

# COVID-19 and the perioperative neuroscience - A narrative review

## ABSTRACT

Among the several medical specialties, anesthesiologists are probably the most affected ones from the coronavirus disease (COVID-19) pandemic as they are at the frontline. In the present stage of the pandemic, where we are observing community transmission, more people with elective neurologic and neurosurgical problems are likely to be tested positive for this virulent disease. Neuroanesthesiologists play an important role in the perioperative period and in neuroradiology suite. It is imperative to know the best available ways by which health care providers can manage their patients and also necessary steps to prevent the spread of infection, not only amongst themselves but also between patients. A high index of suspicion in such patients may help avoid delay in diagnosis and catastrophic sequelae. An overall knowledge about the disease will help plan the clinical management of neurologic patients, during the perioperative period.

**Key words:** COVID-19; neuroradiology; neuroanesthesia; neurocritical care


## Introduction

The pandemic caused by the novel corona virus disease (COVID-19) has stirred medical fraternity tremendously, bringing about significant change in their routine practice. Anesthesiologists are probably the worst inflicted, as they are at the frontline of this pandemic. They are involved in the perioperative care of the patients, dealing with aerosol generating procedures like tracheal intubation and extubation, mechanical ventilation, tracheostomy, cardio-pulmonary resuscitation, placement of central lines and so forth. With more patients of COVID-19 presenting with neurologic symptoms, a rise in neurosurgical emergencies has been observed, along with the routine elective procedures. In the present stage of the pandemic, where we are observing

community transmission, more people with elective neurologic and neurosurgical problems are likely to be tested positive for this virulent disease. It is imperative to know the best available ways by which health care providers can manage their patients and also necessary steps to prevent the spread of infection, not only amongst themselves but also between patients.

## Neurological Presentations of COVID Patients

Some of the initial symptoms related to the disease were fever, respiratory distress, cough, chills, fatigue, headache and palpitations.<sup>[1]</sup> Over a period of time, the neuroinvasive properties of this virus have also been recognized. As the

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## INDU KAPOOR, CHARU MAHAJAN, HEMANSHU PRABHAKAR

Department of Neuroanaesthesiology and Critical Care, All India Institute of Medical Sciences (A.I.I.M.S.), New Delhi, India

**Address for correspondence:** Dr. Hemanshu Prabhakar, Professor, Department of Neuroanaesthesiology and Critical Care, Neurosciences Centre, A.I.I.M.S., New Delhi - 110 029, India. E-mail: prabhakaraiims@yahoo.co.in

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disease progressed, a change in symptomatology was noted and many patients presented with neurologic symptoms.<sup>[2,3]</sup> Neurologic manifestations could be divided into central nervous system manifestations (dizziness, headache, impaired consciousness, acute cerebrovascular disease, ataxia, and seizure), peripheral nervous system manifestations (taste impairment, smell impairment, vision impairment, and nerve pain), and skeletal muscular injury manifestations.<sup>[4]</sup> Some of the severe neurological presentations that have been reported are cases of encephalopathy, encephalitis,<sup>[5]</sup> necrotising haemorrhagic encephalopathy,<sup>[6]</sup> stroke,<sup>[7]</sup> epileptic seizures, rhabdomyolysis and Guillain-Barre syndrome.<sup>[8]</sup>

### General Principles for Elective and Emergent Neurosurgical Procedures

There is a worldwide agreement that elective cases should be postponed at this time to preserve essential supplies which we may desperately need as the cases continuously exponentially rise day after day.<sup>[9]</sup> With a surge in COVID-19 cases, it is wise to rationalize the resources for the benefit of whole population. With many patients presenting with neurologic symptoms, it is of utmost importance to diagnose infection early and correctly. Every case should be taken as a positive case until proven otherwise. Despite a negative test, standard precautions should be followed in every case. Appropriate personal protective equipment (PPE), which includes N95 respirators, protection glasses, face shields, double gloves, water impermeable coverall suits, and shoe covers should be used for all involved in patient care. The neurosurgical patients requiring care can be broadly divided into acute, subacute and chronic cases.<sup>[10]</sup> [Table 1] Though there is ambiguity in clearly defining them and has to be decided strategically on case-to-case basis. The acute cases are the ones where surgical intervention is urgently required. Failing this, patients may sustain significant mortality and morbidity. It is advisable to get COVID-19 testing prior to surgery, if time permits, however emergency surgery should not be delayed. All possible precautions should be taken to avoid spread of infection to other HCPs and patients. The risk-benefit of surgery should be evaluated on case-case basis and should be carried out in a planned manner taking all the precautions. In

