

# Neurorecovery after Critical COVID-19 Illness

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## Abstract

### Keywords

- critical covid illness
- covid recovery
- long covid
- Post-Intensive Care Unit Syndrome
- Post-ICU Clinics
- neurologic rehabilitation

With the hundreds of millions of people worldwide who have been, and continue to be, affected by pandemic coronavirus disease (COVID-19) and its chronic sequelae, strategies to improve recovery and rehabilitation from COVID-19 are critical global public health priorities. Neurologic complications have been associated with acute COVID-19 infection, usually in the setting of critical COVID-19 illness. Neurologic complications are also a core feature of the symptom constellation of long COVID and portend poor outcomes. In this article, we review neurologic complications and their mechanisms in critical COVID-19 illness and long COVID. We focus on parallels with neurologic disease associated with non-COVID critical systemic illness. We conclude with a discussion of how recent findings can guide both neurologists working in post-acute neurologic rehabilitation facilities and policy makers who influence neurologic resource allocation.

Coronavirus disease (COVID-19) has had some of the most far-reaching global health-related and socioeconomic consequences of any modern disease.<sup>1,2</sup> It primarily affects the lungs with clinical manifestations that range from asymptomatic or mildly symptomatic disease to acute respiratory distress syndrome (ARDS) and multiorgan failure.<sup>3</sup> Critical illness complicates the course of approximately 5% of those with COVID-19 infection.<sup>4–6</sup> Those who survive acute COVID-19 infection are at risk of post-acute sequelae of SARS-CoV-2 infection (PASC), the so-called long COVID. The long COVID syndrome is characterized by persistent symptoms or delayed (beyond 4 weeks) long-term complications that can affect a variety of organ systems and further complicate recovery.<sup>7,8</sup> The complex and multifactorial impairments seen in COVID-19 critical illness and long COVID have triggered increased recognition of the need for multidisciplinary care in all stages of COVID-19 disease.<sup>9</sup> With the hundreds of millions of people worldwide who have been, and continue to be, affected by COVID-19 and its chronic sequelae, strategies to improve recovery and rehabilitation from COVID-19 are major global public health priorities.

Neurologic complications, most commonly stroke and encephalopathy, have been associated with acute COVID-19 infection. Long COVID is defined as persistent symptoms, lasting over 4 weeks after infection. In addition to constitutional, respiratory, cardiac, gastrointestinal symptoms, neurologic symptoms are a core part of the symptom constellation of long COVID in many patients.<sup>10,11</sup> There are several key questions relevant to how neurologists participate in the care of COVID-19 patients, both in the acute and chronic phases of disease. What are the mechanisms of neurologic complications in patients with acute COVID-19 infection? Do the neurologic symptoms experienced by COVID-19 survivors in chronic phases directly result from nervous system damage, or are they a result of critical systemic illness? Clear answers to such questions will help guide neurologists managing patients with COVID-19 during both the acute illness phase and through recovery.

Our goal in this article is to tackle these questions with a specific focus on critical COVID-19 illness (i.e., COVID-19 illness requiring the intensive care unit [ICU]). We begin by reviewing the neurologic findings associated with acute and

critical illness with COVID-19. We also review neurologic symptoms and findings associated with recovery from COVID-19 and PASC/long COVID. We discuss the mechanisms by which COVID-19 may cause these nervous system complications. We then discuss neurologic complications of critical systemic illness—what aspects of recovery from COVID-19 might be specific to critically ill COVID-19 patients versus what might be common to critical systemic illness from any cause? Finally, we conclude with implications of these findings for neurologic rehabilitation after COVID-19. Our central thesis is that clarity with regard to the mechanisms of neurologic complications of COVID-19 and to the specificity of neurologic sequelae to the critically ill COVID-19 population will guide neurologic evaluation, post-acute neurologic rehabilitation, and neurologic resource allocation in helping patients recover from critical COVID-19 illness.

