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Neurologic Emergencies during the Coronavirus Disease 2019 Pandemic

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KEYWORDS

• COVID-19 • Neurologic emergencies • Cerebrovascular disease • Thrombolysis • Seizure

KEY POINTS

- Institutions should create protocols for managing neurologic emergencies during the pandemic that allow for rapid and thorough evaluation of patients while also minimizing viral exposure to other patients and staff.
- Less than 5% of patients with coronavirus disease 2019 will have cerebrovascular complications and these typically occur in patients who are critically ill.
- Persons with epilepsy may face significant challenges with regards to care and prevention of seizures, although there does not seem to be an increase in emergency department presentations with seizure.
- Seizure is a rare complication of coronavirus disease 2019 with antiepileptic drug selection impacted by concurrent organ failure, drug–drug interactions with coronavirus disease 2019 therapies, and ongoing drug shortages.

As the coronavirus disease 2019 (COVID-19) pandemic continues, the scientific community is working diligently to rapidly expand knowledge of the disease and disseminate this knowledge worldwide. As of January 2021, there have been more than 90,000 scientific publications relating to COVID-19.[1] The rapid expansion of data on this topic has led to novel means of interpretation and dissemination, including expedited reviews for publication in peer-reviewed journals, open source platforms for review of article preprints, widespread use of social media, and protocol sharing among academic institutions.[2] The literature regarding neurologic features of COVID-19 specifically has been primarily in the form of case reports and a few case series, limiting

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the generalizability of this information owing to the inherent heterogeneity of these studies and patients.[3] Here, we review what has thus far been published about the intersection of COVID-19 and neurology with particular attention to cerebrovascular disease and seizure. Considerations in managing the acute presentations of these conditions in the context of the pandemic can serve as a model for management of other neurologic emergencies.

CONSIDERATIONS FOR MANAGING ACUTE STROKE DURING THE PANDEMIC

Initial Evaluation

Given the rapid sequence of events that unfold upon the activation of a stroke alert, it is critical that hospitals have standardized measures in place to protect staff from potential exposure when patients are known or suspected to be infected with severe acute respiratory syndrome novel coronavirus 2(SARS-CoV-2). Many groups have proposed adjustments to institutional stroke protocols to continue to offer timely stroke care while preserving personal protective equipment (PPE) and limiting provider exposure.[4–6] For regions with high community prevalence of COVID-19, it is reasonable to consider all patients undergoing stroke alerts to be persons under investigation. A surgical mask should be placed on the patient and 1 member of the stroke team should be designated to don PPE and enter the patient's room for the evaluation. This provider, who is charged with interviewing the patient and performing the initial examination, is then able to communicate with other members of the team (either by phone or tablet computer already placed within the room) to facilitate joint decision-making on eligibility for acute intervention. Although it is common practice at many institutions for the stroke team to accompany patients to neuroimaging studies, it is recommended that, in the case of patients with suspected or confirmed COVID-19, the initial evaluator remain in the patient's room with PPE donned to limit PPE use and accidental exposure while doffing. Upon the patient's return to their room, further examination by the designated team member can be used to guide decision-making on thrombolysis and mechanical thrombectomy.

Mechanical Thrombectomy

Unfortunately, a number of centers have seen significant delays in the delivery of mechanical thrombectomy during the pandemic, particularly for those patients arriving from another facility.[7,8] As a result, measures that simultaneously conserve PPE and maintain provider safety while still providing timely interventional therapy during the ongoing pandemic are necessary. In a recent consensus statement, the Society of Vascular and Interventional Neurology outlined several recommendations on the periprocedural management of patients who are deemed candidates for mechanical thrombectomy.[9] Before mechanical thrombectomy, it is recommended that all patients undergo screening (and testing if feasible) for COVID-19 and be placed in negative-pressure isolation if warranted. The Society of Vascular and Interventional Neurology also recommends that the number of involved personnel be limited and endotracheal intubation be avoided if possible to conserve ventilator capacity and decrease the risk of ventilator-associated injury in patients who may be managed with conscious sedation. For those requiring intubation, centers have adapted techniques (such as the use of negative-pressure rooms and barrier enclosure) to minimize the circulation of respiratory droplets.[10,11] After completion of the procedure, the Society of Vascular and Interventional Neurology recommends that initial neurologic and puncture site evaluations take place in the interventional suite while the patient awaits bed placement elsewhere in the hospital to limit donning and doffing of PPE.

Postacute Stroke Care

For acute ischemic stroke patients not meeting criteria for intervention with intravenous (IV) tissue plasminogen activator (tPA) or mechanical thrombectomy, priorities generally shift to postevent monitoring for clinical progression, as well as workup of potential etiologies and initiation of secondary prevention measures. Some institutions have moved toward the use of video evaluation by nursing staff and/or the stroke team to decrease PPE use and limit provider exposure, as well as deferring diagnostic testing that is not thought to impact inpatient management.[4] An example of a modified approach to monitoring poststroke patients who do not undergo thrombolysis or mechanical thrombectomy is shown in **Fig. 1**.

For patients undergoing acute intervention with IV tPA and/or mechanical thrombectomy, postintervention monitoring before the pandemic was largely centered around frequent examination by both bedside nursing and members of the stroke team.[12] A recent study (albeit one conducted before the pandemic) evaluated the safety of a low-intensity monitoring protocol for patients meeting a predefined threshold for low risk for neurologic decompensation and found that selected patients who underwent less frequent neurologic and vital sign checks in the 24 hours after the administration of IV tPA did not see an increased incidence of clinical worsening requiring transfer to an intensive care unit.[13] Similarly, investigations questioning the usefulness of routine surveillance neuroimaging in otherwise stable postintervention patients have called into question their necessity.[14,15] These findings have been extrapolated to inform policy about post-thrombolysis and post-thrombectomy care in the COVID-19 pandemic, when intensive care unit beds have been in short supply and frequent evaluations by providers increase the risk of exposure.[4,16,17] Examples of this process of risk stratification and disposition decision-making are shown in **Figs. 2** and **3**.

Impact on Stroke-Related Outcomes

Hospitals across the world have reported significant reductions in admissions for all types of stroke patients during the pandemic, with the most impact usually occurring during times of local government restrictions on activities and in patients with a transient ischemic attack or minor stroke. Specifically, this phenomenon has been reported in the United States,[18–22] Canada,[23] China,[24] Spain,[25] Amsterdam,[26] Brazil,[27] Bangladesh,[28]

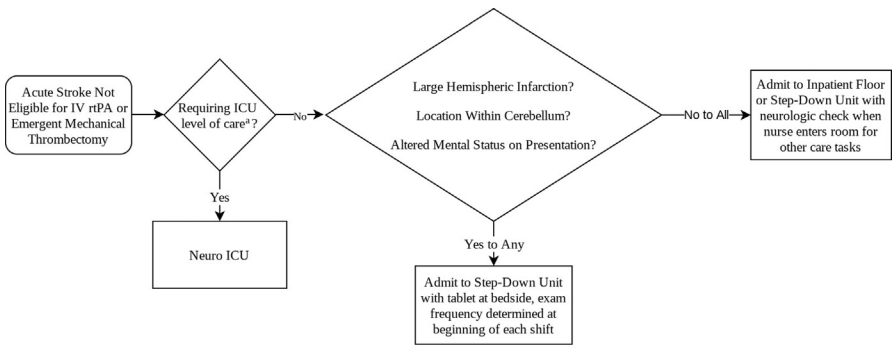

Fig. 1. Neurologic monitoring frequency in patients not receiving IV tPA or emergent mechanical thrombectomy. [a]Indications including (but not limited to) vasoactive medications, insulin drip for hyperglycemia, need for mechanical ventilation. ICU, intensive care unit. (*Adapted from* Optimization of Resources and Modifications in Acute Ischemic Stroke Care in Response to the Global COVID-19 Pandemic. J Stroke Cerebrovas Dis 2020 Aug;29(8):104980, with permission.)

