In acute neurologic care settings, time-sensitive neuro-monitoring is essential for appropriate triage and treatment. Neurologic manifestations of coronavirus disease 2019 (COVID-19) infection (e.g., seizures, cerebrovascular events, and intracranial hemorrhage) are increasingly being recognized.\(^1\) Although clinical neurologic examination remains the standard for monitoring in the neurocritical care unit, changes in the neurologic examination can be late symptoms of neurologic complications, especially when individuals are sedated. Multimodal monitoring in critically ill persons with COVID-19 enables real-time detection of neurologic complications for prompt diagnosis and subsequent management. Common monitoring techniques include EEG, transcranial Doppler ultrasonography (TCD), pupillometry, optic nerve sheath diameter (ONSD), near-infrared spectroscopy (NIRS), and neuroimaging. In this review, we address noninvasive neuromonitoring techniques and their application during the COVID-19 pandemic.

**EEG**

Clinical events concerning for seizures, poor recovery after discontinuing sedation, and persistent encephalopathy are leading reasons for EEG requests in the COVID-19 pandemic.\(^2,3\)

To date, studies have not identified an EEG finding that is more specific to severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) than other viruses.\(^3\) Multiple metabolic abnormalities and ongoing hypoxic and inflammatory processes may contribute to an abnormal EEG background.\(^4\) EEG patterns in hypoxic-ischemic encephalopathy (HIE) can range from generalized periodic discharges (GPDs) to burst suppression and electrographic silence.\(^5\) In patients with COVID-19, the most common EEG findings are background abnormalities (e.g., the absence of a posterior dominant rhythm and generalized theta or delta slowing).\(^3,6-8\)

A study of 94 EEGs from 62 people with COVID-19 suggests that about one-fifth of interictal epileptiform activity was generalized, whereas the rest was focal and most commonly localized to the frontal lobes.\(^7\) A small case series suggests that the principal cause of prolonged comatose state after sedation withdrawal is COVID-19–related encephalopathy, not nonconvulsive status epilepticus, and can manifest with an alpha coma pattern.\(^9\)

Several barriers to EEG monitoring of those with COVID-19, such as prone positioning and contamination risk, have prompted minimizing procedures. Although a full 10 to 20 complement of electrodes with an ECG derivation remains the standard, some hospitals have used an 8-channel headband EEG system (8ch-EEG) to reduce health care personnel exposure to COVID-19. 8ch-EEG can be applied quickly by personnel without prior technological training (Figure 1).\(^3,10\)

The 8ch-EEGs provide a rapid and easy EEG-monitoring option; however, they are not able to detect some abnormalities, such as focal slowing and paroxysmal abnormalities, which may be important for diagnosing and managing acute neurologic complications in critically ill persons with COVID-19.
monitoring method to screen for status epilepticus; however, the electrode coverage, which includes 8 bipolar channels (frontal, temporal, and occipital), can limit the capacity to fully localize and characterize specific waveforms.\textsuperscript{10} Even with this reduced montage, 8ch-EEGs can help triage individuals whose clinical picture is concerning for status epilepticus and determine the need for a complete montage. It is important to note that reduced montages may result in difficulties in identifying artifacts and lateralized periodic discharges of the temporal lobe and inferior frontal lobe.\textsuperscript{11} In the prone position, the reading neurophysiologist may see artifacts commonly seen in the occipital leads of supine patients as they contact the pillow or bed in the frontopolar leads.\textsuperscript{11}

**TCD**

TCD is a sonographic study most commonly used to assess the hemodynamic state of the vertebrobasilar system and the circle of Willis. Clinicians can use TCD to noninvasively monitor cerebral blood flow by measuring the mean flow velocities in the proximal cerebral arteries. TCD evaluates cerebral blood flow in large intracranial arteries; thus, it may not specifically analyze impairment of the microcirculation. To date, no studies detail TCD findings in individuals with COVID-19.