subacute category, delay of surgery by few days to weeks is believed not to jeopardize health of the patients. In chronic cases, there is no risk of increased morbidity by delay in surgery. Patients should be encouraged to stay at home and should be provided advice through telemedicine facility. These form a vulnerable set of patients who can easily acquire infection. However, if the patient's condition deteriorates at any time, surgical intervention may be done after appropriate testing and resource management. Patients can be classified into confirmed, suspected, high and low risk cases based on the history, symptoms and test reports [Figure 1].<sup>[11]</sup>

### Preanesthetic workup

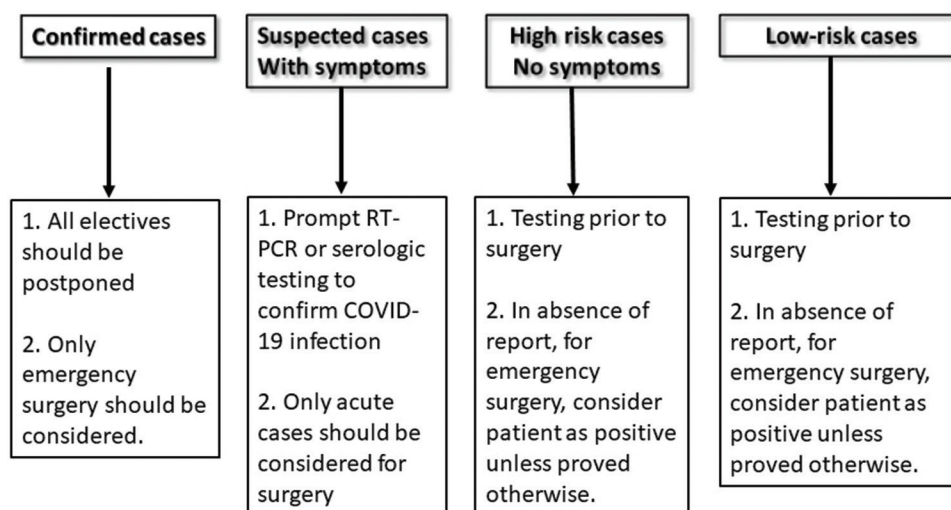
Neurosurgical patients who are admitted should have a dedicated holding area where they can be thoroughly evaluated. Similarly, for intubated patients, a separate dedicated area should be there in neurosurgical ICU for keeping the patients till COVID-19 is ruled out. Personal Protective equipment along with N95 masks should be routinely used while handling these patients.<sup>[12]</sup> All patients should be provided with 3-ply surgical masks for covering their nose and mouth. History of travel, living zone, positive contact history, symptoms and signs focusing on COVID-19 should be elucidated in addition to the neurological complaints. It should be kept in mind that non-symptomatic patients may be infective and pose a threat to HCW and other patients. While there are no clear-cut guidelines to test every patient for COVID-19 prior to surgery, it should be done in all suspected cases who have positive history. All standard investigations as applicable, depending upon indications and type of surgery should be checked. If patient has pulmonary symptoms, arterial blood gas should be checked beforehand. As there is a concern for avoiding auscultation, it is preferable to have a chest X-ray for all patients irrespective of age. Premedication with glycopyrrolate 0.2 mg intravenously before surgery can result in decreased secretions.

### Intraoperative concerns

Suspected cases requiring immediate surgery before availability of the report should be operated in a separate dedicated OR. Segregation of infected patients is important to minimize spread of infection. All precautions should be taken while transfer of patients in hospital, ensuring

**Table 1: Triage of neurosurgical patients during pandemic<sup>[2]</sup>**

Acute	Subacute	Chronic
Raised ICP secondary to Traumatic brain injury Hydrocephalus Tumor Intracranial bleed, Aneurysmal subarachnoid hemorrhage Cauda equina syndrome	Low grade glioma benign tumors arterio-venous malformations unruptured aneurysms Spinal pathology with radiculopathy/myopathy	Benign small intracranial tumors in non-eloquent areas Pituitary adenoma (without vision deterioration), Craniopharyngioma Spine surgeries