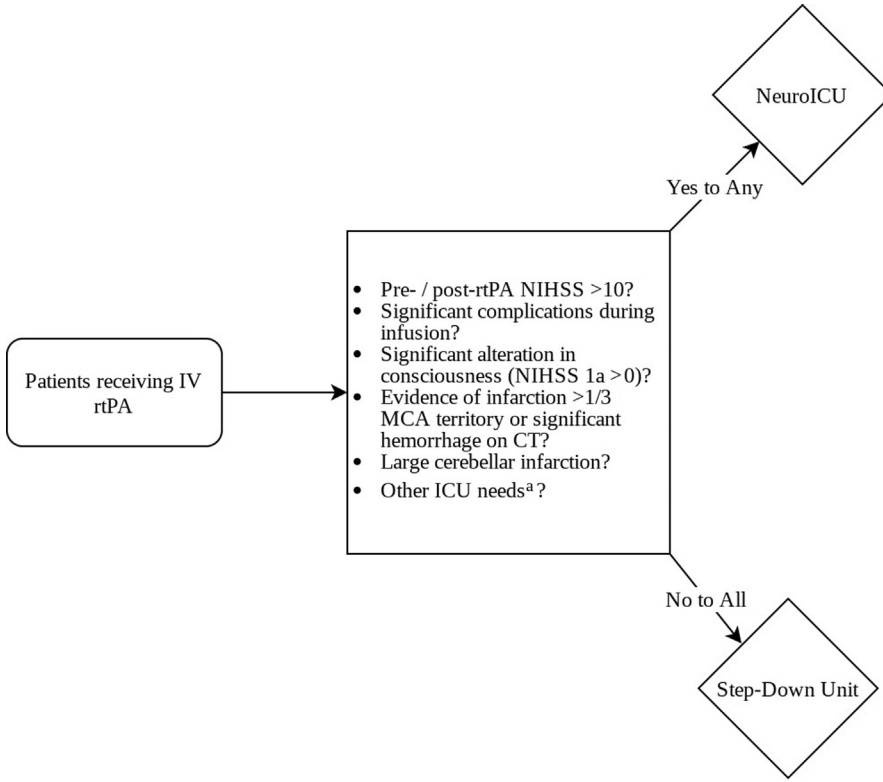

Fig. 2. Disposition determination algorithm after the administration of IV tPA. [a]Indications including (but not limited to) vasoactive medications, insulin drip for hyperglycemia, need for mechanical ventilation. CT, computed tomography; ICU, intensive care unit; MCA, middle cerebral artery; NIHSS, National Institutes of Health Stroke Scale. (*Adapted from* Optimization of Resources and Modifications in Acute Ischemic Stroke Care in Response to the Global COVID-19 Pandemic. J Stroke Cerebrovas Dis 2020 Aug;29(8):104980, with permission.)

Singapore,[29] and Norway,[30] among others. These data suggest that a large number of patients with symptoms of ischemic stroke chose not to seek medical care, a decision that, in many cases, could have a significant impact on their long-term functional status. In addition to a decrease in acute stroke presentations, delays in hospital arrival after symptom onset have been reported for those patients who do seek care,[21] likely owing to the fear of exposure to COVID-19 in a hospital setting. Upon arrival to the emergency department (ED), patients met further delays in arrival time to computed tomography scan,[21] door-to-needle time for IV tPA,[31] and door-to-groin time for mechanical thrombectomy.[8] These in-hospital delays are suspected to be due to the need for donning of PPE and sanitization procedures between patients. Delays in stroke treatment have been shown to significantly increase the risk of poor functional outcomes.[32]

CORONAVIRUS DISEASE 19–ASSOCIATED CEREBROVASCULAR DISEASE

Epidemiology

Infection with SARS-CoV-2 has been associated with a myriad of neurologic complications (**Table 1**) and the presence of neurologic symptoms seem to be quite

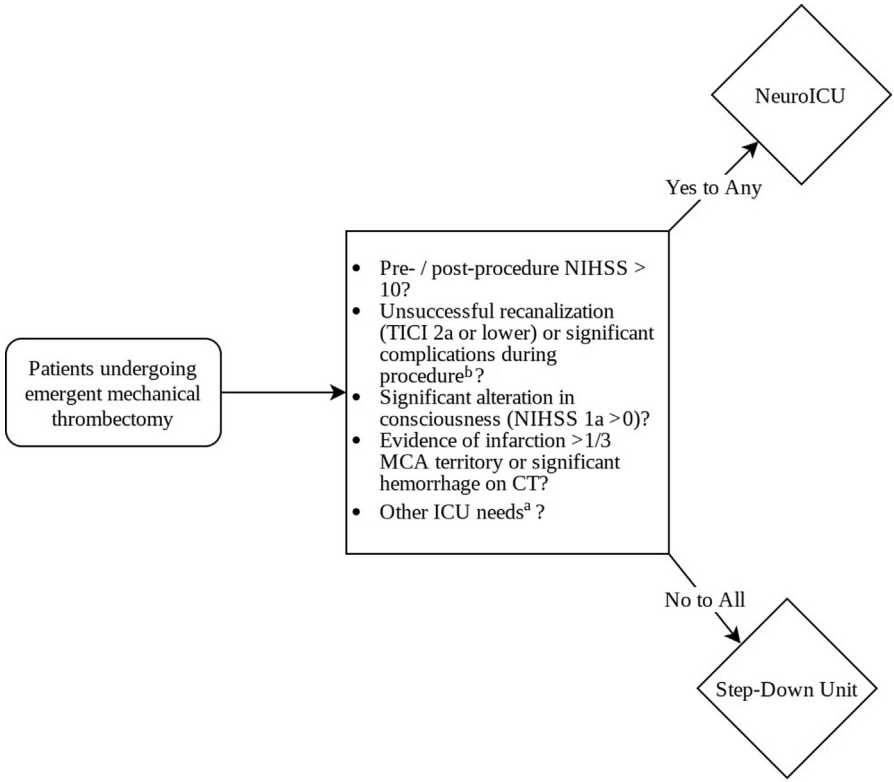

Fig. 3. Disposition determination algorithm after emergent mechanical thrombectomy. [a] Indications including (but not limited to) vasoactive medications, insulin drip for hyperglycemia, need for mechanical ventilation. [b] including (but not limited to) dissection, hemodynamic instability, and respiratory decompensation requiring intubation. CT, computed tomography; ICU, intensive care unit; MCA, middle cerebral artery; NIHSS, National Institutes of Health Stroke Scale; TICI, thrombolysis in cerebral infarction. (*Adapted from* Optimization of Resources and Modifications in Acute Ischemic Stroke Care in Response to the Global COVID-19 Pandemic. J Stroke Cerebrovas Dis 2020 Aug;29(8):104980, with permission.)