Continuous TCDs may allow for real-time detection of acute large vessel occlusions (LVOs), abnormal autoregulation, emboli, and evolving cerebral edema (Figure 2). In individuals undergoing continuous TCD, an increasing waveform pulsatility index (PI), flow resistance, or newly absent flow may prompt an angiogram to evaluate for high-grade stenosis or occlusion.\textsuperscript{12} Ultrasonographers may see arterial dilation, which leads to increased cerebral blood flow during acute hypoxic episodes, especially in the vertebral arteries.\textsuperscript{13,14} These acute changes are reversible after restoring normoxia.\textsuperscript{13} TCDs of patients on mechanical circulatory devices such as venoarterial extracorporeal membrane oxygenation (VA-ECMO) can show continuous flow without clear systolic peaks.\textsuperscript{15} A small case series of people with COVID-19 pneumonia who were mechanically ventilated reported the presence of microbubbles after the injection of agitated saline. In this study, the number of microbubbles detected by TCD was inversely correlated with declining PaO\textsubscript{2}:FiO\textsubscript{2}, suggesting that pulmonary vasodilation may be a significant cause of hypoxemia in patients with COVID-19.\textsuperscript{16}

Although not widely available, robotic TCD can allow the acquisition of uninterrupted extended duration recordings with minimal staff contact.\textsuperscript{17} However, for those with other significant medical issues, including those who require proning, neck cannulation for ECMO, or unstable cervical spines, robotic TCD may not be tolerated.\textsuperscript{17} Physicians can consider limiting routine TCD in asymptomatic patients to the artery of concern to minimize patient and staff exposure.

**Pupillometry**

Pupillometry is a noninvasive neuromonitoring modality frequently used in neurocritical care units. The Neurological Pupil index (NPi) is a standardized measure of pupil size, constriction velocity, latency, and dilation velocity and may be the first sign of impending clinical deterioration.\textsuperscript{18,19} A case series of people with COVID-19 and no evidence of other primary neurologic injury suggests that pupillary light reflex (PLR) is not significantly different in individuals with

![Figure 2. Transcranial doppler of the middle cerebral artery (MCA). A right MCA during a bubble injection shows 1 microembolus (A) and a left MCA shows an abnormally elevated pulsatility index (B).](image-url)
COVID-19. Although further studies are needed, pupillometry remains an important neuromonitoring modality, particularly among the sickest patients who are heavily sedated and paralyzed.

**ONSD**

ONSD is a useful noninvasive technique that can be used to identify individuals with increased intracranial pressure (ICP). Persons with COVID-19 infection are at risk of neurologic complications that may result in increased ICP. The optic nerve is thickest approximately 3 mm behind the retina and then narrows as it continues posteriorly into the orbital cavity. The increased ICP is transmitted through the cerebrospinal fluid in the orbital cavity, causing distention of the optic nerve sheath. Increased ICP has been associated with increased ONSD in patients with subarachnoid hemorrhage (SAH), intracranial hemorrhage (ICH), and traumatic brain injury (TBI).

In the setting of the COVID-19 pandemic, where imaging and testing that are unlikely to change management are minimized to prevent patient and staff exposure, ONSD can be a helpful tool to identify those at risk of increased ICP and in need of head imaging. Although the ONSD measurement technique can vary, axial measurement by the transverse placement of the ultrasound probe through the upper eyelid may be more predictive of high ICP (Figure 3). Currently, there is no optimal cutoff to predict an ICP greater than 20 mm Hg, although studies suggest it is 5 to 6.2 mm.

In addition to TCD and ONSD, cranial ultrasound can be a bedside tool to assess for midline shift, hematoma, or ischemia in those who have undergone hemianectomy. A small study found a similar correlation between ventricular diameter measurements by ultrasound and CT, although ultrasound may slightly underestimate the midline shift. Although head CT remains the standard, cranial ultrasound can be a useful bedside tool to assess the need for further imaging.