### Neurologic Complications Associated with Acute Critical COVID-19 Illness

Early reports from China suggested that over one-third of patients hospitalized with COVID-19 had neurologic complications.<sup>12</sup> The most common neurologic manifestations found in one meta-analysis were myalgias, taste impairments, smell impairments, headache, dizziness, encephalopathy, and stroke (►Table 1).<sup>13</sup> More recent reports have confirmed the high prevalence of neurologic symptoms associated with acute COVID-19 infection.<sup>14,15</sup> Critically ill patients have higher rates of acute neurologic complications than hospitalized COVID-19 patients without critical illness.<sup>12,16</sup> Encephalopathy, stroke, and neuromuscular dis-

orders are the most frequently reported neurologic complications in critical COVID-19 illness (►Fig. 1).<sup>17–19</sup>

Encephalopathy has been reported in up to 90% of ICU patients with COVID-19.<sup>20,21</sup> Notably, studies reporting prevalence of neurologic symptoms in critically ill patients to date have mainly been retrospective and have not controlled for severity of critical illness or amount of sedation required during mechanical ventilation. It may be that the encephalopathy seen in critical COVID-19 illness is primarily due to the unusually high amounts of sedation that have been required to achieve adequate mechanical ventilation.<sup>22</sup> However, even after cessation of sedatives, patients with severe respiratory failure secondary to COVID-19 may have prolonged periods of unconsciousness.<sup>23,24</sup>

Strokes, both acute ischemic and hemorrhage, have been associated with COVID-19 infection. Studies have reported stroke incidence of 1 to 6% of patients hospitalized with COVID-19.<sup>15,25–28</sup> Stroke portends particularly poor outcome in COVID-19 patients.<sup>18</sup> Some reports have found that the incidence of stroke and other thrombotic complications in COVID-19 is high as compared with other comparable viral respiratory infections.<sup>29,30</sup> However, other studies specific to the critically ill population have found similar rates of stroke as compared with non-COVID critical illness.<sup>31,32</sup> A recent study showed that the patterns of cerebral microhemorrhages found in COVID-19 critical illness were similar to patients with non-COVID-related critical illness implying that cerebrovascular disease results from secondary effects of critical illness and hypoxia rather than direct effects of COVID-19 infection.<sup>33</sup>

Several neuromuscular conditions including Guillain-Barré syndrome, rhabdomyolysis, myositis, myopathy, and neuropathy have been associated with acute COVID-19.<sup>34,35</sup> Critical illness polyneuropathy and myopathy have been reported in approximately 10% of critically ill COVID-19 patients.<sup>36</sup> In one case series of three ICU patients with COVID-19 who required mechanical ventilation and developed critical illness myopathy, electron microscopy of biopsied muscle showed coronavirus-like particles arguing for direct viral infection of muscle.<sup>37</sup> Other studies have questioned whether neuromuscular involvement in critically ill COVID-19 patients has distinct features.<sup>38,39</sup>