common, occurring in up to 84% of those with critical illness.[33] The majority of acute cerebrovascular disease associated with COVID-19 infection is acute ischemic stroke, but there have been reports of intracerebral hemorrhage,[34] venous sinus thrombosis,[35] posterior reversible encephalopathy syndrome (PRES),[36] reversible cerebral vasoconstriction syndrome,[37] and endotheliitis without parenchymal infarction.[38]

Ischemic stroke has been reported in 1% to 5% of patients hospitalized with COVID-19, with the higher end of that range coming from very early reports out of Wuhan, China, in predominantly critically ill patients.[39–45] Although nonspecific neurologic symptoms (such as headache, dizziness, and fatigue) are frequently reported early in the course of infection,[3] there is a suggestion that cerebrovascular disease tends to occur an average of 10 days (range, 0–33 days) after the onset of respiratory illness.[39] Most studies report that COVID-19–associated cerebrovascular disease occurs in predominantly male patients who are more than 60 years of age and have known vascular risk factors.[40,41,43–45] However, several studies reported out of New

Table 1
Neurologic complications of COVID-19

Acute Complications	Parainfectious and Postinfectious Complications
Encephalopathy	Acute disseminated encephalomyelitis
Myalgias	Acute necrotizing hemorrhagic encephalopathy
Anosmia/dysgeusia	Steroid responsive (autoimmune) encephalopathy
Headache	Myositis
Cerebrovascular complications	Critical illness neuromyopathy
Seizures	Guillain-Barre syndrome
Meningoencephalitis	Transverse myelitis
Cranial and peripheral neuropathies	Myalgic encephalomyelitis, with or without dysautonomia
Myoclonus	Sudden sensorineural hearing loss
Movement disorders	Unknown late neurologic complications
Psychosis	

York City[42,46] found strokes, particularly large vessel occlusion (LVO) strokes, occurring in younger patients. The majority of strokes reported are attributed to cardioembolism, many considered cryptogenic.[43–47] In the United States, cerebrovascular disease seems to be a complication of COVID-19 seen more commonly in racial minorities (Blacks and Hispanics),[42–44] but this may be due to more data coming from larger urban hospitals and the disproportionate effect COVID-19 has had on minority communities overall.

The mortality of ischemic stroke in COVID-19 is high (25%–44%),[40–45] leading to some speculation that stroke is predominantly associated with preexisting critical illness. Patients admitted with COVID-19 and neurologic disease have been found to have a higher in-hospital mortality (37.5% vs 4.3%) and greater disability at discharge (modified Rankin Scale of 5 vs 2) compared with patients admitted with the same neurologic diagnoses without COVID-19.[48] Similarly, when patients with COVID-19–associated ischemic stroke were compared with propensity score matched patients with stroke alone, they were found to have greater stroke severity (National Institutes of Health Stroke Scale 10 vs 6), higher risk for severe disability (modified Rankin Scale 4 vs 2; $P<.001$), and higher mortality (odds ratio, 4.3).[49] These findings suggest that COVID-19–associated cerebrovascular disease is more severe with worse functional outcomes and higher mortality than non-COVID-19–associated cerebrovascular disease.

Intracerebral hemorrhage occurs less commonly in patients with COVID-19 than acute ischemic stroke. Several reports in the spring in the United States noted that hemorrhage occurred predominantly in hospitalized patients on anticoagulation, often prescribed for elevated D-dimer levels.[34,44,50,51] Other risk factors associated with intracerebral hemorrhage include a prolonged international normalized ratio and partial thromboplastin time independent of anticoagulation use, thrombocytopenia, older age, non-White race, and mechanical ventilation.[34,50,51] Patients with COVID-19 and intracerebral hemorrhage experienced very high in-hospital mortality, up to 84.6% in 1 center.[51]

Cerebral venous sinus thromboses have been infrequently reported despite an abundance of evidence reporting deep vein thromboses elsewhere. Unlike other cerebrovascular complications, cerebral venous sinus thromboses seems to occur more often in females, with a wide age range reported. This finding is similar to patterns seen in non–COVID-associated cerebral venous sinus thromboses. It seems that cerebral venous sinus thromboses associated with COVID-19 may occur at the

same time as typical respiratory or gastrointestinal symptoms, but may also occur in a delayed fashion, up to weeks after initial infection.[35]

Thirteen cases of PRES in the setting of COVID-19 have been reported as of June 30, 2020.[36] Unlike the majority of patients with PRES outside of COVID-19, these patients had only modest fluctuations in blood pressure. Risk factors for COVID-19–associated PRES include an underlying infection or immunomodulatory agents with endothelial effects. In general, as with other associated etiologies, the neurologic prognosis for COVID-19–associated PRES is favorable.[36]

Pathophysiology

Several mechanisms may lead to ischemic stroke in patients with COVID-19 (**Box 1**). One of the more widely accepted hypotheses is that SARS-CoV-2 causes damage to endothelial cells, which leads to activation of inflammatory and thrombotic pathways, microvascular and macrovascular injury, and ultimately coagulopathy similar to that seen in sepsis, characterized by elevated fibrinogen, partial thromboplastin time, D-dimer, and sometimes thrombocytopenia.[3,39] Some studies have also noted a high prevalence of antiphospholipid antibodies[52,53] in critically ill patients with COVID-19. SARS-CoV-2 can also trigger a hyperinflammatory state and cytokine storm similar to that which occurs in hemophagocytic lymphohistiocytosis.[54,55] Cellular entry of SARS-CoV-2 via the angiotensin-converting enzyme 2 receptor leads to the downregulation of receptors with consequent overactivation of the classic renin–angiotensin system axis causing vasoconstriction and a prothrombotic state.[56] Other investigators have suggested a possible direct endothelial invasion and replication within the arterial wall,[57] a process previously described in varicella zoster virus.[58] Finally, the inherent increased risk of stroke in all critically ill patients can also apply to patients with COVID-19, with potential mechanisms including destabilization of atherosclerotic plaque, triggering of atrial fibrillation, or increasing thrombus formation in conditions of hypoxia.[3]

Acute Stroke Treatment for Coronavirus Disease 19–Associated Stroke

In light of the finding that patients with COVID-19 are at risk of mixed hematologic complications,[59–61] the efficacy and safety of administration of IV tPA in this subset of acute ischemic stroke patients has been a topic of debate. Although the efficacy of thrombolysis outside of the context of the COVID-19 pandemic in decreasing

