Concise Definitive Review

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Neurocritical Care for Extracorporeal Membrane Oxygenation Patients

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Objectives: To review the neurocritical care aspects of patients supported by extracorporeal membrane oxygenation, including cerebral physiology, neurologic monitoring, use of sedatives and anti-seizure medications, and prevalence and management of extracorporeal membrane oxygenation associated brain injury.

Data Sources: PubMed database search using relevant search terms related to neurologic complications, neurocritical care management, and brain injury management in patients with extracorporeal membrane oxygenation.

Study Selection: Articles included original investigations, review articles, consensus statements and guidelines.

Data Extraction: A detailed review of publications performed and relevant publications were summarized.

Data Synthesis: We found no practice guidelines or management strategies for the neurocritical care of extracorporeal membrane oxygenation patients. Such patients are at high risk for hypoxic-ischemic brain injury, intracranial hemorrhage, cerebral edema, and brain death. Improving clinical outcomes will depend on better defining the neurologic complications and underlying pathophysiology that are specific to extracorporeal membrane oxygenation. Currently, insufficient understanding of the pathophysiology of neurologic complications prevents us from addressing their etiologies with specific, targeted monitoring techniques and interventions.

Conclusions: A large knowledge gap exists in our understanding and treatment of extracorporeal membrane oxygenation-related neurologic complications. A systematic and multidisciplinary approach is needed to reduce the prevalence of these complications and to better manage the neurologic sequelae of extracorporeal membrane oxygenation in a way that will improve patient outcomes. (*Crit Care Med* 2019; 47:1773–1781)

Key Words: brain injury; extracorporeal membrane oxygenation; neurocritical care; neurologic monitoring

Extracorporeal membrane oxygenation (ECMO) provides temporary emergency cardiopulmonary and circulatory support to patients with acute respiratory or cardiac failure that is refractory to all other conventional therapies (1). Commonly, venoarterial and venovenous ECMO are used for acute cardiac and respiratory failure, respectively. The use of ECMO has increased more than 10-fold in adults with profound cardiopulmonary failure or cardiac arrest over the last decade (2). Furthermore, the Extracorporeal Life Support Organization (ELSO) registry recently reported that survival after ECMO had increased to 58% from an abysmal rate 20–30 years ago (3). Frequently, mortality and poor functional outcomes are driven by neurologic injury that results not only from the underlying disease process but also from complications associated with ECMO support itself (4, 5). As ECMO becomes more widely used and clinical experience accumulates, management of ECMO-associated neurologic injuries is imperative.

GLOBAL BRAIN ISCHEMIA

Global ischemia occurs when cerebral blood flow or oxygen delivery is significantly reduced, causing hypoxic-ischemic brain injury (HIBI). HIBI is one of the most common complications of ECMO, present in 14–61% of patients (6–10). HIBI can occur during any type of ECMO support (cardiac, respiratory, and cardiac arrest).

Recent evidence and guidelines promote the use of extracorporeal cardiopulmonary resuscitation (ECPR) in patients with refractory cardiac arrest as a rescue therapy when the suspected

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etiology of cardiac arrest is potentially reversible (11, 12). ECPR reduces the cerebral postresuscitation hypoperfusion phase, as it restores perfusion immediately upon initiation (13, 14). Recent uncontrolled studies showed that survival and neurologic outcome (Cerebral Performance Category: 1–2) at hospital discharge and 3–6 months postarrest were better in adults who received ECPR than in those who received conventional CPR (15–19). Predictors of post-ECPR neurologic outcome include age, initial rhythm, low- or no-flow time (cardiac arrest-to-ECPR time), use of epinephrine, and inadequate tissue perfusion markers (5, 19–21). Although neurologic outcomes after ECPR have been assessed in many studies by means of a neurologic outcome scoring system, information on the prevalence and characteristics of different types of injury after ECPR is limited.

Patients who receive venoarterial ECMO for other indications also suffer cerebral hypoperfusion from hemodynamic instability, but this hypoperfusion usually occurs pre-ECMO, as ECMO can restore adequate end-organ perfusion, including to the brain. However, certain physiologic perturbations that threaten the brain are specific to ECMO. One example is Harlequin syndrome, which occurs during peripheral venoarterial ECMO cannulation of patients who have severe respiratory failure along with cardiac failure. When the left ventricle is not fully unloaded and continues to eject as it recovers its function, it will be with deoxygenated blood, as a result of pulmonary failure. Depending on where the oxygenated peripherally delivered blood (generally from the femoral artery) and the hypoxic blood ejected from the heart mix, the cerebral blood vessels will be perfused with desaturated blood, potentially injuring the brain (22–24). This mismatch of upper torso hypoxemia and lower torso normoxia, labeled Harlequin Syndrome or North South Syndrome (in the United States), occurs in approximately 9% of patients (22, 23). HIBI was reported in 0–35% of patients in studies of venoarterial ECMO (25–29).