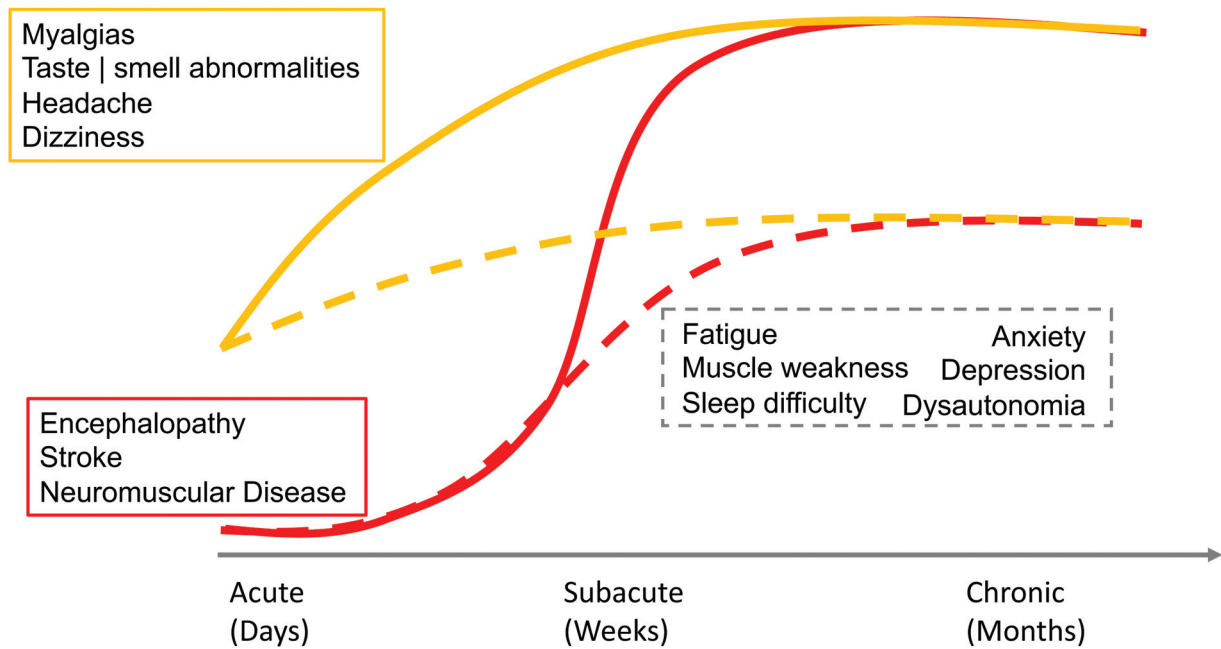
### Neurologic Findings Associated with Long COVID

In addition to acute neurologic complications and recovery from these conditions, it is now well known that survivors of acute COVID-19 continue to have symptoms related to COVID-19 for prolonged periods after the acute infection and hospitalization period (►Fig. 1). Many of these chronic symptoms are neurologic. For example, findings from patients admitted during the initial pandemic months in China in 2020 showed that at 6 months after acute infection, patients previously hospitalized continued to experience fatigue, muscle weakness, sleep difficulties, and anxiety or depression.<sup>40</sup> A 1-year follow-up study reported similar findings.<sup>41</sup>

**Table 1** Acute and chronic neurological complications of COVID-19

Acute complications	Chronic complications
Anosmia	Anxiety
Dysgeusia	Cognitive impairment
Encephalitis	Depression
Encephalopathy <sup>a</sup>	Dysautonomia
Headache	Bowel dysfunction
Neuromuscular <sup>a</sup>	Bladder dysfunction
Guillain-Barré syndrome	Orthostatic tachycardia
Myalgia	Postural hypotension
Myositis	Sexual dysfunction
Neuropathy	Generalized weakness
Rhabdomyolysis	Fatigue
Vascular	Sleep difficulties
Cerebral microhemorrhage	Insomnia
Cerebral venous sinus thrombosis	Hypersomnia
Stroke <sup>a</sup>	
Vertigo	

<sup>a</sup>Commonly reported in critical COVID-19 illness.



**Fig. 1** Covid Recovery Curves and Associated Neurologic Complications. Orange solid line represents mild covid illness. Orange dotted line represents mild covid illness with subsequent development of long-covid. Red solid line represents critical COVID illness with good recovery. Red dotted line represents critical COVID-19 illness with subsequent development of post-icu/long-covid complications. The boxes indicate neurologic symptoms commonly associated with each of these types of COVID recovery.