Box 1
Mechanisms of stroke in COVID-19

- Exacerbation of underlying risk factors
- Viral mediated hematologic derangement/hypercoagulable state
- Effects on the renin–angiotensin system
- Hyperinflammatory condition (cytokine storm)
- Complication of COVID treatments
- General critical illness, hypoxia, hypotension
- Myocarditis, stress cardiomyopathy
- Atrial fibrillation
- Endotheliitis/vasculitis

long-term disability from acute ischemic stroke has been demonstrated clearly,[62,63] there are limited data that address whether this specific patient population is at an increased risk of clinically significant hemorrhagic transformation compared with the general population, thereby altering the risk:benefit relationship. Data on this topic are limited in quality and provide mixed results. One review found that 10.3% of patients with COVID-19 (3/29) receiving IV tPA had clinically significant hemorrhagic transformation,[64] although another did not report any instances (0/13).[65] In the absence of a true consensus regarding the risk of symptomatic hemorrhage in patients with COVID-19 with suspected acute ischemic stroke, the decision to administer tPA is provider-dependent and should be made with consideration of non–COVID-specific contraindications to thrombolysis and other patient-specific factors.

In addition to increased severity of stroke, presentation with LVO stroke has been observed in patients infected with COVID-19.[42,64,66,67] Although emergent mechanical thrombectomy in a patient with confirmed COVID-19 is feasible[11] with appropriate modifications as described elsewhere in this article,[9] the limited data available thus far have unfortunately shown poor outcomes with increased mortality in patients with LVO stroke and COVID-19 compared with LVO stroke alone.[68,69] Specifically, there have been reports of increased procedural complications including clot fragmentation, downstream emboli, and distal emboli to a new vascular territory.[70] An increase in postprocedural complications, including early cerebral reocclusion[69] and deep venous thrombosis and/or pulmonary emboli,[68] has also been reported. Despite these risks, mechanical thrombectomy is recommended in patients with COVID-19 and LVO stroke, with appropriate precautions.

CONSIDERATIONS FOR MANAGING EPILEPSY DURING THE PANDEMIC

Like many chronic illnesses, medical care for persons with epilepsy (PWE) has been impacted by the pandemic. With the shutdowns seen in many countries, there has been a dramatic reduction in the availability of outpatient care such as visits with a neurologist/epileptologist and electroencephalograms (EEGs). Even when in-person visits have been available, many patients chose to defer medical care owing to the fear of viral exposure in the clinic. The advent of widely available telehealth has improved access to care but cannot entirely replicate an in-person evaluation or EEG monitoring. With overcrowding and concerns about infection control, many hospitals have canceled elective admissions and surgeries, delaying care for those awaiting characterization of epileptic spells in epilepsy monitoring units or epilepsy surgery.

The American Epilepsy Society has reported survey data of their membership indicating that 10% of PWE have noted worsening in seizure frequency unrelated to COVID-19 infection during the pandemic, with increased stress, sleep deprivation, and decreased access to medical care and pharmacies cited as potential contributors.[71] This phenomenon has been seen in previous coronavirus outbreaks as well. During the 2003 SARS epidemic in Taiwan, 1 epilepsy center noted that 22% of PWE experienced inability to access antiepileptic drugs (AEDs) owing to lack of access to health care providers and/or pharmacies, leading to increased seizure frequency in 12% (including 2 patients with status epilepticus [SE] who required intensive care unit admission).[72]

However, not all reports about epilepsy care during the pandemic have been negative. Some epileptologists have noted improvement in seizure control in PWE during the pandemic owing to better medication adherence and increased sleep.[71] Despite concerns that ED visits for seizures would increase if patients were not accessing outpatient care, 1 health system in Italy actually observed a decrease in visits for

seizures during the height of the pandemic in their country.[73] Limited evidence has also suggested that PWE without other comorbidities are not at higher risk for acquiring COVID-19 or suffering from more severe complications,[74] unlike patients with a history of cerebrovascular disease.[75,76]

Approach to Managing Seizures and Status Epilepticus During the Pandemic

For the most part, the evaluation and treatment of patients with seizures and/or SE during the pandemic should be unchanged with regard to general management principles, such as those outlined in the Neurocritical Care Society Guidelines.[77] However, there are some key, novel considerations regarding infection control, medications, and resource use.

Convulsive SE should be considered aerosol generating and appropriate PPE should be used for all treating staff. This point is most critical for physicians performing endotracheal intubation. Although debate exists about whether early versus delayed intubation is superior for patient outcomes in severe COVID-19 infection,[78,79] infection control may be considered in some centers. Some centers advocate for earlier intubation in respiratory failure given the potential for increased aerosolization associated with the use of noninvasive ventilation (bilevel or continuous positive airway pressure) and to a lesser extent high-flow nasal cannula, especially in the context of lack of negative pressure rooms and sufficient PPE.[80,81] These factors may influence decision-making for patients with mild respiratory distress after a seizure.

During the pandemic, there have been several shortages of medications frequently used for continuous sedation (IV midazolam, propofol) and AEDs (valproic acid, levetiracetam) that have impacted the care of hospitalized epilepsy patients and in the emergent management of seizures and SE. The main driver for these drug shortages has been the massive increase in simultaneous worldwide need; up to one-third of hospitalized patients with COVID-19 have severe respiratory distress requiring prolonged intubation and sedation.[82] In addition, manufacturing shutdowns in China and closure of exportation from India interrupted the usual supply chain to the United States.[83] Thus, it is important for health care systems to develop alternative sedation and SE treatment protocols to account for potential shortages. In particular, ketamine has experienced a recent resurgence for use in sedation as well as seizures and SE. There may be a particular role in SARS-CoV-2 infection, because ketamine has an anti-inflammatory effect, in particular lowering levels of IL-6, which are often increased in COVID-19 infection.[84,85]

Some patients may present to the ED with seizure or SE as the presenting feature of COVID-19.[86,87] Therefore, it may be reasonable to consider all patients with seizure or SE presenting to the ED as persons under investigation. Irrespective of COVID-19 status, a typical diagnostic work-up for new seizure involves obtaining MRI and EEG. Many investigators suggest the postponement of these studies during the pandemic unless they might provide urgent information that would change management.[74] Because seizure in COVID-19 may occur secondary to conditions like stroke, cerebral venous sinus thromboses, or meningoencephalitis, in our center we advocate for obtaining these studies during admission for a new seizure diagnosis, especially if there are no other provoking factors present.

