Long-Haul COVID: Problems and Opportunities

NY State Commissioner's Grand Rounds October 25, 2021
Abigail Chua, MD, MPH
Assistant Professor, Division of Pulmonary, Critical Care & Sleep Medicine

Stony Brook Medicine
Disclosures

No financial disclosures
Learning Objectives

- Identify the key organ system characteristics of long COVID patients experiencing pulmonary/cardiovascular symptoms.
- Understand the presentation and treatment of pulmonary symptoms in long COVID.
- Identify the management and care approaches for the physical (pulmonary/cardiovascular) symptoms of long COVID.
- Describe the diagnostic, management, and treatment pathways for patients in a post-COVID care clinic, including how patients are referred to/connected with the clinic.
“Victory comes from finding opportunities in problems..”

Sun Tzu
Problem 1: Case Definitions Vary

• Various names in the literature: “long COVID,” “post-COVID syndrome,” “post-acute COVID-19 syndrome,” as well as the research term “post-acute sequelae of SARS-CoV-2 infection” (PASC).
• Heterogenous clinical presentation
• Unknown natural history of disease
Long Haul COVID Can Effect Almost Every Organ System

**Acute Complications of COVID-19**

**Neuropsychiatric**
- Cerebrovascular accident
- Large vessel disease
- Encephalopathy, delirium
- Anosmia, ageusia

**Respiratory**
- Pneumonia
- Hypoxemic respiratory failure, ARDS

**Cardiovascular**
- Arrhythmia
- Myocarditis

**Hematologic, Vascular**
- Coagulopathy
- Thrombotic events

**Renal**
- Acute kidney injury

**Gastrointestinal, Hepatobiliary**
- Diarrhea
- Acute liver injury

**Musculoskeletal**
- Rhabdomyolysis

**Dermatologic**
- Livedo reticularis
- Maculopapular or urticarial rash

**Post-COVID Symptoms, Sequelae**

**Neuropsychiatric**
- Neurocognitive deficits
- Mood changes
- Sensory & motor deficits
- Chronic fatigue and sleep disruption

**Respiratory**
- Persistent dyspnea
- Chronic cough

**Cardiovascular**
- Chest pain
- Palpitations

**Hematologic, Vascular**
- Persistent or recurrent thrombosis

**Renal**
- Chronic kidney disease

**Gastrointestinal, Hepatobiliary**
- Persistent liver dysfunction

**Musculoskeletal**
- Muscle wasting
- Weakness
- Deconditioning

**Dermatologic**
- Hair loss

---

### Type, proportion, and duration of persistent COVID-19 symptoms*

<table>
<thead>
<tr>
<th>Persistent symptom</th>
<th>Proportion of patients affected by symptom</th>
<th>Approximate time to symptom resolution</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Common physical symptoms</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fatigue</td>
<td>15 to 87%(^{1.2.6.9.14})</td>
<td>3 months or longer</td>
</tr>
<tr>
<td>Dyspnea</td>
<td>10 to 71%(^{1.2.6.9.14})</td>
<td>2 to 3 months or longer</td>
</tr>
<tr>
<td>Chest discomfort</td>
<td>12 to 44%(^{1.2})</td>
<td>2 to 3 months</td>
</tr>
<tr>
<td>Cough</td>
<td>17 to 34%(^{1.2.9.12})</td>
<td>2 to 3 months or longer</td>
</tr>
<tr>
<td>Anosmia</td>
<td>10 to 13%(^{1.3.5.9.11})</td>
<td>1 month, rarely longer</td>
</tr>
<tr>
<td><strong>Less common physical symptoms</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Joint pain, headache, sicca syndrome, rhinitis, dysgeusia, poor appetite, dizziness, vertigo, myalgias, insomnia, alopecia, sweating, and diarrhea</td>
<td>&lt;10%(^{1.2.8.9.11})</td>
<td>Unknown (likely weeks to months)</td>
</tr>
<tr>
<td><strong>Psychologic and neurocognitive</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Post-traumatic stress disorder</td>
<td>7 to 24%(^{6.10.14})</td>
<td>6 weeks to 3 months or longer</td>
</tr>
<tr>
<td>Impaired memory</td>
<td>18 to 21%(^{6.15})</td>
<td>weeks to months</td>
</tr>
<tr>
<td>Poor concentration</td>
<td>16%(^{6})</td>
<td>Weeks to months</td>
</tr>
<tr>
<td>Anxiety/depression</td>
<td>22 to 23%(^{2.7.8.10.12.13.14})</td>
<td>Weeks to months</td>
</tr>
<tr>
<td>Reduction in quality of life</td>
<td>&gt;50%(^{8})</td>
<td>Unknown (likely weeks to months)</td>
</tr>
</tbody>
</table>


* These data are derived from an earlier period in the pandemic; information on patient recovery and persistent symptoms is evolving, and these figures may change as longer-term data emerge.

† More than a third of patients with COVID-19 experience more than one persistent symptom.

