Persistent COVID and a Return to Sport.

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Abstract

Coronavirus disease (COVID) has become a global pandemic that has widely impacted athletes at all levels of competition. For many athletes infected with COVID, the course is mild or asymptomatic, and most athletes are able to return to play in a matter of weeks. However, 10% to 15% of people infected with COVID will go on to have prolonged COVID symptoms that last for weeks to months and impact their ability to function and exercise. Not much is known about why certain people become "COVID long-haulers," nor are there any predictive tools to predetermine who may have prolonged symptoms. However, many athletes will suffer from prolonged symptoms that may require further evaluation and may prolong their return to exercise, training, and competition. The purpose of this article is to discuss a framework in which sports medicine and primary care physicians can use to evaluate COVID long-haulers and help them return to sport.

Introduction

SARS-CoV-2 was identified in 2019 as a respiratory coronavirus that causes the coronavirus disease (COVID). COVID has become a global pandemic that has widely impacted athletes at all levels of competition (1–4). For many athletes infected with COVID, the course is mild or asymptomatic and most athletes are able to return to play in a matter of weeks. However, 10% to 15% of people infected with COVID will go on to have prolonged COVID symptoms that last for weeks to months and impact their ability to function and exercise. Not much is known about why certain people become "COVID long-haulers," nor are there any predictive tools to predetermine who may have prolonged symptoms (5). However, many athletes will suffer from prolonged symptoms that may require further evaluation and may prolong their return to exercise, training, and competition. The purpose of this article is to discuss a framework in which sports medicine physicians and primary care physicians can use to evaluate COVID long-haulers and help them return to sport.

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What Is the COVID Long-Haul?

Mayo Clinic defines COVID long-haulers as patients with symptoms attributed to SARS-CoV-2 infection for four or more weeks after positive COVID polymerase chain reaction (PCR) or symptomatic start of a clinically diagnosed SARS-CoV-2 infection (1). The Centers for Disease Control (CDC) uses the term "postacute COVID syndrome" to describe health issues that persist more than 4 wk after a person is first infected with SARS-CoV-2 (6). Others have described it as "not recovering [for] several weeks or months following the start of symptoms that were suggestive of COVID, whether you were tested or not" (7). Raveendran et al. (8) proposed a diagnostic criterion involving a positive COVID test (or positive serology), history of a COVID symptom cluster, and appropriate duration of symptoms (>4 weeks). Whatever definition is used, symptoms that linger or last longer than 4 wk are consistent with persistent COVID. The most common symptoms of those suffering from prolonged COVID is profound fatigue, while others may have a range of other symptoms to include muscle and body aches, chest pressure, shortness of breath, cough, palpitations, brain fog, and/or other neurological symptoms. A commonly described feature of the prolonged symptom is their relapsing, remitting nature (7).

It is unclear exactly which patients will develop prolonged COVID symptoms; however, several studies have found that women are more likely to develop this than men (1,4). Patients with more than five symptoms in the acute phase of COVID infection also are more likely to develop prolonged symptoms (9). Other factors found associated with patients who develop prolonged symptoms include age between 45 and 60 years, normal body mass index (BMI), and White race (1,2). Of note, a nature study found 52% of young adults between the age of 16 and 30 years who had mild to moderate COVID symptoms treated at home ended up with persistent symptoms (10).

The exact mechanism of prolonged COVID symptoms is unclear; however, there are several theories. Two of the more common theories are inflammatory or immunologic (11,12). These inflammatory or immune responses can occur in a variety of end organs, including the brain, lungs, heart, endothelial system, muscles, gut, and nervous system, which lead to the symptoms. One proposed mechanism for prolonged COVID symptoms in some patients is perhaps immunologic reactivation of

latent Epstein-Barr virus, which may present very similarly to myalgic enchaphilitis/chronic fatigue syndrome (13).

Approach to Athlete

The first step in the approach to the athlete with possible prolonged COVID is to take a detailed history and perform a clinical examination focusing on timeline of onset, duration and severity of symptoms, primary systems involved, and extent of functional limitation. In patients with suggestive symptoms without a diagnosis of COVID, a positive antibody test can help confirm the diagnosis. However, antibody levels may wane over time, so a negative antibody test does not definitely rule out prolonged COVID.