Electroencephalography

Many health care systems decreased the use of EEG during the initial surge for all patients or modified indications and restricted access. Some eliminated the use of EEG for inpatients suspected to have COVID-19 altogether or created treatment algorithms

which modified the standard of care for typical evaluations such as myoclonus, encephalopathy, and nonconvulsive SE.[88]

Pursuing EEG for patients with COVID-19 requires consideration of the risk:benefit ratio, given the risk of potential viral transmission to the technologist. If the study is unlikely to change management decisions for the patient, strong consideration should be given to foregoing the study. Most studies require prolonged set-up times and close proximity to patients' faces, which increase the risk of viral transmission (which may be lessened by proper use of PPE). Although an EEG in itself is not an aerosolizing procedure, the patient population requiring EEG may have behavioral unpredictability with the potential for yelling or coughing. For this reason, we recommend the use of N95 respirators, face shields, gowns, and gloves for all technologists during EEG lead placement and adjustment of all patients. Other infection control measures may include having a dedicated machine exclusively for patients with COVID-19 or using only disposable electrodes and cables.[89]

We recommend obtaining an EEG in cases of known SE who remain encephalopathic or comatose after the initial treatment of the seizure, for myoclonus and encephalopathy that has not responded to an empiric trial of an AED,[88] and for encephalopathy or coma evaluation when other explanations have been excluded. If EEG is pursued, a standard 10 to 20 EEG complement of electrodes with electrocardiogram should be used. Expedited studies with simplified montages to screen for SE (generalized and most regional or focal types), encephalopathy, and reactivity may be helpful in the intensive care unit setting if there are concerns about resource use.[90] The interpretation of specific patterns on the intensive care unit EEG suggestive of encephalopathy, nonconvulsive SE, focal slowing (suggestive of a lesion, such as a stroke), and postanoxic changes are beyond the scope of this article, but we recommend EEG scoring as per the American Clinical Neurophysiology Society guidance.[91] We suggest continuous video EEG monitoring to limit technologist active hands-on time in the room as well as to allow the electroencephalographer to make clinical correlations with the EEG findings. With reduced montages, however, there may be difficulty in identifying artifacts and a failure to identify lateralized periodic discharges. Most societies have recommended against the use of hyperventilation during EEG to decrease the risk of viral transmission.[89,90]

Because patients with COVID-19 are often intubated (sometimes with less common ventilation strategies), the electroencephalographer may be aided in interpretation of the study if the mode and rate of ventilation is recorded. There is no reason why EEG cannot be used for patients requiring the prone position, but experience with interpretation is very limited. When prone, the typical artifacts that are usually seen in the occipital leads (representing contact with bedding for supine patients) would instead be in the frontopolar leads.[90] Furthermore, positioning affects the cerebrospinal fluid (CSF) layer surrounding the brain parenchyma and shifts from supine to prone will redistribute CSF by up to 30% owing to gravity. As CSF is more conductive than brain parenchyma, and this factor will change the scalp potentials with thicker CSF layers associated with a decreased EEG signal.[92]

CORONAVIRUS DISEASE 19–ASSOCIATED SEIZURES AND STATUS EPILEPTICUS

Seizures seem to be an infrequent complication in patients with COVID-19, with a reported incidence of less than 1.6% in single health system studies[40,93–95] There are many mechanisms by which seizures may occur in COVID-19 (**Box 2**). PWE may be at greater risk of seizure during COVID-19 (similar to other common

Box 2
Mechanisms of seizure in COVID-19

- Exacerbation of underlying epilepsy
- Metabolic derangements
- Hypoxia
- Hyperinflammatory condition (cytokine storm)
- Complication of COVID treatments
- General critical illness
- Meningoencephalitis, infectious, or parainfectious
- Secondary consequence of cerebrovascular disease

infections), although the American Epilepsy Society reported survey data indicating that most PWE (>80%) did not experience worsening of seizure frequency, although they had symptoms of COVID-19 infection.[71] Metabolic derangements, organ failure, hypoglycemia, hypoxia, and some medications used during critical illness may all lower the seizure threshold. Moreover, subclinical seizures or nonconvulsive SE are common in patients with other forms of critical illness and depressed mental status.[96] There have been reports of new-onset epilepsy in COVID-19, most of which have been described in patients with a preexisting risk factor that lowered their seizure threshold. However, not all patients have a history of epilepsy, identified preexisting risk factor, or current metabolic derangement to explain new-onset seizures.[86,97] Some of these patients have been determined to have meningoencephalitis either from SARS-CoV-2 infection or as a parainfectious process.[88,97–99] Finally, COVID-related cerebrovascular complications may also lead to seizures.

The management of seizures and SE in COVID-19 may have some notable differences with regard to AED selection. In general, we advocate for the use of an IV AED formulation to avoid concerns of malabsorption. Critically ill patients with COVID-19 are at risk for multiple organ system failures. Cardiac complications in COVID-19 may be exacerbated by the combined effects of both COVID treatments and AEDs that lead to PR and/or QT prolongation (such as hydroxychloroquine and phenytoin). Hepatic injury and potential anticoagulation use may limit the use of phenytoin, valproate, and carbamazepine. Acute kidney injury leading to the need for renal replacement therapy or placement of patients on extracorporeal membrane oxygenation may require dose adjustments to maintain therapeutic concentrations of AEDs in serum.[100] Finally, as noted elsewhere in this article, key drug shortages may influence management decisions.

SUMMARY

Significant attention must be paid to the logistical challenges of managing neurologic emergencies in the setting of the COVID-19 pandemic. Thoughtful modifications of protocols allow for efficient delivery of high-quality care for all patients while protecting health care providers from viral exposure during the pandemic. Although the percentage of SARS-CoV-2 infections associated with neurologic emergencies is small, the large and still growing number of total infected individuals will likely result in a high burden of COVID-19 associated neurologic disease.[39] COVID-19–associated

cerebrovascular disease and seizure are areas of active research that require further investigation to clarify their pathophysiology and determine optimal treatment measures.

CLINICS CARE POINTS

- Institutions should create protocols for managing neurologic emergencies during the pandemic that allow for rapid and thorough evaluation of patients while also minimizing viral exposure to other patients and staff.
- Less than 5% of patients with COVID-19 will have cerebrovascular complications and these typically occur in patients who are critically ill.
- PWE may face significant challenges with regards to care and prevention of seizures, but thus far there does not seem to be an increase in ED presentations with seizure
- Seizure is a rare complication of COVID-19 with AED selection impacted by concurrent organ failure, drug–drug interactions with COVID therapies, and ongoing drug shortages.

DISCLOSURE

The authors have nothing to disclose.