HIBI in venovenous ECMO is most often caused by hypoxia from refractory respiratory failure. A second mechanism is Co_2 dysregulation and cerebral vasoconstriction, which can lead to cerebral ischemia. The prevalence of HIBI in patients with venovenous ECMO is unclear. HIBI may be inappropriately categorized as ischemic stroke (4, 30), and variations in neuromonitoring and neurologic diagnosis commonly lead to misreporting of neurologic complications (26, 31–33).

It is important to reverse hypoxia and ischemia as soon as possible to prevent HIBI, but the precise effect of ECMO on cerebral circulation remains unclear. At present, the management of ECMO-associated HIBI is similar to that of any typical cardiac arrest and includes targeted temperature management (the ECMO circuit can be used to control temperature); neurologic monitoring; and management of seizures, cerebral edema, and elevated intracranial pressure (ICP) (34). Advantages of ECMO, however, are that it allows support of cerebral circulation without vasopressors, or with far less vasoactive support, prevents hemodynamic instability, and facilitates end-organ recovery.

ISCHEMIC STROKE

The prevalence of acute ischemic stroke (AIS) in patients supported with venoarterial ECMO is 3.5–14% (5, 25, 28, 35–42). The diagnosis of AIS is based on history, neurologic examination, and CT brain findings. The timing of strokes among patients on ECMO is frequently uncertain, as they may precede ECMO, occur during cannulation (43, 44), or result from a prothrombotic state with emboli from the ECMO circuit (45–47). Furthermore, the development of emboli will be affected by the intensity of antithrombotics, arrhythmia with cardiogenic shock (48, 49), hemolysis (50, 51), and acute infection. Mechanisms for infection-related stroke include septic embolism, mycotic aneurysms, and inflammation-related hypercoagulable states (52–55). The relationship between bloodstream infection and stroke in patients with a left ventricular assist device (LVAD), similar to ECMO, has been described (56–61).

The prevalence of AIS in patients with venovenous ECMO is less than that with venoarterial ECMO and reported to be approximately 2–6%, but the mechanism of stroke is poorly described (4, 38, 62). Possible etiologies include cerebral venous sinus thrombosis (CVST) and emboli from the circuit through a patent foramen ovale (PFO). Elevated right heart pressure can reverse the shunt (through a PFO), allowing for a paradoxical embolism to cause ischemic stroke. Use of the internal jugular vein as a cannulation site is certainly a risk factor for CVST, and this risk probably increases with a dual-lumen venovenous catheter.

A CT angiogram is strongly recommended to rule out hemorrhage and look for large vessel occlusion (LVO). IV alteplase is contraindicated for ECMO patients because they already require anticoagulation, and alteplase increases their risk of bleeding. Therefore, mechanical thrombectomy should be considered for patients with acute LVO (63). Nevertheless, because CT angiography is rarely obtained in patients on ECMO, the true prevalence of acute LVO during ECMO remains unknown. It is concerning, yet informative, that 33% of patients with LVAD-associated AIS had an acute LVO (64). Currently, CT venography and echocardiography are recommended for patients on venovenous ECMO who have a cerebral event. Antiplatelet therapy may be administered regardless of the infarct size. The optimal timing of initiation or resumption of anticoagulation after AIS in patients with ECMO is unknown. For patients with atrial fibrillation, it is recommended that anticoagulant be started 4–14 days after the stroke (65, 66). Resumption can be earlier for those with mild ischemic stroke (67), but little information is available on the resumption of anticoagulation in patients with moderate to large AIS. For those on venovenous ECMO who experience a moderate to large stroke and are at risk for hemorrhagic transformation, holding anticoagulation for few days may be recommended. For patients on venoarterial ECMO, the risks and benefits of holding anticoagulation should be thoroughly discussed and the risk of thromboembolism and bleeding assessed daily. For AIS caused by CVST, anticoagulation is recommended and should be continued. If embolus via a PFO is the cause of stroke in patients with venous thromboembolism, antiplatelet therapy is recommended; PFO closure may be considered in carefully selected patients with a large shunt (68).

Permissive hypertension is allowed in cases of AIS, but higher pressures may decrease myocardial recovery owing to increased afterload, which not only reduces stroke volume but increases myocardial work in situations where the heart is not vented and is being asked to eject. Furthermore, no guideline exists for optimal mean arterial blood pressure (MAP) (63). One study showed that survival was best when MAP was higher than 90 mm Hg (71%) and worst when MAP was less than 70 mm Hg (69). Therefore, titration of MAP within this range allowing patients with AIS to autoregulate seems reasonable as long as the heart can tolerate higher pressures.