While it is helpful to consider the effect of the symptoms to the entirety of the patient, the evaluation of the patient with prolonged COVID is primarily symptom and organ system driven (Table 1). The symptoms of prolonged COVID can be divided into different categories to better direct evaluation and testing. The macro view of the categories is persistent fatigue, cardiorespiratory, and neuropsychiatric (8). Subcategorization by organ system may further help the evaluation process.

As far as diagnostic testing goes, most standard tests in those with persistent COVID, such as chest radiographs, spirometry, echocardiogram, and autonomic reflex testing turn up normal or nondiagnostic (14). However, using a more selective and targeted testing pattern can improve diagnostic yield. Suggested laboratory tests include complete blood count, complete metabolic panel, creatine kinase, C-reactive protein, brain naturietic peptide, and ferritin. These laboratory tests would assess for other potential causes of fatigue, dyspnea, or existing underlying medical condition such as anemia, myocarditis, myositis, or iron deficiency. Additional standard studies may include a chest radiograph and an electrocardiogram to assess for cardiac or pulmonary pathology (15).

Treatments Available

The Mayo Clinic has developed a multidisciplinary clinic to provide comprehensive care to patients with persistent COVID consisting of physical/occupational therapy, brain rehabilitation, reestablishing self-care routines, and psychosocial-based treatment (1). When it comes to prolonged COVID symptoms in athletes, this team should be expanded to include the sports medicine physician, athletic trainer, and psychologist (in the appropriate setting).

Table 1.
Target approach to evaluation/treatment of post-COVID syndrome.

Category	Symptoms	Possible Causes	Evaluation	Treatment[a]
Fatigue	Profound fatigue	Anemia, hypothyroid, postviral effects, relative hypoxia, post viral cardiomyopathy, inflammatory syndrome,	CBC, TSH, PO2, ECG, echocardiogram, chest X-ray, CRP	Graded exercise, CBT, SSRI/SNRI, nutrition, sleep hygiene, stress management
Cardiopulmonary				
Cardiac	Chest pain, palpitations, dyspnea on exertion	Myocarditis, cardiomyopathy, pericarditis, endocarditis	Chest X-ray, ECG, echocardiogram, CRP, (+/−) cardiac MR	As indicated by cardiac testing, thromboprophylaxis
Pulmonary	Cough, shortness of breath, chest pain	Pneumonia, pneumonitis, pulmonary embolus	Chest X-ray, CT chest, CT pulmonary angiogram, D-dimer, CRP	Beta agonists, PPIs, pulse oximetry monitoring, pulmonary rehab
Neuro/Psych				
Neurologic	Headache, dizziness, brain fog	Encephalitis, ischemic stroke, seizures, cranial neuropathy	MR or CT brain, EEG, lumbar puncture, neuropsychological testing	Aerobic exercise, focus on nutrition, sleep, consider fish oil supplement
Psychologic	Low mood, hopelessness, anxiety, insomnia	Depression, anxiety, posttraumatic stress response	PHQ9, GAD7, psychological evaluation	CBT, SSRI/SNRI, melatonin (if needed for sleep)
Other				
Gastrointestinal	Abdominal pain, diarrhea, constipation, vomiting	Post-COVID sequelae, medication induced	CBC, abdominal radiograph, stool studies	Ondansetron, loperamide, oral hydration
Musculoskeletal	Myalgias, weakness, arthralgia	Myopathy, electrolyte imbalance, inflammatory arthralgia, prolonged inactivity	CK, CMP, CRP, joint aspiration	NSAIDs, consider steroid taper for recalcitrant symptoms, aquatherapy
Dermatologic	Vesicular, maculopapular, urticarial, or vasculitis lesions on extremities	Endothelial dysfunction, complement activation, coagulopathy	CBC, CRP, possible biopsy	As directed by dermatologic testing

[a]Not evidence based.

CK, creatine kinase; CMP, comprehensive metabolic panel; CRP, C-reactive protein; NSAIDs, Non-steroidal anti-inflammatory drugs.