REFERENCES

1. LitCovid. Available at: https://www.ncbi.nlm.nih.gov/research/coronavirus/. Accessed November 10, 2020.
2. Cervantes-Arslanian A, Lau KHV, Anand P, et al. Rapid dissemination of protocols for managing neurology inpatients with COVID-19. Ann Neurol 2020; 88(2):211–4.
3. Pezzini A, Padovani A. Lifting the mask on neurological manifestations of COVID-19. Nat Rev Neurol 2020. https://doi.org/10.1038/s41582-020-0398-3.
4. Ford T, Curiale G, Nguyen TN, et al. Optimization of resources and modifications in acute ischemic stroke care in response to the global COVID-19 pandemic. J Stroke Cerebrovasc Dis 2020. https://doi.org/10.1016/j.jstrokecerebrovasdis.2020.104980.
5. Khosravani H, Rajendram P, Notario L, et al. Protected code stroke: hyperacute stroke management during the coronavirus disease 2019 (COVID-19) pandemic. Stroke 2020. https://doi.org/10.1161/STROKEAHA.120.029838.
6. On Behalf of the AHA/ASA Stroke Council Leadership. Temporary emergency guidance to US stroke centers during the coronavirus disease 2019 (COVID-19) pandemic: on behalf of the American Heart Association/American Stroke Association Stroke Council Leadership. Stroke 2020;51(6):1910–2.
7. Yang B, Wang T, Chen J, et al. Impact of the COVID-19 pandemic on the process and outcome of thrombectomy for acute ischemic stroke. J Neurointerv Surg 2020. https://doi.org/10.1136/neurintsurg-2020-016177.
8. Kerleroux B, Fabacher T, Bricout N, et al. Mechanical thrombectomy for acute ischemic stroke amid the COVID-19 outbreak: decreased activity, and increased care delays. Stroke 2020. https://doi.org/10.1161/STROKEAHA.120.030373.
9. Nguyen T, Abdalkader M, Jovin T. Mechanical thrombectomy in the era of COVID-19. Emergency preparedness for the neuroscience teams. Stroke 2020;51(6):1896–901.

10. Canelli R, Connor CW, Gonzalez M, et al. Barrier enclosure during endotracheal intubation. N Engl J Med 2020;382(20):1957–8.
11. Mansour OY, Malik AM, Linfante I. Mechanical Thrombectomy of COVID-19 positive acute ischemic stroke patient: a case report and call for preparedness. BMC Neurol 2020. https://doi.org/10.1186/s12883-020-01930-x.
12. Powers WJ, Rabinstein AA, Ackerson T, et al. Guidelines for the Early Management of Patients With Acute Ischemic Stroke: 2019 Update to the 2018 Guidelines for the Early Management of Acute Ischemic Stroke: a guideline for healthcare professionals from the American Heart Association/American Stroke Association. Stroke 2019;50(12). https://doi.org/10.1161/STR.0000000000000211.
13. Faigle R, Butler J, Carhuapoma JR, et al. Safety trial of low-intensity monitoring after thrombolysis: optimal post tpa-iv monitoring in ischemic STroke (OPTIMIST). Neurohospitalist 2020;10(1):11–5.
14. George AJ, Boehme AK, Dunn CR, et al. Trimming the fat in acute ischemic stroke: an assessment of 24-h CT Scans in tPA Patients. Int J Stroke 2015;10(1):37–41.
15. Guhwe M, Utley-Smith Q, Blessing R, et al. Routine 24-hour computed tomography brain scan is not useful in stable patients post intravenous tissue plasminogen activator. J Stroke Cerebrovasc Dis 2016;25(3):540–2.
16. Dafer RM, Osteraas ND, Biller J. Acute stroke care in the coronavirus disease 2019 pandemic. J Stroke Cerebrovasc Dis 2020. https://doi.org/10.1016/j.jstrokecerebrovasdis.2020.104881.
17. Gioia LC, Poppe AY, Laroche R, et al. Streamlined Poststroke Treatment Order Sets During the SARS-CoV-2 pandemic: simplifying while not compromising care. Stroke 2020. https://doi.org/10.1161/STROKEAHA.120.031008.
18. Esenwa C, Parides MK, Labovitz DL. The effect of COVID-19 on stroke hospitalizations in New York City. J Stroke Cerebrovasc Dis 2020. https://doi.org/10.1016/j.jstrokecerebrovasdis.2020.105114.
19. Cummings C, Almallouhi E, Al Kasab S, et al. Blacks are less likely to present with strokes during the COVID-19 pandemic: observations from the buckle of the stroke belt. Stroke 2020. https://doi.org/10.1161/STROKEAHA.120.031121.
20. de Havenon A, Ney J, Callaghan B, et al. A Rapid Decrease in Stroke, Acute Coronary Syndrome, and Corresponding Interventions at 65 United States Hospitals Following Emergence of COVID-19. medRxiv 2020. https://doi.org/10.1101/2020.05.07.20083386.
21. Ghanchi H, Takayanagi A, Savla P, et al. Effects of the COVID-19 pandemic on stroke patients. Cureus 2020. https://doi.org/10.7759/cureus.9995.
22. Sharma M, Lioutas V-A, Madsen T, et al. Decline in stroke alerts and hospitalisations during the COVID-19 pandemic. Stroke Vasc Neurol 2020. https://doi.org/10.1136/svn-2020-000441.
23. Bres Bullrich M, Fridman S, Mandzia JL, et al. COVID-19: stroke admissions, emergency department visits, and prevention clinic referrals. Can J Neurol Sci 2020. https://doi.org/10.1017/cjn.2020.101.
24. Wang J, Chaudhry SA, Tahsili-Fahadan P, et al. The impact of COVID-19 on acute ischemic stroke admissions: analysis from a community-based tertiary care center. J Stroke Cerebrovasc Dis 2020. https://doi.org/10.1016/j.jstrokecerebrovasdis.2020.105344.
25. Meza HT, Lambea GÁ, Saldaña AS, et al. Impact of COVID-19 outbreak on ischemic stroke admissions and in-hospital mortality in North-West Spain. Int J Stroke 2020;15(7):755–62.