For hemispheric infarct or malignant middle cerebral artery infarct, the use of hyperosmolar therapy may be considered. However, we found no data on decompressive hemicraniectomy in patients with ECMO.

CEREBRAL AIR EMBOLISM

Cerebral air embolism (CAE) is a rare but serious complication of ECMO that is associated with alveolar air trapping and low pulmonary venous pressure caused by decreased venous return in the ECMO circuit, traumatic chest compression prior to ECPR, air entry from vascular access, endoscopy, lung injury from bag-valve-mask resuscitation, and positive-pressure ventilation (70–72). The common locations for CAE are subarachnoid space, parenchyma, and venous sinuses. Patients may have acute onset of neurologic symptoms such as focal neurologic deficits, coma, seizures, sudden hemodynamic instability, encephalopathy, and headache (73). CAE can mimic the symptoms of stroke, and a CT brain study should be obtained. CAE is managed with supportive care, including volume resuscitation, oxygenation improvement, and seizure management. The use of hyperbaric oxygen therapy in ECMO patients has not been described and may not be feasible. The risk of air embolisms from the oxygenator being delivered to the patient via the outflow from the ECMO circuit may be reduced by using an oxygenator that contains a venous bubble trap and prevented by maintaining the circuit pressure higher than the gas pressure within the oxygenator (74, 75).

INTRACRANIAL HEMORRHAGE

The prevalence of intracranial hemorrhage (ICH) is similar for venoarterial and venovenous ECMO, with rates of 2–18% and 4–19%, respectively (4, 5, 76–83). Types of ICH seen in patients on ECMO include intraparenchymal hemorrhage (IPH), subarachnoid hemorrhage (SAH), and subdural hematoma (SDH). IPH is the most common, followed by SAH and SDH (76, 77). As with AIS, the timing of ICH is not well characterized. Risk factors for ICH include the use of anticoagulant and antiplatelet therapy (78, 79), female sex (78, 80), thrombocytopenia (77, 80), central cannulation (80), high transfusion requirements (77), a large dual-lumen venovenous cannula (81), ECMO duration (82), bloodstream infections (79), renal failure, and dialysis (62, 78). Most of these risk factors are associated with multiple organ failure, coagulopathy, massive transfusions, and thrombocytopenia. Endothelial dysfunction with acquired von Willebrand Syndrome is always a possible contributor, as it invariably occurs with nonpulsatile continuous flow pumps (83). Furthermore, anticoagulation combined with antiplatelet therapy likely increases the risk for hemorrhagic transformation of AIS.

In practice, differentiating ischemic and hemorrhagic strokes requires a brain CT scan, in addition to clinical history and neurologic examination. CT is a sensitive tool for detecting hemorrhage and should be performed in a timely manner. A noninvasive intracranial vascular study may be considered when cerebral aneurysm or arteriovenous malformation is suspected or to identify patients at risk for hematoma expansion (84). Cerebral angiography may be considered to look for mycotic aneurysm or vascular malformation in patients with a bloodstream infection (79). When a patient who has experienced a cerebral hemorrhagic event successfully separates from ECMO, MRI may be used to assess the etiology of the hemorrhage and the burden of microhemorrhage.

One of the key management strategies in ICH is to prevent hemorrhagic expansion by discontinuing anticoagulation, lowering blood pressure, utilizing seizure management, avoiding hypoglycemia and fever, and providing supportive critical care (84). The optimal duration of anticoagulation cessation is unclear. Recommendations for non-ECMO patients are to avoid anticoagulation for at least 4 weeks, or 2 weeks when protection is needed for an artificial heart valve. However, as ECMO patients are among those with the highest risk of thrombosis, only a few reports show the feasibility of using heparin-free venovenous ECMO with a heparin-coated circuit (85–87). In one cohort ($n = 32$), venoarterial ECMO was used without systemic anticoagulation, and the risk of thromboembolism did not increase; however, the duration of ECMO support was less than 2 days (88). Based on limited evidence, for patients on venovenous ECMO that experience ICH, withholding systemic anticoagulation until decannulation may be acceptable, but only for short periods, given that a circuit clot may require pump and oxygenator exchanges and stroke may be the first sign of failure.

No studies have investigated reversal of anticoagulation during ECMO. Clinicians should carefully discuss the risks and benefits while considering the size and expansion of ICH and the thrombotic risk of ECMO. The Neurocritical Care Society recommends an urgent reversal of anticoagulation in patients with ICH (89); however, the ECMO population was not considered during establishment of the guideline. In a cohort of 405 patients with LVADs, the reversal of anticoagulation was deemed feasible and safe (90). However, LVADs do not include an oxygenator, the most thrombogenic aspect of an ECMO circuit. Reversal of anticoagulation may be considered to prevent hematoma expansion, but it is not without risk.

