

# COMMENTARY

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## Recovering Coronavirus Disease Patients in the Active Duty Military Population: A Review of Current Evidence and Special Considerations for Uniformed Providers

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**ABSTRACT** Patients acutely infected by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) coronavirus disease (COVID-19) may continue to have symptoms well beyond 2 weeks. The range of symptoms and physiological sequelae can impact medical readiness even in a relatively young and healthy cohort of service members. It is important to monitor, document, and investigate symptoms from all service members recovering from COVID-19. Military medicine must be prepared to support and manage cases of patients who are recovered from acute COVID-19 but are suffering from post-COVID-19 complications.

### INTRODUCTION

Emerging data indicate patients acutely infected by severe acute respiratory syndrome—coronavirus 2 (SARS-CoV-2), also referred to as coronavirus disease 2019 (COVID-19), may continue to have sequelae that last for many months after resolution of their initial infection. These can include simply a prolonged recovery from their acute illness or symptoms that present after they have fully recovered. Persistent signs and symptoms after COVID-19 recovery are variable and can include effects on nearly all body systems. Two notable exceptions include gastrointestinal and renal: during the acute phase of COVID-19 infection, patients can experience anorexia, nausea, vomiting, and diarrhea, and acute kidney injury can occur; however, the presence of these sequelae in the convalescent period is not well described.

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Long-term sequelae of other infectious diseases are well described and include enteric pathogens, Lyme disease, mononucleosis, and various other viral infections. Several aspects of COVID-19 recovery have manifested similarly to the SARS-CoV-1 outbreak in 2003. There is a possibility that long-term outcomes may be similar. Ngai et al. found that 2 years after their acute illness, 1 in 2 SARS survivors had poorer exercise capacity compared to those who never had the disease. Only 78% of SARS patients were able to return to full-time work 1 year after infection.<sup>1</sup> Lam et al. found that 40% of people recovering from SARS still had chronic fatigue syndrome 3.5 years after being diagnosed. A post-viral chronic fatigue syndrome was associated with SARS, but it was unclear if symptoms were because of reactivation of a persistent infection, reinfection, or infection with another virus or bacteria during the same period.<sup>2</sup>

Individuals who suffered severe COVID-19 requiring hospitalization are most notably affected by these post-viral symptoms, but physiologic sequelae have also been reported in patients with mild or moderate disease. To date, over 150,000 DoD service members have recovered or are recovering from acute COVID-19.<sup>3</sup> We present a review of persistent symptoms in patients who have recovered from acute COVID-19 infection, grouped according to body system. We also discuss the unique impact on the active duty military population.

### PROLONGED RECOVERY FROM COVID-19

Many cases of mild or moderate COVID-19 acute infection have resulted in an extended recovery period lasting weeks or months. Anecdotally, at the time of this writing, we have

encountered cases with persistent chest pain, dyspnea and fatigue, and recurrent respiratory symptoms. The CDC conducted a multi-state phone survey involving 274 recovering COVID-19 patients 2-3 weeks after their initial diagnosis. The most common symptoms were fatigue, cough, and headache, reported by 71%, 61%, and 61% of the respondents, respectively. Twenty-six percent of adults aged 18-34 years, and 32% of adults aged 35-49 years had not yet returned to their normal state of health at a median of 16 days after diagnosis.<sup>4</sup> An Italian longitudinal study evaluating 143 patients between 19 and 84 years of age (median 56.5 years) who were initially hospitalized for COVID-19 found that 32% had one or two lingering symptoms and 55% had three or more symptoms 2 months after discharge. A high proportion of individuals still reported fatigue (53.1%), dyspnea (43.4%), joint pain, (27.3%), and chest pain (21.7%). A diminished quality of life was observed in 44.1% of patients.<sup>5</sup> A full range of symptoms that can be experienced in post-acute period are presented in (Table S1).

### NEUROLOGIC COMPLICATIONS

COVID-19-related neurological effects include anosmia, headaches, delirium, encephalitis, and strokes.<sup>6,7</sup> Patterson et al. from University College London reported neurological symptoms in 43 COVID-19 positive patients. The authors identified 10 cases of transient encephalopathy with delirium, 12 cases of encephalitis, 8 cases of stroke, and 8 others with nerve damage, primarily from Guillain-Barré syndrome. Nine of 12 cases with encephalitic conditions were diagnosed with acute disseminated encephalomyelitis, a rare entity typically seen in children and triggered by viral infections.<sup>6</sup> Lu et al. conducted a prospective study utilizing diffusion tensor imaging of 60 recovered COVID-19 patients. In the recovery phase, 55% of patients had neurological symptoms, and imaging revealed possible disruption to micro-structural and functional brain integrity, suggesting lasting neurological consequences of COVID-19 infection.<sup>7</sup>