Dedicated follow-up and characterization of critically ill COVID-19 patients have been more limited. One study showed that among 246 COVID-19 ICU survivors who completed questionnaires, 74% had generalized weakness, 26% had anxiety and depression, and 16% had cognitive impairment.<sup>42</sup> Other studies have shown similar rates of anxiety and depression<sup>43</sup> as well as cognitive disorders.<sup>44</sup> However, outcomes after critical COVID-19 illness remain heterogeneous and difficult to predict.<sup>45</sup> A key question is whether rates of long-term neuropsychiatric and cognitive impairments among critically ill COVID-19 survivors are different from survivors of non-COVID severe illness. One study which used propensity matching suggests that rates are similar between COVID-19 and non-COVID severe illness.<sup>46</sup>

Persistence of symptoms or development of new sequelae beyond 4 weeks from the onset of acute symptoms of COVID-19 is termed long COVID or PASC, post-acute sequelae of SARS-CoV-2 infection (► Fig. 1).<sup>47</sup> A range of organ systems, including the lungs, heart, brain, kidneys, and liver, are known to be affected by long COVID.<sup>48</sup> Neurologic symptoms, the most frequent being chronic fatigue, cognitive impairment, diffuse myalgia, depression and anxiety, and nonrestorative sleep, represent core features of long COVID.<sup>8,48</sup> There is overlap with other post-viral syndromes.<sup>49</sup> Dysautonomia is also a feature commonly seen in long COVID: patients develop orthostatic tachycardia, postural hypotension, persistent fever, and bowel, bladder, or sexual dysfunction.<sup>50–52</sup> Research into risk factors for the development of long COVID continues to evolve; preexisting health conditions such as diabetes, autoantibodies, and concomitant infection with other viruses may play a role.<sup>53</sup> One study showed that experiencing more than five symp-

toms during the first week of illness was associated with long COVID.<sup>54</sup> A critical remaining question is whether COVID-19 critical illness, compared with noncritical illness, puts patients at higher risk of long COVID and its associated neurologic complications. Studies examining this question have shown mixed findings (► Table 2).<sup>55</sup>

### Mechanisms of Neurologic Dysfunction in Acute COVID-19

COVID-19 could lead to nervous system complications through direct nervous system invasion or through indirect effects from systemic disease.<sup>56</sup> The angiotensin-converting enzyme-2 (ACE2) receptor is the main route of cell entry for the COVID-19 virus.<sup>57</sup> ACE2 has been found in human brain vessels as well as in choroid plexus and neocortical neurons.<sup>58</sup> It has been proposed that the SARS-CoV-2 virus might enter the brain via the olfactory system, across the blood-brain barrier, or the virus may accompany immune cells entering the nervous system.<sup>59</sup>

Clinical studies that have tested for the presence of virus in brain or cerebrospinal fluid (CSF) have had mixed results.<sup>60</sup> Some studies have shown evidence of RNA in postmortem brains of patients with COVID-19-related encephalitis,<sup>61,62</sup> while other studies could not detect viral invasion, despite inflammatory CSF.<sup>63</sup>

Acute systemic COVID-19 infection, especially critical illness, can lead to several indirect effects on the brain. Respiratory failure can lead to severe hypoxia and resulting hypoxic brain injury.<sup>64</sup> COVID-19 may lead to cytokine storm, a maladaptive host immune response characterized by high levels of circulating cytokines (e.g., IL-6, IL-1 $\beta$ , tumor

**Table 2** Summary of recommendations to promote neurologic recovery after COVID-19 across care phases

ICU management	Inpatient rehabilitation	Outpatient clinics
<ul style="list-style-type: none"> <li>• Minimize sedatives, analgesics, and neuromuscular blocking agents to facilitate serial neurologic examinations.</li> <li>• Develop local protocols to guide a balanced approach for use of sedatives, analgesics, and neuromuscular blockade.</li> <li>• Maintain a low threshold for EEG monitoring in patients with signs of encephalopathy or altered mental status.</li> <li>• Be vigilant for critical illness myopathy and polyneuropathy, especially as length of ICU stay increases.</li> <li>• Consider early mobilization</li> </ul>	<ul style="list-style-type: none"> <li>• Individualize rehabilitation plans targeting not only recovery of respiratory and cardiovascular conditioning but also mobility, functioning, and cognition.</li> <li>• Pay particular attention to cognitive functioning; consider standard neuropsychological evaluations for all admitted patients.</li> <li>• Implement mental health screening for anxiety and depression</li> </ul>	<ul style="list-style-type: none"> <li>• The first clinic visit should occur 2–4 wk after hospital discharge; discharge navigators (nursing, case management, social work) may be particularly helpful in this role.</li> <li>• Implement standardized tools to screen for known post-COVID complications.</li> <li>• Consider the systematic development of post-COVID-19 critical care multidisciplinary clinics</li> </ul>