Symptom-Based Approach

- Fatigue: The fatigue seen in COVID long-haulers is like chronic fatigue syndrome seen in SARS, MERS, and community-acquired pneumonia. There has been controversy about the use of graded exercise in chronic fatigue, therefore exercise in these patients should be introduced gradually, performed prudently, and stopped if any fever, breathlessness, or muscle aches develop (7). Further, some athletes will develop profound postexertional fatigue like that seen in chronic fatigue syndrome or fibromyalgia. When this postexertional fatigue flares, it can be quite extreme. This is especially important as consideration is given to athletes returning to sport specific activities. Cognitive behavioral therapy (CBT) may have a role in the treatment of post COVID fatigue. This CBT is much like is used for concussion or postconcussion syndrome in sports settings. CBT has positive effects on fatigue levels, work and social adjustment, depression, anxiety, and postexertional malaise (16). While no specific pharmacologic treatments exist specifically for post-COVID fatigue, focusing on symptomatic treatment of the common postviral fatigue symptoms (physical pain, recurrent headaches, malaise, cognitive impairment, unrefreshing sleep, recurrent sore throats, and lymphadenopathy) can be helpful (17). Medications to treat these symptoms to include selective serotonin reuptake inhibitors (SSRIs), serotonin and norepinephrine reuptake inhibitors (SNRIs), melatonin to assist with mood, energy and sleep may be useful. Further, attention to nutrition, sleep hygiene, and stress management should be addressed. Athletes with poor sleep, nutrition, or stress management will continue to stay in a "stressed" inflammatory state, which may worsen symptoms and delay recovery.
- Cardiopulmonary symptoms: the main cardiopulmonary symptoms seen in COVID and in post-COVID include cough, shortness of breath, chest pain, and dyspnea on exertion.
  - Chest pain should be worked up as usual with a history, risk factor assessment, and physical examination. Myocarditis, pericarditis, myocardial infarction, dysrhythmias, and pulmonary embolus can be cardiopulmonary complications in young otherwise healthy patients several weeks after COVID infections. Therefore, a high index of suspicion for these conditions in required and diagnostic testing should be employed in patients with these symptoms. Further testing may include echocardiogram, cardiac magnetic resonance (MR), and chest computed tomography (CT) to assess for cardiomyopathy, myocarditis or underlying cardiac or pulmonary pathology. Nonathlete patients with myocarditis or pericarditis should limit vigorous cardiovascular exercise for 3 months, while due to the vigorous nature of practice and competition, athletes may need to wait 3 to 6 months with specialist follow-up before a return to full sports activities. Although it is unclear how long patients remain hypercoagulable after COVID, higher risk patients who have been hospitalized should have thromboprophylaxis extended for at least 10 d (7).
  - Pulmonary symptoms: coughing and breathlessness seen in persistent COVID is best managed with simple breathing control exercises to normalize breathing patterns and increase respiratory muscle efficiency and medication when appropriate, such as a PPIs for reflux symptoms and short acting beta agonists for wheezing or persistent cough. Pulse oximeters are useful for monitoring objective oxygen level when patients are having subjective respiratory symptoms, which may help reduce breathing-related anxiety in patients. Pulmonary rehabilitation is suggested for those who had significant respiratory illness, required oxygen, or had a prolonged hospital stay (7).
  - Dyspnea: The severity of dyspnea should be assessed. Mild dyspnea would include those patients with a respiratory rate <24, pulse oximetry >95%, and no oxygen requirement. Moderate dyspnea includes respiratory rate >24, pulse oximetry between 92% and 95%, with or without oxygen need. Severe dyspnea is demonstrated by an inability to maintain pulse oximetry >92% or moderate dyspnea that is decompensating. Mild dyspnea can be observed with follow-up within 48 h. Moderate dyspnea should be evaluated with complete blood count, B-type natriuretic peptide, chest radiograph, electrocardiogram, and limited echocardiogram. Severe dyspnea should be referred for emergency evaluation (7). It is important to note that dyspnea following COVID can persist for some time, therefore it may be prudent to delay extensive dyspnea work-up until it has persisted for 3 months, if it is getting worse, or if patient had preexisting underlying lung disease prior to infection (18).
- Neuropsychologic: Nonspecific neurological symptoms, including headaches, dizziness, and cognitive blunting should be treated with supportive management with symptom monitoring. Rarer, but serious, complications of persistent COVID include stroke, seizures, encephalitis, and cranial neuropathies. These patients should be referred and comanaged with a neurologist and imaging, such as CT or MR may be indicated. For more cognitive symptoms, further neuropsychological testing and evaluation may be needed (7).
- Mental Health: 20% to 50% of patients may develop symptoms of depression, anxiety, and insomnia post-COVID (19). Mental health referral for general therapy/psychology or CBT is recommended (7). Medications to consider for patients with persistent mental health symptoms following COVID include SSRIs and SNRIs for the treatment of anxiety and depressive symptoms. Sleep aids such as melatonin may be considered for persistent insomnia.

