.*

# Neuropsychiatric



- 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, post traumatic stress disorder (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)
- PC-PTSD-5 Screen / PCL-5 checklist
- Insomnia Severity Index Link
- 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

## Dyspnea

Differential diagnosis:

- Infectious pneumonia
- Organizing pneumonia
- Post-inflammatory pulmonary fibrosis
- Venous thromboembolic disease
- Post-viral syndrome
- Anemia
- Thyroid disease
- Cardiac disease

## Cough

Contributing Factors:

- Transient inflammation of the lower airways with or without bronchial hyperresponsiveness
- Mucus hypersecretion with impaired mucociliary clearance
- Persistent inflammation of the upper airways with or without secretion drainage into the hypopharynx (upper airway cough syndrome)
- Aggravation of concomitant gastroesophageal reflux (GERD) resulting from increased abdominal pressure from coughing.

## Hypoxemia

- 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.
- 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.

## OUTPATIENT EVALUATION (6-12 WEEKS AFTER DIAGNOSIS OR DISCHARGE)

**Dyspnea, Cough and/or Hypoxemia**

**Intake Information:**

- Date of COVID-19 illness
- Hospitalization / ICU Admission
- Treatments
- Oxygen requirements
- Symptoms present (dyspnea, cough, edema)

***Hospitalization, ICU admission*** → *Lower threshold for early referral for patients with severe disease*

- History and Physical Examination
- Pulse oximetry at rest and with exertion
- 6 Minute Walk Test

***NO Hospitalization,*** *Pulmonary referral is always available earlier, if needed*

| Improving hypoxemia and symptoms | No hypoxemia with dyspnea +/- chest pain | Hypoxemia or symptoms NOT improving | Palpitations |
|---|---|---|---|
| Re-evaluate 6-8 Weeks | Echocardiogram | • Pulmonary referral<br>• Chest CT: High resolution and PE protocol (0.6-1 mm cuts)<br>• PFTs<br>• CPET | • EKG<br>• Holter monitor<br>• Tilt table, if possible POTS |

- Cardio referral
- Chest CT; High resolution and PE protocol (0.6-1 mm cuts)
- Cardiac MRI (indication: evaluate myocarditis)
- Trop / BNP
- EKG
- CPET

**Consider pulmonary or cardiac rehabilitation**

# Cardiopulmonary



| | Persistent Dyspnea | Venous Thromboembolic Disease | Hypoxemia | Persistent dyspnea or hypoxia after 3 months of acute PE |
|---|---|---|---|---|
| **Testing** | ▪ High-sensitivity troponin<br>▪ Echocardiogram<br>▪ Chest CT: High resolution and PE protocol (0.67 – 1 mm thickness cuts)<br>▪ Pulse oximetry at rest<br>▪ 6 minute walk (including pulse oximeter evaluation with exertion)<br>▪ Labs: CBC with differential, chem7, LFTs, BNP, TSH with reflex<br>▪ Chest X-Ray<br>▪ Full pulmonary function studies: spirometry, lung volumes, DLCO<br>▪ D-dimer, lower extremity venous ultrasonography<br>▪ ECG +/- transthoracic echocardiogram | ▪ Diagnosis of possible venous thromboembolic disease<br>o D-Dimer<br>o Venous ultrasonography<br>▪ Chest CT: High resolution and PE protocol (0.67 – 1 mm thickness cuts)<br>▪ pulmonary angiography (CT PE study)<br>▪ VQ Scan (if dyspnea not improving after 3 months of acute episode)<br>▪ Echocardiogram (if dyspnea not improving after 3 months of acute episode) | ▪ Pulse oximetry evaluation at rest and with exertion at 2-3 months after diagnosis or discharge<br>▪ Chest X-Ray<br>▪ Chest CT: High resolution and PE protocol (0.67 – 1 mm thickness cuts)<br>▪ Full pulmonary function studies (spirometry, lung volumes, DLCO)<br>▪ 6 minute walk at time of referral (see below) | ▪ Echocardiogram<br>▪ VQ scan<br>▪ Chest X-Ray<br>▪ Right Heart Catheterization, if evidence of CTEPH |
| **Treatment** | ▪ Based on testing results and etiology | ▪ Anticoagulation for 3 months for the acute episode<br>▪ Discussion of benefits and risks of anticoagulation beyond 3 months on a case by case basis | | ▪ Treatment based on RHC results |
| **When to Refer (eConsult)** | Patients without history of COVID-19 related hospitalization:<br>▪ Abnormal pulmonary tests (Chest X-Ray or pulmonary function studies)<br>▪ Unrevealing dyspnea evaluation (“unexplained dyspnea”) 2-3 months after the diagnosis<br><br>Patients with history of COVID-19 related hospitalization<br>▪ Not improving or unresolved hypoxemia | ▪ Not necessary for routine management of acute episodes<br>▪ Dyspnea that is not improving at the conclusion of treatment of the acute episode (3 months) for evaluation for chronic thromboembolic pulmonary hypertension | ▪ Hypoxemia that is worsening<br>▪ Hypoxemia that is not improving at 2-3 month evaluation<br>▪ Hypoxemia that has not resolved or returned to baseline at 3-4 month evaluation | |