necrosis factor) found particularly in patients with severe illness.<sup>65</sup> This systemic hyperinflammatory state can affect brain homeostasis and neuronal cell function via disruptions in the blood–brain barrier.<sup>66</sup> Several studies have suggested that intracerebral microvascular injury characterized by disrupted endothelial cells, fibrinogen leakage, and microhemorrhages may play a role in neurologic dysfunction.<sup>67,68</sup> These mechanisms are further supported by the high frequency of coagulation-related events including strokes and hemorrhages associated with COVID-19.

### Mechanisms of Neurologic Dysfunction in Long COVID

The neurobiological underpinnings of long COVID are less well understood, but similar direct viral or indirect effects on the nervous system likely play a role.<sup>69</sup> Given that microglia and macrophages are key to learning and memory systems, dysregulated neural-immune interactions may play a central role in the cognitive impairment often seen with long COVID.<sup>70</sup> Supporting this hypothesis, the extent of cognitive deficits in patients with long COVID correlate with structural neuroimaging abnormalities (e.g., global decrease in brain volume, structural abnormalities in the limbic system and cerebellum, white matter hyperintensities, and changes in diffusivity in many structures),<sup>71,72</sup> which may represent biomarkers of the neuroinflammatory response.

### Parallels with Neurologic Complications of Critical Systemic Illness

#### Acute Neurologic Complications

A central question in caring for patients with acute and chronic COVID-19-related neurologic complications is whether the symptoms seen during recovery are unique to COVID or seen more generally in critical systemic illness and other post-viral syndromes. Insights can be gained from examining neurologic complications in general critical care populations both in the acute and follow-up phases. Nervous

system tissue has high metabolic demands and, as a result, is one of the organ systems most susceptible to critical systemic illness. In one classic study of 1,850 patients admitted to a medical ICU, neurologic complications, most commonly encephalopathy and stroke, occurred in 12%. Encephalopathy was frequently associated with sepsis.<sup>73</sup> In another study of more than 18,000 patients admitted to the ICU for non-neurologic illness, 1.2% had strokes.<sup>74</sup> Encephalopathy, stroke, seizures, and peripheral nerve and muscle dysfunction are all well-described neurologic symptoms associated with critical illness.<sup>75</sup> Neurologic complications are associated with poor ICU outcomes and increased mortality.<sup>76</sup>

#### Post-Viral Syndromes

Post-viral syndromes and associated neurologic syndromes have also been well described.<sup>77</sup> For example, Ebola virus infection, West Nile virus infection, polio, Lyme disease, and infections with prior coronaviruses all have known post-viral syndromes with remarkable symptom similarity to long COVID. Hallmarks are fatigue, cognitive impairment, anxiety and depression, muscle and joint pain, and sleep disturbances.<sup>78</sup> A study of 22 SARS survivors who remained unable to work for 1 to 3 years following acute SARS infection revealed a syndrome characterized by fatigue, diffuse myalgias, weakness, depression, and sleep abnormalities.<sup>79</sup> Autonomic dysfunction also seems to be a hallmark of post-viral syndromes.<sup>80</sup>