For those athletes with persistent COVID symptoms, who have not been vaccinated, as many as 30% to 40% of those

Table 2.
Return to sports after persistent COVID.

Degree of Symptoms	Level of Exercise
Recovery from mild symptoms	1 wk of flexibility/mobility before beginning graduated return to exercise
Persistent mild symptoms	Start with low intensity exercise such as walking, allow symptoms to guide duration, avoid high intensity exercise Once able to complete 20 min of walking without increase of symptoms may progress activity.
Persistent symptoms	Limit activity to mild to moderate (60% of max) until 2 to 3 wk after symptoms resolve then may progress activity
Patients with severe symptoms that required oxygen or cardiac evaluation	Need respiratory and/or cardiac clearance before beginning stage 1 exercise

Modified from the Stanford-Hall Consensus statement for post-COVID rehabilitation.

Barker-Davies RM, O'Sullivan O, Senaratne KPP, *et al.* The Stanford Hall Consensus Statement for Post-COVID Rehabilitation. *Br J Sports Med*. 2020; 54 (16). doi: 10.1136/bjsports-2020-102596.

who receive the vaccine have had improvements in some or all their symptoms. Although the mechanism for this is unclear, it is believed that the vaccine may help the body fight off residual virus, may decrease adverse immune response, or may serve to reset the immune system. Either way, vaccination should be considered in those with persistent post COVID symptoms (20).

Return to Play

Return to play guidelines for short-term, limited COVID have been published and adopted by many different sporting organizations (7,21,22). Guidelines for return to play in athletes have been suggested and take into consideration the risks of transmission, potential for symptomatic worsening, and possible myocarditis associated with COVID (23–26). Throughout the pandemic, individuals have returned to exercise after recovery from COVID and a gradual return to sport has occurred at all levels of competition (27–29). Most return-to-sport guidelines are based on expert opinion, developed for team sports, and have been targeted at youth, high school, collegiate, or professional athletes. However, little is known about the optimal return-to-play following prolonged COVID in athletes.

The Stanford-Hall Statement may serve as a good template for return to play in athletes with prolonged COVID (18) (Table 2). Those who had cardiopulmonary symptoms, or those who demonstrate any exercise intolerance with return to training, will require cardiac evaluation (electrocardiogram, troponin, echocardiogram) before resuming exercise. It is recommended that for those who had persistent symptoms to limit activity to 60% of maximum heart rate for 2 to 3 wk after symptoms resolve. Once completion of the 2- to 3-wk submaximal aerobic period, a graduated return to activity may commence. This can follow the framework of the *BJSM* suggested return to sport progression (30).

Conclusion

Although most athletes are younger and healthier than the general population, they are still susceptible to the SARS CoV-2 virus and 10% may even develop prolonged COVID (long-hauler) syndrome. It is important to use a categorical, symptom-based, organ-specific focus in the evaluation to direct a targeted approach to pathology so that potential treatments can be recommended. Fatigue and cardiopulmonary complaints are the main limiters for return to exercise. Exercise may be resumed once symptoms have decreased in a graduated process. More research is needed to direct an evidence-based approach to return to play following prolonged COVID.

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