26. Rinkel LA, Prick JCM, Slot RER, et al. Impact of the COVID-19 outbreak on acute stroke care. J Neurol 2020. https://doi.org/10.1007/s00415-020-10069-1.
27. Diegoli H, Magalhães PSC, Martins SCO, et al. Decrease in hospital admissions for transient ischemic attack, mild, and moderate stroke during the COVID-19 era. Stroke 2020. https://doi.org/10.1161/STROKEAHA.120.030481.
28. Hasan ATMH, Das SC, Islam MS, et al. Impact of COVID-19 on hospital admission of acute stroke patients in Bangladesh. PLoS One 2020. https://doi.org/10.1101/2020.09.28.316448.
29. Paliwal PR, Tan BYQ, Leow AST, et al. Impact of the COVID-19 pandemic on hyperacute stroke treatment: experience from a comprehensive stroke centre in Singapore. J Thromb Thrombolysis 2020. https://doi.org/10.1007/s11239-020-02225-1.
30. Saxhaug Kristoffersen E, Holt Jahr S, Thommessen B, et al. Effect of COVID-19 pandemic on stroke admission rates in a Norwegian population. Acta Neurol Scand 2020. https://doi.org/10.1111/ane.13307.
31. Neves Briard J, Ducroux C, Jacquin G, et al. Early impact of the COVID-19 pandemic on acute stroke treatment delays. Can J Neurol Sci 2020. https://doi.org/10.1017/cjn.2020.160.
32. Darehed D, Blom M, Glader E-L, et al. In-hospital delays in stroke thrombolysis: every minute counts. Stroke 2020;51(8):2536–9.
33. Helms J, Kremer S, Merdji H, et al. Neurologic Features in Severe SARS-CoV-2 Infection. N Engl J Med 2020;382(23):2268–70.
34. Melmed KR, Cao M, Dogra S, et al. Risk factors for intracerebral hemorrhage in patients with COVID-19. J Thromb Thrombolysis 2020. https://doi.org/10.1007/s11239-020-02288-0.
35. Nwajei F, Anand P, Abdalkader M, et al. Cerebral Venous Sinus Thromboses in Patients with SARS-CoV-2 infection: three cases and a review of the literature. J Stroke Cerebrovasc Dis 2020. https://doi.org/10.1016/j.jstrokecerebrovasdis.2020.105412.
36. Anand P, Lau KHV, Chung DY, et al. Posterior reversible encephalopathy syndrome in patients with coronavirus disease 2019: two cases and a review of the literature. J Stroke Cerebrovasc Dis 2020;29(11):105212.
37. Dakay K, Kaur G, Gulko E, et al. Reversible cerebral vasoconstriction syndrome and dissection in the setting of COVID-19 infection. J Stroke Cerebrovasc Dis 2020;29(9):105011.
38. Pugin D, Vargas M-I, Thieffry C, et al. COVID-19–related encephalopathy responsive to high-dose glucocorticoids. Neurology 2020;95(12):543–6.
39. Ellul MA, Benjamin L, Singh B, et al. Neurological associations of COVID-19. Lancet Neurol 2020;19(9):767–83.
40. Mao L, Jin H, Wang M, et al. Neurologic manifestations of hospitalized patients with coronavirus disease 2019 in Wuhan, China. JAMA Neurol 2020. https://doi.org/10.1001/jamaneurol.2020.1127.
41. Li Y, Li M, Wang M, et al. Acute cerebrovascular disease following COVID-19: a single center, retrospective, observational study. Stroke Vasc Neurol 2020;5(3):279–84.
42. Majidi S, Fifi JT, Ladner TR, et al. Emergent large vessel occlusion stroke during New York City's COVID-19 outbreak: clinical characteristics and paraclinical findings. Stroke 2020. https://doi.org/10.1161/STROKEAHA.120.030397.
43. Kihira S, Schefflein J, Mahmoudi K, et al. Association of Coronavirus Disease (COVID-19) with large vessel occlusion strokes: a case-control study. AJR Am J Roentgenol 2020;29:1–6.

44. Rothstein A, Oldridge O, Schwennesen H, et al. Acute cerebrovascular events in hospitalized COVID-19 patients. Stroke 2020. https://doi.org/10.1161/STROKEAHA.120.030995.
45. Jillella DV, Janocko NJ, Nahab F, et al. Ischemic stroke in COVID-19: an urgent need for early identification and management. PLoS One 2020. https://doi.org/10.1371/journal.pone.0239443.
46. Yaghi S, Ishida K, Torres J, et al. SARS-CoV-2 and Stroke in a New York Healthcare System. Stroke 2020;51(7):2002–11.
47. Siegler JE, Cardona P, Arenillas JF, et al. Cerebrovascular events and outcomes in hospitalized patients with COVID-19: the SVIN COVID-19 Multinational Registry. Int J Stroke 2020. https://doi.org/10.1177/1747493020959216. 174749302095921.
48. Benussi A, Pilotto A, Premi E, et al. Clinical characteristics and outcomes of inpatients with neurologic disease and COVID-19 in Brescia, Lombardy, Italy. Neurology 2020;95(7):e910–20.
49. Ntaios G, Michel P, Georgiopoulos G, et al. Characteristics and outcomes in patients with COVID-19 and acute ischemic stroke: the Global COVID-19 Stroke Registry. Stroke 2020. https://doi.org/10.1161/STROKEAHA.120.031208.
50. Dogra S, Jain R, Cao M, et al. Hemorrhagic stroke and anticoagulation in COVID-19. J Stroke Cerebrovasc Dis 2020;29(8):104984.
51. Kvernland A, Kumar A, Yaghi S, et al. Anticoagulation use and Hemorrhagic Stroke in SARS-CoV-2 Patients Treated at a New York Healthcare System. Neurocrit Care 2020. https://doi.org/10.1007/s12028-020-01077-0.
52. Beyrouti R, Adams ME, Benjamin L, et al. Characteristics of ischaemic stroke associated with COVID-19. J Neurol Neurosurg Psychiatry 2020;91(8):889–91.
53. Zhang Y, Xiao M, Zhang S, et al. Coagulopathy and antiphospholipid antibodies in patients with Covid-19. N Engl J Med 2020;382(17):e38.
54. Bhaskar S, Sinha A, Banach M, et al. Cytokine storm in COVID-19-immunopathological mechanisms, clinical considerations, and therapeutic approaches: the REPROGRAM Consortium position paper. Front Immunol 2020;11:1648.
55. Divani AA, Andalib S, Di Napoli M, et al. Coronavirus disease 2019 and stroke: clinical manifestations and pathophysiological insights. J Stroke Cerebrovasc Dis 2020;29(8):104941.
56. South AM, Tomlinson L, Edmonston D, et al. Controversies of renin-angiotensin system inhibition during the COVID-19 pandemic. Nat Rev Nephrol 2020;16(6):305–7.
57. Gulko E, Overby P, Ali S, et al. Vessel Wall Enhancement and Focal Cerebral Arteriopathy in a Pediatric Patient with Acute Infarct and COVID-19 Infection. AJNR Am J Neuroradiol 2020;41(12):2348–50.
58. Shulman JG, Cervantes-Arslanian AM. Infectious Etiologies of Stroke. Semin Neurol 2019;39(4):482–94.
59. Bhattacharjee S, Banerjee M. Immune thrombocytopenia secondary to COVID-19: a systematic review. SN Compr Clin Med 2020;1–11. https://doi.org/10.1007/s42399-020-00521-8.
60. Tang N, Li D, Wang X, et al. Abnormal coagulation parameters are associated with poor prognosis in patients with novel coronavirus pneumonia. J Thromb Haemost 2020;18(4):844–7.
61. Thachil J, Tang N, Gando S, et al. ISTH interim guidance on recognition and management of coagulopathy in COVID-19. J Thromb Haemost 2020;18(5):1023–6.