#### Post-Intensive Care Unit Syndrome

Post-intensive care syndrome (PICS) refers to physical, cognitive, and psychiatric impairments persisting after ICU discharge.<sup>81</sup> It is estimated that more than half of ICU survivors suffer from some component of PICS.<sup>82,83</sup> The most common symptoms include generalized weakness, fatigue, decreased mobility, anxiety, depression, cognitive dysfunction, sexual dysfunction, and sleep disturbance.<sup>84</sup> Given the resulting functional disability from core impairments, PICS confers a substantial socioeconomic and public health burden. Many ICU survivors face challenges returning to work.<sup>85</sup> Risk factors can be broadly divided into preexisting factors (e.g.,

preexisting neuromuscular disorders, dementia, or psychiatric illness) versus ICU course factors which generally are associated with severity of critical illness (e.g., mechanical ventilation, sepsis, acute encephalopathy).<sup>86</sup> It is worth noting that preexisting risk factors for developing PICS such as asthma, COPD, and concomitant medical conditions (e.g., diabetes and hypertension) are also risk factors for developing severe illness with COVID-19.<sup>87</sup> PICS symptoms can last months to years after the acute injury. Standardized approaches including ICU bundles have been developed to help prevent PICS.<sup>88</sup>

COVID-19 critical illness survivors, given preexisting conditions (e.g., asthma and COPD) as well as ICU-related factors (long duration of mechanical ventilation, encephalopathy during acute illness), are at particularly high risk of developing PICS.<sup>89</sup> In one study of COVID-19 ICU survivors from New York, the overall prevalence of PICS was 90%.<sup>90</sup> Another study conducted in Australian ICUs compared 6-month outcomes in mechanically ventilated, critically ill COVID-19 versus non-COVID survivors. Disability, measured with a battery of patient-reported outcomes which screened for global health, health status, anxiety and depression, posttraumatic stress disorder (PTSD), cognition, and activities of daily living, was similar between the two groups.<sup>91</sup>

Taken together, there is a high degree of overlap between the neurology of recovery from COVID-19 and known neurologic complications of other forms of critical systemic illness, well-described post-viral syndromes, and PICS. These insights will inform our recommendations for neurologic rehabilitation after critical COVID-19 illness and particularly for implementing ICU follow-up clinics to promote recovery.

## Recommendations to Promote Neurologic Recovery after COVID-19

With this background of neurologic complications associated with critical COVID-19 illness and a discussion of mechanisms, we now offer suggestions to optimize neurologic recovery after COVID-19 ICU illness during different phases of disease—acute illness, inpatient rehabilitation, and outpatient rehabilitation.

### Critical Illness

Given the high prevalence of neurologic complications during acute critical illness with COVID-19, the ICU team should maintain a high vigilance for new neurologic syndromes—such as encephalopathy, stroke, and neuromuscular complications. Many COVID-19 ICU patients require high and prolonged amounts of sedatives, analgesics, and neuromuscular blocking agents to achieve lung protective ventilation in the setting of ARDS.<sup>92</sup> These medications should be minimized as much as possible to allow for serial neurologic examinations, which are important to allow monitoring for neurologic complications. Neurology consultation should be sought if there is suspicion of a new neurologic syndrome. Given the high overlap between encephalopathy and seizures in critically ill patients, there should be a low threshold for EEG monitoring. Local protocols should be developed to guide the balance between the required sedation, analgesia, and neuromuscular blockade for mechanical ventilation and need to lighten these medications to enable close and

frequent neurologic examination. Weaning of high doses of sedation, particularly opioids, can lead to withdrawal syndromes. Including pharmacists on rounds in the ICU is especially valuable for the development of strategies and protocols to minimize this risk.<sup>93,94</sup>

Early mobilization helps prevent decline in muscle mass, strength, and aerobic efficiency seen with bedrest and is overall beneficial for outcomes in many different populations of mechanically ventilated patients.<sup>95–97</sup> COVID-19 patients who require ventilator support for extended periods of time may be particularly susceptible to the negative effects of immobility. Early mobilization thus may prevent some of the neurologic complications related to and improve overall outcomes from COVID-19 critical illness.<sup>98</sup> Yet, enthusiasm for early mobilization needs to be balanced with knowledge of specific disease pathophysiology. For example, in patients with large strokes, early and intense mobilization may be harmful given the loss of cerebral autoregulation.<sup>99</sup> In addition, protocols for early mobilization in COVID-19 patients may be complicated by the need for prolonged respiratory positioning (i.e., prone positioning) due to lung de-recruitment with changes in position. More studies on the optimal timing of and protocols for mobilization for critically ill COVID-19 patients are needed.<sup>100,101</sup>