**Figure 1: Decision making for patients classified into confirmed, suspected, high and low risk cases**

minimal contact with bystanders. Sanitization of paths, lifts may be required if patient's report is positive. An OR closest to entrance and exit gates makes the path of travel shorter for these patients and reduces the risk of viral spread. The total personnel working in OR should be limited to minimum number required to avoid exposure. OR should be closed at all times and restricted for movement. All should be completely aware of correct steps of donning and doffing of PPE. Negative pressure OR prevents spread of infection. In case of positive pressure OR, air exchange cycle rate  $\geq 25$  cycles/hr helps to decrease viral load inside OR.<sup>[13]</sup> OR should ideally have an independent ventilation system with HEPA filters. The anaesthetic machine and other equipment (USG machine, monitor) may be covered with transparent sheets to reduce contamination as far as possible. For a conscious patient, preoxygenation with rapid sequence intubation, avoiding manual breaths, hypnotic agent followed by opioid and muscle relaxant are some of the suggested steps to decrease aerosol generation.<sup>[14]</sup> A large transparent sheet to cover the patient or aerosol boxes may be used to decrease environment contamination, according to the availability and comfort of the attending anaesthesiologist. Video laryngoscopes can be invaluable in these times avoiding the need to be too close to the patient.<sup>[14]</sup> Awake intubation should be avoided in these patients. If the patient has cervical spine instability, MILS can be used along with VL for intubation. Closed suction should be used whenever possible. Once the tracheal intubation is done, gloves should be removed and replaced with a new pair. HEPA (high-efficiency particulate air) filters should be connected to the patient end of the breathing circuit and other between the expiratory limb and the anaesthetic machine. These filters should be discarded safely and soda lime changed after each case. The use of bone drills and

smoke from use of cautery can produce significant aerosols. Instead of drills, saw has been suggested for cutting bone along with liberal saline irrigation to avoid environmental contamination.<sup>[15]</sup>

There should be minimum change in staff during course of surgery. The extubation requires the application of same principles for minimal aerosol generation. Different techniques of extubation have been described for reducing the environment contamination by generated aerosols.<sup>[16]</sup> Precaution should be taken to avoid cough during extubation. As soon as the patient is extubated, 3-ply surgical mask should be worn over the patient face and over which face mask delivering oxygen can be applied. A barrier enclosure constituted by a transparent plastic box with ventilation ports can be used to cover the head end of the patients while transporting them. Large transparent plastic sheets can be used to cover the patients completely while allowing significant space for breathing comfortably. Any of the techniques may be used depending upon the availability. For patients who are shifted intubated, ensure that the patient is sedated and preferably paralyzed to avoid coughing and bucking on tracheal tube. The phase of disconnecting tracheal tube from anesthesia machine and connecting to transport ventilator is the time for generation of significant aerosol production. To minimize it, the gas flow from the anesthesia machine should be switched off followed by application of a tracheal tube clamp. This should be followed immediately by connecting the patient to transport ventilator. The same steps need to be followed when patient is switched over from transport ventilator to ICU ventilator. This shifting of patients should be done under the cover of large transparent sheets to further minimize environmental contamination.<sup>[17]</sup> Patients should be handed over to another person wearing

appropriate PPE, at the exit of OR, for safe transportation to ICU. Doffing should be done extremely carefully in a dedicated area and medical record should be completed only after doffing. All biomedical wastes should be adequately discarded. The OR along with equipment should be cleaned and sanitized completely.

### Specific scenarios

Transsphenoidal endonasal approach for pituitary surgery is considered one of the high risk procedures for aerosol generation and contamination.<sup>[15]</sup> The nasal mucosa is a source of viral shedding and can easily transmit infection to operating team. The need to operate should be assessed on case-case basis and craniotomy may be considered as an alternative approach for pituitary tumors. All possible precautions should be taken during such procedures.

Another surgery which poses risk in particular during this pandemic is awake craniotomy, which is more of a subacute indication. It should only be done when absolute indicated. Patient is awake and capable of producing significant aerosols if coughs. Minimizing airway manipulation by a combination of RSB and dexmedetomidine can be quite safe and efficient anaesthetic technique for carrying out AC. The oxygen flow should be kept to a minimum desirable level to avoid generation of aerosols by high flow oxygen.

Patients having traumatic brain injury with hematomas and refractory intracranial hypertension require immediate surgery. There will be instances when the COVID-19 testing report will not be available and patient has to be operated immediately. In those scenarios, every patient should be considered as infective and all standard precautions mentioned before should be followed.