62. National Institute of Neurological Disorders and Stroke rt-PA Stroke Study Group. Tissue plasminogen activator for acute ischemic stroke. N Engl J Med 1995;333(24):1581–7.
63. Hacke W, Kaste M, Bluhmki E, et al. Thrombolysis with alteplase 3 to 4.5 hours after acute ischemic stroke. N Engl J Med 2008;359(13):1317–29.
64. Tan Y-K, Goh C, Leow AST, et al. COVID-19 and ischemic stroke: a systematic review and meta-summary of the literature. J Thromb Thrombolysis 2020. https://doi.org/10.1007/s11239-020-02228-y.
65. Carneiro T, Dashkoff J, Leung LY, et al. Intravenous tPA for Acute Ischemic Stroke in Patients with COVID-19. J Stroke Cerebrovasc Dis 2020. https://doi.org/10.1016/j.jstrokecerebrovasdis.2020.105201.
66. Oxley TJ, Mocco J, Majidi S, et al. Large-vessel stroke as a presenting feature of Covid-19 in the young. N Engl J Med 2020;382(20):e60.
67. Baracchini C, Pieroni A, Viaro F, et al. Acute Stroke Management Pathway During Coronavirus-19 Pandemic. Neurol Sci 2020;41:1003–5.
68. Pop R, Hasiu A, Bolognini F, et al. Stroke thrombectomy in patients with COVID-19: initial experience in 13 cases. AJNR Am J Neuroradiol 2020. https://doi.org/10.3174/ajnr.A6750. ajnr;ajnr.A6750v1.
69. Escalard S, Maïer B, Redjem H, et al. Treatment of acute ischemic stroke due to large vessel occlusion with COVID-19: experience from Paris. Stroke 2020;51(8):2540–3.
70. Wang A, Mandigo GK, Yim PD, et al. Stroke and mechanical thrombectomy in patients with COVID-19: technical observations and patient characteristics. J Neurointerv Surg 2020;12(7):648–53.
71. Albert DVF, Das RR, Acharya JN, et al. The Impact of COVID-19 on epilepsy care: a survey of the American Epilepsy Society membership. Epilepsy Curr 2020;20(5):316–24.
72. Lai S-L, Hsu M-T, Chen S-S. The impact of SARS on epilepsy: the experience of drug withdrawal in epileptic patients. Seizure 2005;14(8):557–61.
73. Cheli M, Dinoto A, Olivo S, et al. SARS-CoV-2 pandemic and epilepsy: the impact on emergency department attendances for seizures. Seizure 2020;82:23–6.
74. French JA, Brodie MJ, Caraballo R, et al. Keeping people with epilepsy safe during the COVID-19 pandemic. Neurology 2020;94(23):1032–7.
75. Florez-Perdomo WA, Serrato-Vargas SA, Bosque-Varela P, et al. Relationship between the history of cerebrovascular disease and mortality in COVID-19 patients: a systematic review and meta-analysis. Clin Neurol Neurosurg 2020;197:106183.
76. Pranata R, Huang I, Lim MA, et al. Impact of cerebrovascular and cardiovascular diseases on mortality and severity of COVID-19-systematic review, meta-analysis, and meta-regression. J Stroke Cerebrovasc Dis 2020;29(8):104949.
77. Brophy GM, Bell R, Claassen J, et al. Guidelines for the evaluation and management of status epilepticus. Neurocrit Care 2012;17(1):3–23.
78. Rola P, Farkas J, Spiegel R, et al. Rethinking the early intubation paradigm of COVID-19: time to change gears? Clin Exp Emerg Med 2020;7(2):78–80.
79. Matta A, Chaudhary S, Bryan Lo K, et al. Timing of Intubation and Its Implications on Outcomes in Critically Ill Patients With Coronavirus Disease 2019 Infection. Crit Care Explorations 2020;2(10):e0262.
80. Tran K, Cimon K, Severn M, et al. Aerosol generating procedures and risk of transmission of acute respiratory infections to healthcare workers: a systematic review. PLoS One 2012;7(4):e35797.

81. Schünemann HJ, Khabsa J, Solo K, et al. Ventilation techniques and risk for transmission of coronavirus disease, including COVID-19: a living systematic review of multiple streams of evidence. Ann Intern Med 2020;173(3):204–16.
82. Wunsch H. Mechanical ventilation in COVID-19: interpreting the current epidemiology. Am J Respir Crit Care Med 2020;202(1):1–4.
83. Choo EK, Rajkumar SV. Medication shortages during the COVID-19 crisis: what we must do. Mayo Clin Proc 2020;95(6):1112–5.
84. Ortoleva J. Consider Adjunctive Ketamine in Mechanically Ventilated Coronavirus Disease-2019 Patients. J Cardiothorac Vasc Anesth 2020;34(10):2580.
85. Dale O, Somogyi AA, Li Y, et al. Does intraoperative ketamine attenuate inflammatory reactivity following surgery? A systematic review and meta-analysis. Anesth Analg 2012;115(4):934–43.
86. Anand P, Al-Faraj A, Sader E, et al. Seizure as the presenting symptom of COVID-19: a retrospective case series. Epilepsy Behav 2020;112:107335.
87. Vollono C, Rollo E, Romozzi M, et al. Focal status epilepticus as unique clinical feature of COVID-19: a case report. Seizure 2020;78:109–12.
88. Anand P, Zakaria A, Benameur K, et al. Myoclonus in patients with coronavirus disease 2019: a multicenter case series. Crit Care Med 2020. https://doi.org/10.1097/CCM.0000000000004570.
89. Alotaibi F, Althani Z, Aljaafari D, et al. Saudi Epilepsy Society consensus on epilepsy management during the COVID-19 Pandemic. Neurosciences (Riyadh) 2020;25(3):222–5.
90. Gélisse P, Rossetti AO, Genton P, et al. How to carry out and interpret EEG recordings in COVID-19 patients in ICU? Clin Neurophysiol 2020;131(8):2023–31.
91. Hirsch LJ, LaRoche SM, Gaspard N, et al. American Clinical Neurophysiology Society's Standardized Critical Care EEG Terminology: 2012 version. J Clin Neurophysiol 2013;30(1):1–27.
92. Rice JK, Rorden C, Little JS, et al. Subject position affects EEG magnitudes. Neuroimage 2013;64:476–84.
93. Lu L, Xiong W, Liu D, et al. New onset acute symptomatic seizure and risk factors in coronavirus disease 2019: a retrospective multicenter study. Epilepsia 2020;(6):61. https://doi.org/10.1111/epi.16524.
94. Narula N, Joseph R, Katyal N, et al. Seizure and COVID-19: association and review of potential mechanism. Neurol Psychiatry Brain Res 2020;38:49–53.
95. Anand P, Zhou L, Bhadelia N, et al. Neurologic findings among inpatients with COVID-19 at a safety-net US hospital. Neurol Clin Pract 2020. https://doi.org/10.1212/CPJ.0000000000001031.
96. Claassen J, Mayer SA, Kowalski RG, et al. Detection of electrographic seizures with continuous EEG monitoring in critically ill patients. Neurology 2004;62(10):1743–8.
97. Sohal S, Mansur M. COVID-19 presenting with seizures. IDCases 2020;20:e00782.
98. Moriguchi T, Harii N, Goto J, et al. A first case of meningitis/encephalitis associated with SARS-Coronavirus-2. Int J Infect Dis 2020;94:55–8.
99. Karimi N, Sharifi Razavi A, Rouhani N. Frequent convulsive seizures in an adult patient with COVID-19: a case report. Iranian Red Crescent Med J 2020;22(3). https://doi.org/10.5812/ircmj.102828.
100. Asadi-Pooya AA, Attar A, Moghadami M, et al. Management of COVID-19 in people with epilepsy: drug considerations. Neurol Sci 2020;41(8):2005–11.