Given that many COVID-19 patients have prolonged ICU stays, vigilance to neuromuscular complications (e.g., critical illness myopathy and polyneuropathy) is important, especially in patients with the longest ICU stays. Neurology consultation for nerve conduction studies will be helpful in identifying and differentiating causes.

### Inpatient Rehabilitation

Almost all patients who experience COVID-19 critical illness will require inpatient rehabilitation to maximally restore function. Studies have shown that COVID-19 patients make significant gains during inpatient rehabilitation.<sup>102</sup> This is true even for patients who have the most severe illness at the time of admission to rehabilitation.<sup>103</sup> Rehabilitation hospitals and systems experienced substantial strain during the heights of the COVID-19 pandemic.<sup>104</sup> Given the multiorgan dysfunction often seen in COVID-19, the multidisciplinary rehabilitation team is critical for framing the ongoing impairments of recovering COVID-19 patients within the biopsychosocial rehabilitation model. The individualized rehabilitation formulation plan should not only target recovery of respiratory and cardiovascular conditioning but also mobility, functioning, and cognition. The ultimate goal of rehabilitation, implemented within the framework of the International Classification of Functioning, Disability, and Health,<sup>105</sup> is to restore function so that individuals can achieve optimal levels of independence after critical illness. Strategies specific to optimizing inpatient rehabilitation for COVID-19 patients are still emerging. Lessons, including guidelines for best practices and anticipation and mitigation of new health-related challenges, can likely be learned from sepsis patients.<sup>106</sup> For example, practices aimed at screening for new mental health impairments, medication optimization, and monitoring for health deterioration after acute hospital discharge for sepsis survivors have been shown to result in reduced morbidity and mortality.<sup>107</sup>



It is important for rehabilitation care teams to be aware of neurologic complications experienced during the acute phase as well as potential new neurologic complications that might arise. Incident neurologic complications in COVID-19 patients are associated with greater post-acute rehabilitation needs.<sup>108</sup> Particular attention during the inpatient rehabilitation phase should be paid to cognitive functioning. In one study, over 80% of patients admitted to an inpatient rehabilitation unit for COVID-19 had evidence of cognitive impairment.<sup>109</sup> Improvements in cognition tracked with functional gains made by these patients. Standard neuropsychologic evaluations such as the Montreal Cognitive Assessment should be considered for all COVID-19 patients admitted to rehabilitation units and strategies to improve cognitive functioning, and minimize encephalopathy, should be optimized.

Finally, long COVID symptoms, if present, will most likely start to appear during the inpatient rehabilitation phase. Rehabilitation practitioners should actively screen for long COVID symptoms. If patients with continued symptoms reach discharge, resources for continued treatment and engagement with the healthcare system should be provided.<sup>110</sup> Given quarantine restrictions, telehealth may be a particularly effective healthcare delivery model during the outpatient phase.<sup>111</sup>

### Outpatient Clinics

Although limited evidence exists to inform the optimal neurologic support for recovering COVID-19 patients once they have transitioned back to the community, the substantial overlap with the neurology of recovery from critical systemic illness argues that outpatient systems developed for patients recovering from critical illness could be effective for recovering COVID patients. Post-ICU clinics have been developed to evaluate and manage the downstream effects of critical illness, particularly PICS.<sup>112</sup> Intensivists who provide acute critical care for patients are likely best equipped to lead these clinics because of their ability to provide continuity of care and give closed-loop feedback to inpatient care teams for acute care process improvement.<sup>113</sup> In the case of neurologic recovery from severe COVID-19, neurointensivists may be best fit to serve in this role given their training in both neurologic disease processes and critical care. The multidisciplinary provider team is fundamental to the success of post-ICU clinics.<sup>114</sup> Multidisciplinary post-ICU teams for the assessment of post-COVID recovery deficits could include neurologists, pulmonologists, physiatrists, physical, occupational, and speech therapists, nurses, clinical psychologists, pharmacists, palliative care specialists, nutritionists, case managers, and potentially others.