**NIRS**

NIRS can be used to measure cerebral oxygenation noninvasively. NIRS devices estimate regional cerebral oxygenation by using 2 photoelectrodes, 1 shallow and 1 deep. The difference between the data from the shallow electrode and the deep electrode yields the regional cerebral tissue oxygen saturation (rSO2), which is a combination of the venous, arterial, and microcirculatory hemoglobin concentration. As NIRS only measures 2.5 cm beneath the skin of the frontal bone, its use is limited in cases of frontal pneumocephalus, contusion, and hematoma. Electrodes are placed within the watershed area between the middle cerebral artery (MCA) and anterior cerebral artery (ACA) territories, which are sensitive to oxygenation changes.

Lower rSO2 has been linked with worse neurologic outcomes after cardiac surgery, cardiopulmonary resuscitation, decompensated heart failure, and aneurysmal subarachnoid hemorrhage. In addition, rSO2 may decrease during hemodialysis sessions, which is especially relevant considering that renal failure is seen with COVID-19. Individuals who are critically ill with delirium also tend to have lower rSO2.

More research is needed on the role of NIRS during the COVID-19 pandemic. Potential uses include monitoring for fluctuations in cerebral oxygenation, early identification of cerebral hypoxia in patients using noninvasive ventilation, and potentially a role in prognosticating cognitive function in survivors of COVID-19 associated severe acute respiratory distress syndrome (ARDS). The ongoing NIRS-COVA trial, is recruiting participants to investigate whether cerebral oxygenation could be a more useful parameter than peripheral oxygen saturation to guide clinical titration of permissive hypoxemia in those with COVID-19 ARDS.

**CT and MRI**

The need for sedation and paralysis for ventilator management can preclude neurologic examination in severe COVID-19. The most common indications for brain imaging in hospitalized people with confirmed COVID-19 are delirium or confusion, new focal neurologic deficits, and depressed level of alertness. Considering the risk for serious
neurologic complications, patients with new focal neurologic deficits or prolonged altered mental status should undergo urgent brain imaging to rule out neurologic emergencies (eg, ICH or large territory ischemic stroke), which may prompt changes in management.

In some, transportation to a CT or MRI suite may be difficult owing to patient instability or the need for monitoring staff and equipment.36 CT and MRI availability may also be limited by the need for constant decontamination and concern for viral spread throughout the hospital, which may cause delays in image acquisition. Some hospitals have made point-of-care CT and MRI available. Portable CT scanners have the added benefit of providing imaging results faster than conventional CT scanners, although poorer spatial resolution may limit evaluation of subtle cerebral edema or early infarct signs (Figure 4).37 Whereas transporting a person who is critically ill to an imaging suite and obtaining the images may take approximately 50 minutes, a portable CT scan can be done in approximately 20 minutes.37 Likewise, point-of-care MRI is compatible with nearby ferromagnetic materials and eliminates the need for a controlled environment.38 Portable MRI scanners acquire images at low magnetic-field strength and have an open design convenient for patient positioning.39 Sequences available on portable MRIs include T1-weighted, T2-weighted, T2 fluid-attenuated inversion recovery (FLAIR) sequences, and diffusion-weighted imaging (DWI).38 Images obtained with portable CT and MRI scanners may have lower resolution, however, they remain a viable option for those who are critically ill with COVID-19.

The imaging manifestations of COVID-19 can vary. The most common MRI findings include FLAIR cortical signal abnormalities, cortical diffusion restriction, and leptomeningeal enhancement.39,40 Other abnormalities have been identified, including microhemorrhages, multifocal white matter hyperintense lesions, infarcts, microhemorrhages, acute necrotizing encephalopathy, inflammatory syndromes (eg, acute disseminated encephalomyelitis [ADEM]), and medial temporal lobe abnormalities.40,41 Gadolinium-enhanced MRI should be used in cases where an inflammatory etiology is suspected (eg, encephalitis or myelitis).42

Figure 4. Portable head CT showing diffuse poor grey-white differentiation.