Anosmia (loss of the sense of smell) and ageusia (loss of the sense of taste) emerged as significant symptoms several months into the outbreak. Lee et al. sought to determine the prevalence and diagnostic significance of both symptoms by interviewing 3,191 patients. Acute anosmia or ageusia was observed in 15% of patients in the early stages of COVID-19. This observance was more common in females and younger patients. Most patients recovered from symptoms of anosmia and ageusia within 3 weeks; median time to recovery was 7 days.<sup>8</sup> Chary et al. also noted these symptoms more often in young female patients with a 15-day median time to recovery.<sup>9</sup> Brann et al. recently reported that COVID-19-associated anosmia appears to be because of an infection of the olfactory cells found in the nasal cavity rather than sensory neurons themselves. The difference in rates of cellular regrowth is believed to be the mechanism behind why COVID-19-associated anosmia lasts from weeks to months.<sup>10,11</sup>

Although symptoms like anosmia or vertigo may be an annoyance among civilians who have recovered from acute COVID-19 infection, the impact of these neurological complications on the active duty military population cannot be overstated. For example, chronic vertigo in a pilot or diver could result in disastrous consequences, and anosmia in a service member who is working in a closed compartment could rob them of their body's early warning of a toxic or flammable gas leak. Close monitoring of these persistent symptoms and consideration of their impact on a service member's ability to execute their mission is of vital importance.

### MENTAL HEALTH COMPLICATIONS

The stress of the COVID-19 pandemic has caused a range of mental health symptoms in the general population. Czeisler et al. queried 5,285 adults of 18 years and older about mental health and behavioral health symptoms during the pandemic. Respondents reported anxiety and depression (33%), COVID-19-related stress or trauma disorder (29.6%), increased substance use (15.1%), and contemplated suicide (11.9%).<sup>12</sup> Those who experienced COVID-19 infection had higher levels of mental health symptoms.

A systematic review of the mental health consequences of the COVID-19 pandemic by Vindegaard and Benros found higher levels of post-traumatic stress symptoms in hospitalized patients with COVID-19 and elevated levels of depression in all COVID-19 patients as compared to quarantined and general populations. The review also evaluated 16 papers examining the mental health of medical and frontline workers, of which 14 described increases in symptoms of depression, anxiety, or sleep disorders among medical workers.<sup>13</sup> Although beyond the scope of this review, this aspect of occupational stress and mental resilience is important to consider among military medical providers, many of whom are providing care on the front lines, far from home and their usual support systems.

### CARDIOVASCULAR COMPLICATIONS

Acute cardiac injury was estimated to occur in 22% of critically ill COVID-19 patients and greater than 7% of all COVID-19 patients as evidenced by cardiac biomarkers or new electrocardiogram abnormalities. Several patterns of cardiac injury have been described: microthrombotic cardiac injury, viral myocarditis, acute stress myocarditis, and cardiac injury from immune-mediated cytokine storm.<sup>14</sup> Exact pathophysiology of how COVID-19 causes chronic cardiac damage has yet to be described, but myocarditis secondary to myocyte invasion may be mediated by angiotensin-converting enzyme 2 receptors, which lead to cardiac dysfunction, arrhythmias, and death.<sup>15</sup> German authors described 100 study participants, 45-53 years old, 67% of whom recovered from COVID-19 at home and 33% of whom required hospitalization. Participants underwent a cardiac MRI 2-3 months after COVID-19 diagnosis. Seventy-eight percent of all patients had evidence

of heart damage on MRI, and 60% had evidence of ongoing myocardial inflammation, 18% of whom were entirely asymptomatic, with 49% of their study cohort having mild-to-moderate symptoms.<sup>16</sup> This raises significant concerns for the future of the active duty military population, particularly with arrhythmia or inflammatory cardiomyopathy as a complication of COVID-19. Although most military members are young and healthy and may present with mild symptoms, cardiac complications are still a risk.