Δ Time course for recovery varies depending on premorbid risk factors and illness severity and may be shorter or longer than that listed. Hospitalized patients, and in particular critically ill patients, are more likely to have a more protracted course than

Mikkelsen ME, Abramoff B. COVID-19: Evaluation and management of adults following acute viral illnessIn: UpToDate, Post TW (Ed), UpToDate, Waltham, MA. (Accessed on October 22, 2021.)
Opportunity 1: Recognition of the need for case definition flexibility

CDC Defines Post-Covid Conditions:
“We use post-COVID conditions as an umbrella term for the wide range of health consequences that are present four or more weeks after infection with SARS-CoV-2. The time frame of four or more weeks provides a rough approximation of effects that occur beyond the acute period, but the timeframe might change as we learn more.”
Problem 2: Case presentation and severity of post-covid symptoms may not be related to severity of initial illness

• Despite early data suggesting a shorter recovery (eg, two weeks) for those with mild disease and a longer recovery (eg, two to three months or longer) for those with more severe disease, more recent studies have found that this does not always hold true.

• In addition three separate recent studies have found that while many patients have persistent symptoms 4 weeks after discharge, many of these patients have no objective evidence of physiologic or radiographic abnormalities

• The preponderance of published studies have been in patients who have been hospitalized with COVID- and there is a dearth of data on long term outcomes of non-hospitalized patients with persistent symptoms
In discharged patients post COVID-19, relatively normal oxygen saturations can be demonstrated. However, with PFT testing, the most common abnormality of lung function is impairment of diffusion capacity.
Opportunity 2: Our understanding of medicine and pulmonary physiology has advanced in the last two years

Opportunity 3: Our understanding of medicine and pulmonary physiology has advanced in the last two years

Normal ventilatory responses:
- Respiratory rate increases throughout exercise
- Tidal volume at least doubles over baseline
- Tidal volume reaches 50 to 60% of FVC or 70% of IC
- Breathing reserve 30 to 40%
- VD/VT <0.3 to 0.4 at rest and 0.2 with exercise

Normal cardiovascular responses:
- Heart rate increases linearly with VO₂ up to >90% predicted maximum
- BP increases gradually during exercise, but increase in diastolic pressure <20 mmHg
- Peak oxygen pulse (VO₂/HR) >80% predicted and does not plateau early
- AT occurs at >40% of predicted maximal VO₂
- Nadir of VE/VCO₂ is <34 or slope of VE versus VCO₂ <32
- No evidence of arrhythmia or ischemic changes on ECG

Normal gas exchange responses:
- SaO₂ >96% at rest and minimal or no decrease with exercise
- A-a O₂ difference with exercise <35

Treatment possibility 1: What do we do with our Corticosteroids?

<table>
<thead>
<tr>
<th>Lung Function</th>
<th>Before Treatment</th>
<th>After Treatment</th>
<th>Mean Difference (95% CI)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>FVC, L</td>
<td>3.07 ± 1.12</td>
<td>3.36 ± 1.11</td>
<td>0.42 (0.28–0.56)</td>
<td>0.014</td>
</tr>
<tr>
<td>FVC, %</td>
<td>86.8 ± 18.5</td>
<td>99.2 ± 19.1</td>
<td>9.63 (4.49–14.7)</td>
<td>0.004</td>
</tr>
<tr>
<td>TLCO, SI</td>
<td>5.56 ± 2.56</td>
<td>7.05 ± 2.42</td>
<td>1.72 (1.18–2.25)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>TLCO, %</td>
<td>59.7 ± 21.1</td>
<td>82.6 ± 15.7</td>
<td>22.3 (14.1–32.5)</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

Improvement Is Possible

Treatment possibility 2: Antifibrotics

# Data Collection Ongoing: Antifibrotics

<table>
<thead>
<tr>
<th>Trial</th>
<th>Location and Status</th>
</tr>
</thead>
<tbody>
<tr>
<td>Phase-II Randomized Clinical Trial to Evaluate the Effect of Pirfenidone Compared to Placebo in Post-COVID19 Pulmonary Fibrosis</td>
<td>Completed Spain</td>
</tr>
<tr>
<td>Pirfenidone vs. Nintedanib for Fibrotic Lung Disease After Coronavirus Disease-19 Pneumonia (PINCER) -</td>
<td>Ongoing since March 2021 India</td>
</tr>
<tr>
<td>BIO 300 Oral Suspension in Discharged COVID-19 Patients (1500mg Genistein QD for 12 weeks)</td>
<td>University of Colorado Anschutz Medical Campus Aurora, Colorado NYU Langone Health New York, New York, United States Houston Methodist Research Institute Houston, Texas, United States</td>
</tr>
<tr>
<td>Use of Nintedanib in Slowing Lung Fibrosis in Patients With Pulmonary Infiltrates Related to COVID-19</td>
<td>Mount Sinai Beth Israel New York, New York, United States Icahn School of Medicine at Mount Sin</td>
</tr>
</tbody>
</table>
Treatment possibility 3: Pulmonary Rehabilitation