The patients with aneurysmal SAH require frequent transportation between ICU, interventional neuroradiology (INR) suite and OR. The intubation should be carried out in a negative pressure isolation room. If not available, patient may be intubated electively in ICU before shifting to INR suite. The areas for donning and doffing should be allocated near the suite. Proper sanitization of radiation protective gear is needed after every case. The radiation protective aprons need to be worn below PPE and may cause significant fatigue when the case runs for a long time. Proper design and fit of aprons should be chosen carefully. The in-hospital transportation needs all precautions as discussed before. The suite needs to be sanitized properly along with all high-touch equipment.

### Postoperative management

All postoperative patients should be shifted to a dedicated area for suspected cases until the COVID-19 infection report

is negative. Subsequently, they can be shifted to other ICU areas, ward or designated COVID-19 area accordingly. The critical care part shall be discussed later on.

## General Principles for Elective and Emergent Neuroradiological Procedures

It is clear that many of the procedures in neuroradiology, may be considered urgent or emergent. These include cranial space occupying lesions with mass effect, intracranial bleeds with impending herniation, intracranial aneurysms, trauma, spine compressions, myelopathy and cauda equina syndrome. Authors from the Endovascular Neurosurgery Research Group provide useful guidance for appropriate prioritization of common neurovascular procedures.<sup>[18]</sup> The Neurointervention staff should be properly trained about the handling of COVID-19 suspected and positive patients; they should be aware of disinfection and sterility and ways to prevent the spread of this contagious disease and at the same time take care of themselves and their immunity status be enhanced by providing improved balanced diet, proper rest and moderate exercise.<sup>[19]</sup> For the safety of the HCPs, all patients posted for procedures in the neuroradiology suite should be erstwhile tested for COVID-19.

Procedures in neuroradiological suites can be performed under monitored anesthesia care (MAC), or general anesthesia (GA). However, the choice of GA versus MAC should be individualized based on the neurological status of the patient and the risk of infection to healthcare personnel. The Consensus Statement from the Society for Neuroscience in Anaesthesiology and Critical Care,<sup>[20]</sup> recommends the use of MAC as best suited for experienced centres with a low rate of conversion from MAC to GA. Irrespective of anaesthetic technique, hemodynamic stability and oxygenation/ventilation should be optimized and maintained within optimal range

## Critical Care Management of Neurologic/Neurosurgical Patients

These patients pose a special challenge as the steps for optimizing oxygenation like high PEEP and permissive hypercapnia may result in aggravation of secondary brain injury by disrupting cerebral homeostasis. Moreover, propensity to multi-organ failure in these patients may make matters worse.

The neurological management of these patients is as per standard protocols keeping in mind cerebral haemodynamics. In addition, the management of the COVID-19 infection

remains more or less symptomatic. The indications of intubation and mechanical ventilation remain same as for any other neurological patient. There are several aerosol producing procedures in ICU like administering high flow oxygen, bag and mask ventilation, intubation, chest physiotherapy, suctioning, non-invasive ventilation, extubation, bronchoscopy, procedures in agitated patients, tracheostomy, circuit changes and cardio-pulmonary resuscitation (CPR).<sup>[21]</sup> All the personnel working in COVID-19 and COVID-19 suspected areas should adorn complete PPE. Those in COVID-19 negative areas still need basic PPE at all times.

### **Pulmonary management**

The probability of this interaction is strong in neurological patients having COVID-19 infection.<sup>[22]</sup> The lung protective ventilation may be opposite to the brain protective strategy and needs to be balanced for optimisation of both. Depending upon lung condition, patients can be categorized into mild, moderate, severe disease. If oxygen saturation is <93%, supplemental oxygen is required.<sup>[14]</sup> Use of bag valve mask or a tight-fitting mask may help to contain aerosol generation.<sup>[14]</sup> Instead of nebulization, multidose inhalers (MDI) may be preferred in spontaneously breathing patients to avoid generation of aerosolized particles. In intubated patients, closed suction system should be used at all times. Mechanical ventilation needs to be implemented early in patients with COVID-19 pneumonia in respiratory failure. Empiric antimicrobials agents may be given till antibiotic sensitivity reports are available.<sup>[23]</sup> Acetaminophen should be used for temperature control.