### **PULMONARY COMPLICATIONS**

COVID-19 can lead to a variety of respiratory diseases including pneumonia, pulmonary embolism, and acute respiratory distress syndrome.<sup>17,18</sup> Huang et al. studied the influence of COVID-19 on lung function in the early convalescence phase. To do this, they conducted serial assessments of 57 COVID-19 cases (40 non-severe and 17 severe cases). The severe category was reserved for patients with any one of the following: intensive care unit requirement, organ failure, shock, mechanical ventilation, respiratory rate > 30, oxygen saturation at rest < 93%, or dyspnea. Abnormalities were detected in pulmonary function tests in 75.4% of patients. Impaired diffusion capacity, lower respiratory muscle strength, and lung imaging abnormalities were detected in more than half of their patient population. Compared with non-severe cases, severe COVID-19 cases had a higher incidence of diffusing lung capacity of carbon monoxide impairment and encountered more total lung capacity decrease.<sup>17</sup> Zhao and colleagues utilized high-resolution computerized tomography and lung function to assess pulmonary status of 55 COVID-19 patients 3 months after discharge. Radiological (70%) and physiological (25%) abnormalities were still found in a considerable proportion of COVID-19 survivors.<sup>18</sup> Although not currently well studied, both pulmonary fibrosis<sup>19-21</sup> and pulmonary thromboembolic vasculature sequelae leading to perfusion dysfunctions are possible complications. What remains unknown is the incidence of these sequelae and if they will constitute a future public health crisis in the form of chronic illness. Compounding the effects of pulmonary disease post-COVID-19 is factor such as combustible tobacco product use. Recent review of self-reported tobacco use by active duty service members reveals that 18.8% use combustible tobacco (including vape devices or electronic cigarettes, traditional cigarettes, or similar products).<sup>22</sup> The compounded effects of smoking as well as the long-term chronic symptoms described above secondary to COVID-19 can have considerable impact on the active duty population, particularly those in the dive and flight communities, and those stationed in areas of higher altitude or poor air quality.

### **EXERCISE INTOLERANCE/RETURN TO EXERCISE**

Although the exact pathophysiologic mechanisms of chronically decreased exercise tolerance in the active duty population after recovery from acute COVID-19 is not well

described, the cardiopulmonary effects discussed above can reasonably be inferred as contributing factors. In a recent study by Cramer et al., a population of 199 Swiss military recruits experienced an outbreak of COVID-19. The median age of the recruit population was 21 years old, and they were predominantly male (87%). Exercise tolerance was measured before the outbreak and measured again 45 days after the outbreak, comparing non-infected recruits with recruits that were symptomatic for COVID-19 or were asymptomatic with COVID-19. There was a significant decrease in predicted maximal aerobic capacity among symptomatic COVID-19 recruits as compared to their counterparts, with VO<sub>2</sub> max decrease of 10% or greater. Interstitial lung disease is one possible cause of this sharp decline. It is unknown if these findings were reversible, and further studies were recommended.<sup>23</sup> In addition to the decreased aerobic exercise tolerance, the subjectively increased myalgia and arthralgia (as common as 27.3%)<sup>5</sup> in patients with persistent symptoms would limit a service member's ability to perform physical fitness testing. This would also hinder their ability to carry gear, drag a wounded comrade off the battlefield, pursue the enemy, and ultimately achieve mission success. Phelan et al. recently discussed the impact on sports and exercise resumption after COVID-19 and recommended utilizing an algorithm for athletes to return to intense physical activity.<sup>24</sup> As there are currently no evidence-based guidelines for returning recovered athletes to exercise or training, this professional opinion guideline may be useful to consider. DoD practice management guidance on returning active duty members to exercise was published in the DoD COVID-19 Practice Management Guide outlining cautious increase in exercise activity in a stepwise fashion to address this issue (see [Table I](#)).<sup>25</sup>

### **COLLECTION OF DATA BY PATIENT NETWORKS AND ONGOING RESEARCH**

There are several studies around the world enrolling patients to study lasting post-COVID-19 sequelae. The Post-Hospitalisation COVID-19 Study in the UK is set to examine the long-term effects of COVID-19 on patient health of ~10,000 patients. The National Heart Blood Lung Institute's COVID-19 Observational Study (CORAL) involves 3,000 patients at 50 hospitals. The patients will be followed up to 6 months after discharge to better understand the epidemiology and recovery of patients after COVID-19. The National Institutes of Health is currently enrolling for the Longitudinal Study of COVID-19 Sequelae and Immunity (RECON\_19) in order to better understand the long-term impacts on health of COVID-19 infection in adults. The goal is to also characterize the individual immune response and effects on close contacts, and describe the mental health implication of COVID-19 on recovered patients.<sup>26</sup> Many patient networks are also documenting and collating their experiences via surveys and plan on publishing their findings.