# Cardiopulmonary



## Pulmonary

### Persistent Cough

**Testing**

- Chest X-Ray

**Treatment**

*No role for antibiotics*

- Post-infectious cough is self-limited
- Inhaled short acting bronchodilators
  - Inhaled ipratropium
  - Inhaled short acting beta agonists
- Inhaled glucocorticoids if cough adversely affecting quality of life
- Oral glucocorticoids
  - 30-40 mg prednisone tapered over 2-3 weeks
  - Low quality evidence

**Upper airway cough syndrome**

- Antihistamine-decongestant combinations
- Intranasal glucocorticoids
- Intranasal anticholinergics

**GERD**

- H2-antihistamines
- Proton pump inhibitors

**When to Refer (eConsult)**

- Abnormal chest radiograph
- Persistence of cough beyond 8 weeks for evaluation and management of chronic cough

## Cardiovascular

| | Chest pain or chest heaviness at rest or exertion | New onset HF (LVEF < 45%) or Myocarditis | Palpitations |
|---|---|---|---|
| **Testing** | ▪ High-sensitivity troponin<br>▪ Echocardiogram<br>▪ ECG<br>▪ Stress testing<br>▪ Left and/or right heart catheterization, based on symptoms | ▪ Cardiac MRI with contrast (indication: evaluate myocarditis)<br>▪ Right Heart Catheterization<br>▪ VO2 testing, based on symptoms | ▪ High-sensitivity troponin<br>▪ Echocardiogram<br>▪ Holter monitor<br>▪ Tilt table testing, if suspicion for Postural orthostatic tachycardia syndrome (POTS) |
| **Treatment** | ▪ Aspirin, statin, beta-blockers, if new onset CAD<br>▪ Colchicine / Aspirin, if consistent with pericarditis | ▪ Guideline directed therapy for HFrEF | ▪ Based on testing results and etiology |

**When to Refer (eConsult)**

- If symptoms persist after evaluation and clinical concern or high risk individual (e.g., athlete, aviation etc.)
- EP referral for POTS or arrhythmias

## 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* | ▪ Avoid medications previously known to be associated with delirium, such as:<br>○ Benzodiazepines<br>○ Antihistamines, both $H_1$ and $H_2$<br>○ High dose opioids<br>○ Scopolamine<br>○ Other medications with anticholinergic side effects<br>▪ Avoid intra-operative hypotension. Keep mean arterial pressure within 20% of pre-op values |
| *PTSD* | ▪ Consider avoiding ketamine administration |
| *Anxiety* | ▪ Premedication with agents other than benzodiazepines are encouraged. These include:<br>○ Low dose opioids<br>○ Alpha 2 agonists such as: guanfacine or dexmedetomidine |
| **Cardiovascular System** | **Consideration** |
| *Medications* | ▪ No change in ACE-I use is recommended. Follow institutional guidelines regarding pre-op administration<br>▪ Continue aspirin and beta-blockers per institutional guidelines |
| *Chest pain, shortness of breath, exercise intolerance, and palpitations* | ▪ 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:<br>○ ECG to evaluate arrhythmias<br>○ Echocardiography to evaluate biventricular function and pulmonary artery pressures |
| *Intra-operative hypotension* | ▪ Be cognizant of potential need for inotropic agents, especially in patients with right ventricular dysfunction who developed pulmonary fibrosis |
| **Respiratory System** | **Consideration** |
| *Ongoing symptoms* | For continued symptoms of shortness of breath, persistent oxygen requirements, and exercise intolerance:<br>▪ These should be address pre-operatively in a multidisciplinary fashion. Day of surgery evaluation is discouraged unless urgent or emergent. |
| *Fibrosis* | ▪ Consider pressure modes of ventilation<br>▪ Be cognizant of increased pulmonary artery hypertension and right ventricular dysfunction<br>▪ Follow lung protective ventilation guidelines (4-6 ml/kg)<br>▪ Promote good respiratory mechanics. Consider using Sugammadex for neuromuscular blocker reversal<br>▪ Avoid excessive administration of intravenous fluids. "Dry" lungs are happy lungs |
| **Renal System** | **Consideration** |
| *Acute Kidney injury and chronic kidney disease* | ▪ Ensure man arterial pressure within 20% of baseline<br>▪ Avoid excessive administration of intravenous fluids |
| **Hematologic System** | **Consideration** |
| *Thromboembolic Disease* | ▪ Patients with previously described clots should have a plan regarding bridge therapy for systemic anticoagulation<br>▪ Patients should receive perioperative chemical and mechanical prophylaxis<br>▪ Systemic anticoagulation should be restarted as soon as possible after surgery<br>▪ Aspirin should be continued |

**Other**

- 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

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## Guideline Approved

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