Patients developing ARDS need to be managed according to the standard ARDS protocol, while ensuring PEEP doesn't compromise cerebral perfusion or decreases blood pressure. The different ventilatory strategies used are volume-controlled mode/pressure control mode, high PEEP, fraction of inspired oxygenation (FiO<sub>2</sub>) as per requirement. For patients having raised ICP, cervical spine instability or decompressive craniectomy, prone positioning may not be an option in these patients. Regular ABG analysis may guide the treatment strategy. Intermittent boluses of neuromuscular blocking agents may be given for decreasing ventilator asynchrony in moderate-severe ARDS. Use of auscultation is discouraged and instead radioimaging or ultrasonography lung can be of immense help.<sup>[24]</sup> Lower respiratory tract samples may be obtained in intubated and mechanically ventilated patients instead of nasopharyngeal/oropharyngeal samples. It is advisable to collect endotracheal aspirates over bronchial wash or bronchoalveolar lavage samples.<sup>[23]</sup> In COVID-19 patients having refractory hypoxemia, the benefit of

veno-venous extracorporeal membrane oxygenation (ECMO) is not clear and possibly risk-benefit ratio will be high.<sup>[23]</sup>

### **Hemodynamic management**

Institution of PEEP, osmotic agents and diuretics may make these patients predisposed to hypotension. These patients may have associated stress cardiomyopathy. Euvolemia should be maintained in each patient, keeping in mind the brain injury and harmful effects of hypotension. Hemodynamic monitoring by USG and cardiac output measurement can guide the management. Dynamic parameters for fluid responsiveness like skin temperature, capillary refilling time, and/or serum lactate should be used for managing patients. Though surviving sepsis guidelines favour conservative over liberal fluid strategy but for neurosurgical patients, care should be taken to maintain cerebral perfusion pressure (CPP) and avoid hypotension.<sup>[23]</sup> Use of crystalloids is recommended over colloids and use of hydroxyethyl starches should be avoided.<sup>[23]</sup> Balanced salt solutions may be preferred over unbalanced solutions. Albumin should not be routinely used for initial resuscitation. Norepinephrine may be used as first-line vasoactive agent followed by vasopressin or epinephrine.<sup>[23]</sup> Besides, echocardiography can guide the choice of vasopressor/ionotropes. For cardiac dysfunction and persistent hypoperfusion despite fluid resuscitation and norepinephrine, dobutamine may be added. Low-dose corticosteroid therapy may be added for refractory hypotension but the evidence is not strong enough.<sup>[23]</sup>

### **Gastrointestinal and renal care**

These patients can have nausea, vomiting (raised ICP) or even diarrhoea (COVID-19 manifestation). The management should be symptomatic with replacement of water and electrolytes. The RT feed should be started in intubated patients as soon as feasible.

For renal care, basic principles have to be followed like maintaining hydration, blood pressure and reducing nephrotoxic agents.

### **Venous thromboembolism prophylaxis**

With a propensity of COVID-19 infection causing thrombosis, Patients may develop deep vein thrombosis, pulmonary embolism and sagittal sinus thrombosis.<sup>[21]</sup> The principles are same as for any neurosurgical patient. Mechanical prophylaxis should be started in every patient and may be switched over to pharmacological prophylaxis as per institutional protocol.

### **Considerations for Special Patient Population**

Without differentiating, the COVID-19 pandemic has affected all ethnicity, gender and ages. The only weapon that fight

against this pandemic is body's immune system which help a person with COVID-19 to cop up with infection and early recovery from disease.

It has been already reported that it has greater impact on geriatric population compared to others. Because of age-related co-morbidities like diabetes, hypertension, cardiovascular disease, and cerebro-vascular disease and change in immune system, geriatric patients are at significant risk of acquiring COVID-19 infection.<sup>[25]</sup> According to a study by Liu *et al.*, the mortality of elderly patients with COVID-19 is higher than that of young and middle aged patients, and the proportion of patients with pneumonia severity index (PSI) grade IV and V is significantly higher than that of young and middle-aged patients.<sup>[26]</sup> They concluded that the elderly patients with COVID-19 are more likely to progress to severe disease compared to younger ones. During this COVID-19 pandemic, another sensitive group are pediatric patients due to their underdeveloped immune system to fight this disease. If we do literature search on children and COVID-19, it show scant initial data on burden of COVID-19 in children.<sup>[27]</sup> However Dong *et al.* observed children of all ages appeared susceptible to COVID-19. There wasn't any significant gender difference. They also concluded that although clinical manifestations of children's COVID-19 cases were generally less severe than those of adult patients, young children, particularly infants, were vulnerable to infection. Furthermore, their study provided strong evidence of human-to-human transmission in infected children.<sup>[28]</sup>