**TABLE I.** Algorithm for Return to Physical Activity and Exercise After Acute COVID-19

	Stage 1	Stage 2	Stage 3A	Stage 3	Stage 4	Stage 5
Activity description	Minimum rest period after 10 days of activity restriction	Light activity	Light moderate	Moderate activity	Prolonged moderate activity	Normal training
Exercise allowed	Walking and activities of daily living	Walking, light jogging (15 min/mile) for 0.5-0.75 mile Stationary bike (60 rpm, 0-25 Watts). No resistance training.	Jogging (12-15 min/mile) for 1 mile Stationary bike (60 rpm, 25-50 Watts). Low resistance training.	Slow run 10-15 min/mile for 1.5 miles Stationary bike (60 rpm 50-125 Watts) Moderate resistance training	Run 10-12 min/mile for 1.5-2.5 miles Stationary bike (60 rpm, 150+ Watts) Moderate to High resistance training	Normal training exercise activities
% Heart rate max (220 age)	Varies based on medical and activity history	<70%	<80%	<80%	<80%	Normal training
Duration	Depends on the activity history of the patient	<15 min	<30 min	<45 min	<60 min	Normal training duration
Objective	Allow time for recovery. Protect cardiorespiratory system	Gradual increase in HR (Heart Rate)	Increase load gradually. Manage post-viral fatigue syndrome.	Exercise coordination and skills.	Restore confidence and assess functional skills	Resume standard fitness routine
Monitoring	Persistence of symptoms (shortness of breath (SOB), increased work of breathing, difficulty breathing)	Presence or new onset of cardiopulmonary symptoms. Recurrence of initial COVID-19 symptoms.				

This table was adapted from DoD COVID-19 Practice Management Guide v6, Supplementary Appendix 1<sup>25</sup>.

Within the DoD, the Joint Trauma System (JTS) has created a COVID-19 infectious disease registry to collect and analyze clinical data on all COVID-19 positive and suspected symptomatic cases. The goals of the registry include investigating COVID-19 risk factors and examining the safety and effectiveness of COVID-19-related treatments and outcomes. This information can be made available for performance improvement initiatives.<sup>27</sup>

**CONCLUSION**

The list of residual COVID-19 symptoms will likely continue to grow as more data become available and the pandemic continues. COVID-19 infections affect the military population.<sup>28-30</sup> Generally, those who have had more severe illness will require more intensive and lengthy post-acute care. What we are likely to encounter in our young, healthy active duty patient population based on our current experience and the trend in infections are mild COVID-19 cases with constellations of vague residual symptoms. Our local experience has reinforced this point, with patients now presenting with

ill-defined symptoms after recovery from their acute illness, presenting a challenge to providers in how to care for them. It is therefore important to monitor, document, and investigate symptoms from all service members recovering from COVID-19, since these conditions impact service members' health and medical readiness. What remains to be understood about these symptoms is whether or not work up will reveal physiological sequelae that require longer periods of rest, recovery, or interventions. Regardless, military medicine must be prepared to support and manage cases of patients who are recovered from acute COVID-19 but are suffering from post-COVID-19 complications, in order to preserve our fighting force.

**RECOMMENDATIONS FOR MANAGING ACTIVE DUTY MILITARY RECOVERED COVID-19 PATIENTS WITH POST-COVID-19 SYMPTOMS**

The authors recommend consideration of the following aspects of care in patients recovered from acute COVID-19 with persistent symptoms, in order to optimize patient



tracking, patient outcomes, and a return to full-duty status:

1. Thorough and accurate documentation in the electronic medical record is a key. Detection and deliberate recording of what may seem to be obscure or unrelated findings may go on to impact others.
2. Medicine is still medicine; work up symptoms as you normally would. Some symptoms (chest pain, dyspnea, and neurologic symptoms) are more concerning than others and require timely attention.
3. Early management of patient expectations during encounters is essential. Explain that a work up will be conducted, but there is a possibility that some symptoms may persist for months or longer. Explain to patients that data are still evolving and that we may have a better understanding of what is happening to them in the near future. If there is interest, consider encouraging them to enroll in clinical trials.
4. We have a large population of young active duty service members. They may want to return to previous extreme exercise routines or training, but their body may resist because of persistent fatigue from one or many of the sequelae discussed here. A well thought-out, graduated increase in physical activity will need to be informed by military medical providers.<sup>25</sup>
5. Be alert for mental health issues and substance abuse. Do not wait for your patient to bring it up; ask direct questions about stigma, mental and spiritual coping, and well-being.
6. Consider establishing a local registry of patients with post-COVID-19 symptoms and/or collaborating with the existing JTS infectious disease registry.
7. In the absence of dedicated ICD-10 codes to describe post-COVID-19 symptoms, coordinate with a medical coder to standardize coding at the local level to facilitate accurate longitudinal tracking of COVID-19 patients.
8. A multidisciplinary approach will likely be required for some patients. The team may include but is not limited to a primary care manager, a pulmonologist, an infectious disease specialist, a neurologist, a psychiatrist, a physiatrist, physical therapists, and an occupational therapist. Specialists should rule out life-threatening or urgent conditions and provide clear instructions for management. Dedicated clinics or multidisciplinary teams to support post-COVID-19 patient care are being created by other health systems. Adaptation of these paradigms to our military health system may serve as unified support to thoroughly evaluate and support returning active component military members to duty.

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#### SUPPLEMENTARY MATERIAL

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#### CONFLICT OF INTEREST STATEMENT

None declared.

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