Consensus guidelines recommend that the first visit to a post-ICU clinic occurs 2 to 4 weeks after hospital discharge, but this may vary depending on length of stay of patients at inpatient rehabilitation.<sup>86</sup> Discharge navigators may be particularly helpful in identifying and recruiting patients to post-ICU clinics and serving as point of contacts for patients and families between hospital discharge and first ICU clinic follow-up. This role can be filled by individuals

with backgrounds in nursing, case management, or social work.<sup>115</sup>

During the clinical visit, standard tools for the evaluation of known post-ICU complications (i.e., PICS) and in this case post-COVID complications should be implemented. Tools such as the Montreal Cognitive Assessment, the Hospital Anxiety and Depression Scale, the Impact of Events Scale—Revised, and the Fatigue Severity Scale might be used to assess cognitive impairment, anxiety/depression, PTSD, and fatigue, respectively. Additional assessments should be guided by the history and physical examination. A comprehensive medical reconciliation should be performed, potentially by a pharmacist, to reduce the risk of polypharmacy by eliminating unnecessary medications. Evaluation for new and persistent symptoms and signs including long COVID and critical illness myopathy/polyneuropathy will be important. Including caregivers and family members in the evaluation and interview will likely lead to additional insights. After comprehensive evaluation, providers in the clinic should counsel patients on expected recovery trajectory. Evaluation will also lead to the treatment of any new complications of critical illness and referral to additional services, as necessary. For example, referrals to physical, occupational, and speech therapy, as well as psychotherapy will likely be common given the spectrum of symptoms seen in chronic COVID-19. Finally, with the social and public health restrictions imposed by the pandemic and the resultant rise in access to telehealth, these visits might be conducted via telemedicine with additional in-person follow-up scheduled as needed.

Ultimately, the success of the post-critical care clinic will depend on a larger healthcare system investment in this model of care. Indeed, in one recent study, ICU and COVID recovery clinics were surveyed and shown to depend heavily on volunteer support and discretionary institutional support.<sup>116</sup> As more patients survive the acute phase of critical illness, improving ICU care will also necessitate focus on reducing disability and improving long-term function. Post-ICU and post-COVID clinics are a valuable venue for collecting data on long-term outcomes to improve understanding of downstream effects of practices in the critical care unit. For ICU staff, post-ICU clinics have been shown to reduce burn-out, likely because of the perspectives and unique relationships built with patients and families in the outpatient setting.<sup>117</sup> Increased investment in the model of post-ICU/COVID recovery clinics may ultimately improve outcomes for all critically ill patients.

### Conclusion

Neurologic complications, including stroke, encephalopathy, and neuromuscular disorders, are commonly associated with COVID-19, particularly critical COVID-19 illness, and these complications portend poor outcomes and prolonged recovery. Many survivors of critical COVID-19 illness face long COVID, a syndrome which has many core features that are neurologic, including cognitive impairment. There are many parallels with the neurologic complications of COVID-19 and other non-COVID respiratory and critical illnesses, which

may indeed share common mechanisms, primarily reflecting the indirect effects of critical illness on the central nervous system. Providers caring for patients throughout the acute care and inpatient rehabilitation phases of COVID-19 should be vigilant in screening for neurologic complications. Outpatient management of patients recovering from critical COVID-19 illness could learn valuable lessons from the recent development of multidisciplinary post-ICU clinics. Increased investment in the model of multidisciplinary post-ICU care will likely improve critical illness outcomes overall.

#### Conflict of Interest

None declared.

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