Next, extremely high-risk patient group in this medical crisis are pregnant women due to their altered physiology and immune functions which make them more susceptibility to infection. Current epidemic data indicate that COVID-19 more often affects men than women, but there is still too little data on pregnant women to be certain of the prognosis in this group.<sup>[29]</sup> There are few studies on the incidence of COVID-19 in pregnant women. In a study by Chen *et al.*, 9 women were diagnosed with COVID-19 during the third trimester of pregnancy.<sup>[30]</sup> The clinical symptoms of these pregnant patients were similar to those in adult patients. Liu *et al.* observed that out of 13 pregnant patients, caesarean section was performed in 5 patients (38%). Only one woman had multi-organ failure and was mechanically ventilated and there was a single case of stillbirth.<sup>[31]</sup>

Amongst these highly sensitive groups, geriatric patients had shown significant neurological symptoms which include headache, light headedness and stroke. Mao *et al.* had observed that 36.7% of patients who had neurological manifestation with severe disease were old and had

co-morbidities.<sup>[4]</sup> Out of them, 5.7% of patients with severe coronavirus infection developed cerebrovascular disease later in the course of illness. It has also been found that the total incidence of stroke in COVID-19 patients is about 5% with a median age of 71.6 years.<sup>[7]</sup>

## Resuscitation and Long-term Sequelae

Unexpected cardiac arrest may not be common amongst COVID-19 patients, but it is one of the conditions, HCPs encountering almost every day during present time. They are extremely anxious whether to perform cardiopulmonary resuscitation in these patients or not and thus need clear directions. CPR is one of the high-risk procedures during present COVID-19 pandemic. It involves many steps that aerosolize the virus, thus increases the risk of transmission amongst HCPs.<sup>[32]</sup> World Health Organisation [WHO] has listed CPR as one of the high-risk aerosol generating procedure, for which full PPE should be used which include, PPE gown, N95 mask, gloves, and facial protection.<sup>[33]</sup>

Worldwide, there is confusion over CPR in COVID-19 patients, whether it should be done or not? The current situation shows a system that is in disarray, unprepared, slow, confused, and impassive to frontline workers.<sup>[34]</sup> According to the International Liaison Committee on Resuscitation (ILCOR) recommendation, compression-only resuscitation should be considered with public-access defibrillation.<sup>[35]</sup> They also suggest that it may be reasonable for HCPs to consider defibrillation before donning aerosol generating personal protective equipment in situations where the provider assesses the benefits may exceed the risks.<sup>[35]</sup> The American Heart Association (AHA) has given an interim guidance that resuscitation should be done with door closed during in-hospital cardiac arrest in COVID-19 patients to prevent airborne contamination of adjacent indoor space.<sup>[36]</sup> Patients on ventilator should be left on mechanical ventilator with HEPA filter to maintain a closed circuit and reduce aerosolization. Ventilation mode should be changed to pressure-controlled mode with increase in FiO<sub>2</sub> to 1.0. Limit the pressure as needed to generate adequate chest rise (6 mL/kg ideal body weight for adults, 4-6 mL/kg for neonates).<sup>[36]</sup> On the other hand, the University Hospitals Birmingham NHS Foundation trust has recommended against the CPR in COVID-19 patients unless they are in the emergency department or if the staff are wearing full PPE. According to them, if cardiac arrest in a COVID-19 patient occurs outside the emergency department, defibrillator treatment can be given if they have a "shockable" rhythm. But if it fails to restart the heart, then further resuscitation is considered futile.<sup>[37]</sup> From literature search, it is very clear that the clinicians all over the world are

divided on consensus, whether HCPs should keep low or high threshold for performing CPR in COVID-19 patient in cardiac arrest.<sup>[38]</sup> Furthermore, clear data is required for clinicians to direct towards the management of COVID-19 patients in cardiac arrest.

## Conclusion

To conclude, neurologic manifestations as the primary presenting symptom are quite common in COVID-19 infection. A high index of suspicion in such patients may help avoid delay in diagnosis and catastrophic sequelae. An overall knowledge about the disease will help plan the clinical management of neurologic patients, during the perioperative period.

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## Conflicts of interest

There are no conflicts of interest.

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