# Treatment Possibility 4: Lung Transplantation

Considerations Before Transplantation in Outpatients With Post-COVID Fibrosis

<table>
<thead>
<tr>
<th>Consideration</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Assess for evidence of preexisting ILD</strong></td>
</tr>
<tr>
<td>- History: Symptoms before COVID-19 infection, family history of ILD, connective tissue disease history or signs/symptoms, occupational or other exposures associated with chronic hypersensitivity pneumonitis</td>
</tr>
<tr>
<td><strong>Review available chest imaging from before COVID-19 infection</strong></td>
</tr>
<tr>
<td><strong>Consider connective tissue disease testing</strong></td>
</tr>
<tr>
<td><strong>Obtain baseline PFTs, 6MWT, and imaging, and monitor serially</strong></td>
</tr>
<tr>
<td><strong>Consider a trial of corticosteroids</strong></td>
</tr>
<tr>
<td><strong>Consider anti-fibrotic (pirfenidone or nintedanib) if evidence of progression</strong></td>
</tr>
<tr>
<td><strong>Refer for pulmonary rehabilitation</strong></td>
</tr>
<tr>
<td><strong>Transplantation is reserved for severe debility failing to improve with time, medical therapy, and rehabilitation or progressive disease</strong></td>
</tr>
</tbody>
</table>
Treatment Possibility 4: Lung Transplantation = Last Resort

Does the patient have traditional contraindications to transplant?
- Recent or active malignancy
- BMI < 17 or > 35
- Age > 65 (> 70 in exceptionally fit patients)
- Active substance abuse
- Inadequate social support
- Inability to comply with complex regimen
- Inadequate financial resources for transplant
- Highly virulent bacterial, mycobacterial or fungal pathogens
- Multi-organ dysfunction

Has the patient had appropriate medical therapy and adequate time to recover?

Has the patient cleared their COVID infection?

Is the patient strong enough for transplant?

Continue medical therapy
- If deemed unrecoverable, discuss goals of care and consider palliation

Continue medical therapy and allow more time for recovery

Proceed with lung transplant evaluation

Preliminary Data: Lung Transplantation

- A query of the United Network for Organ Sharing (UNOS) showed that as of April 30, 2021, only 78 lung transplants carrying a recipient diagnosis of COVID-19 had been performed in the United States: 50 for COVID ARDS and 28 for COVID Fibrosis.

- As of April 23, 2021, the Eurotransplant consortium (responsible for organ allocation in Austria, Belgium, Croatia, Germany, Hungary, Luxemburg, the Netherlands, and Slovenia) reported only 21 patients undergoing transplantation for a diagnosis of COVID-19.

- Very little data exists on patients post-transplant, however one study of 54 patients transplanted at UT Southwestern demonstrated that a significant proportion of COVID-19 survivors suffer persistent allo-graft injury.
Problem 3: Diagnosis is made difficult with varying risk factors, varying natural history of disease and the

- The development of long COVID has been identified with more frequency in patients with higher body mass index (BMI), older age and Black, Asian and Minority ethnic groups

- The post-acute COVID-19 Chinese study demonstrated that women were more likely to experience fatigue and anxiety/depression at 6 months follow-up


Tracking Social Determinants of Health During the COVID-19 Pandemic Published: Oct 21, 2021 Kaiser Family Foundation
Opportunity 3: Diagnosis is made easier with well coordinated integrated primary and subspecialty care

Stony Brook University Hospital  Post-COVID Clinic

- Opened November 2020
- Offers comprehensive follow up and evaluation of patients recovering from COVID 19
- 500 patients have been seen by the program
- Patients are seen initially at the clinic and then referred for subspecialty care to ensure integration
Stony Brook University Hospital Post-COVID Clinic

Specialty Services Offered in the Post-COVID Clinic:
• Cardiology
• Infectious Disease
• Internal Medicine
• Mental Health Services, including Stony Brook Medicine's COVID-19 Support Group
• Nephrology
• Neurology
• Pulmonary
• Vascular Care

Diagnostic Services offered:
• Pulmonary Function Testing
• Cardiopulmonary Exercise Testing
• 6 Minute Walk Testing
• Stress Test Lab
• Echocardiography
• Imaging
• Laboratory Services

Sritha Rajupet, MD MPH
Family and Preventive Medicine

Jenna Palladino PsyD
How To Make An Appointment

Post COVID-19 Clinic Appointment Request

Stony Brook Medicine Advanced Specialty Care
500 Commack Road, Suite 203
Commack, NY 11725
(631) 638-0597

Please provide the information requested below and we will be in touch to help schedule your appointment. We try our best to respond within 16 business hours. If you are having urgent symptoms, please speak with your physician and go to the nearest emergency room for care.

1. FIRST NAME *
   Enter your First Name exactly as it appears on your license.

2. LAST NAME *
   Enter your Last Name exactly as it appears on your license.

(631) 638-0597
Advanced Specialty Care
500 Commack Road
Suite 203
Commack, NY 11725