The utility of neurosurgical intervention for ECMO-associated ICH is limited (91) and associated with a high mortality rate, increased by the presence of anticoagulation, critical illness, and multiple organ failure (92). Despite the hazardous effect of ongoing anticoagulation and the thrombotic risk after reversal of anticoagulation, neurosurgical intervention may be

indicated in carefully selected patients when no other management strategies are available and the risk-benefit profile favors the surgery.

POSTERIOR REVERSIBLE ENCEPHALOPATHY SYNDROME

Only one case report has described the occurrence of posterior reversible encephalopathy syndrome (PRES) in a patient with venoarterial ECMO (93). Venoarterial ECMO carries a high degree of cerebral autoregulation impairment, as assessed with near-infrared spectroscopy (NIRS). Even when sufficient cerebral blood flow was maintained by adjusting ECMO flow rates, impaired cerebral autoregulation was noted (94). PRES can be an underlying cause of both ischemic and hemorrhagic stroke because it results from cerebral autoregulation breakdown and endothelial dysfunction, both of which occur in patients receiving ECMO. Owing to the paucity of reports, there is no definitive management recommendation. Additional research is necessary to characterize ECMO-associated PRES and to develop a management strategy.

CEREBRAL EDEMA AND ACUTE INTRACRANIAL HYPERTENSION

Cerebral edema is a severe complication of ischemic stroke and ICH and is associated with an elevated ICP. Although studies into ICP monitoring of ECMO patients should be encouraged, such monitoring is not essential because evidence of intracranial mass effect and brain herniation can be made clinically from CT scans and cranial nerve examination, as shown for other brain injuries (95, 96). One limitation of using an invasive ICP monitor is that it requires cessation of anticoagulation, which has its own risks. As such, ICP monitor placement should be considered with temporary cessation of anticoagulation to allow clinicians to adequately manage acute intracranial hypertension (AIH).

A step-wise AIH management algorithm should be pursued to improve outcomes. When AIH is suspected, the first action should be to elevate the head of bed to greater than 30 degrees to reduce ICP (97). Reverse Trendelenburg position can be considered to avoid kinking of femoral-femoral venoarterial ECMO cannulae. Hyperventilation is a quick way to acutely reduce ICP. Lowering $Paco_2$ to a goal of 30 mm Hg by increasing sweep gas flow also can effectively lower ICP. Cerebral edema and AIH can be effectively managed with hyperosmolar therapy (98). Acute elevation of osmolarity can be achieved and maintained by an infusion of hypertonic saline and/or mannitol. The factors that increase ICP, including agitation, pain, seizure, and fever, should be aggressively managed and avoided. The use of analgesia and sedatives can be effective. Normothermia or mild hypothermia (easy to accomplish but risky because of the potential to exacerbate ever-present coagulopathy) can be considered to prevent the vasodilatory effect of fever and its impact on ICP. Propofol and barbiturates can be used to reduce cerebral blood flow and cerebral metabolic rate of oxygen for refractory AIH. The ultimate and most effective therapy for AIH is decompressive craniectomy. However, the utility and benefit of neurosurgical intervention is unknown, and this radical intervention should be considered cautiously and used judiciously owing to the severe underlying critical illness of patients who need ECMO support.

BRAIN DEATH

There is no standardized protocol or guideline to assess brain death in patients receiving ECMO. An apnea test may be challenging because patients with ECMO may have hemodynamic instability and severe acidemia, and no guideline exists for choosing an ancillary test when an apnea test is deemed unsafe or difficult (99). A systematic review of eight studies, mostly case reports, concluded that an apnea test can be conducted as part of brain death criteria in patients on ECMO by reducing sweep gas flow or adding exogenous CO_2. Electroencephalograms (EEGs), cerebral angiograms, and nuclear scans are preferred ancillary tests in cases of hemodynamic instability (100). Standardized practice guidelines are needed for brain death determination in patients on ECMO.

SEIZURES AND ANTI-SEIZURE MEDICATIONS

Seizures are reported in 1–6% of ECMO patients (3–5, 39, 101). Given that EEGs of comatose patients are not systematically monitored, anesthetics are used routinely during ECMO, and brain injury is common in this patient population, these values are likely an underestimation. Comatose patients should be monitored with continuous EEG to rule out nonconvulsive seizures.

Drug treatment in patients supported by ECMO is affected by altered pharmacokinetics and pharmacodynamics (102). ECMO circuits can sequester drugs, thereby increasing the volume of distribution, but the circuit saturates over time (103). After treatment is discontinued, the circuit may continue to release sequestered drug, resulting in unpredictable effects (102). Lipophilic and highly protein-bound drugs such as propofol and midazolam are particularly susceptible to such alterations (104). Other lipophilic anti-seizure medications include carbamazepine, tiagabine, felbamate, and phenobarbital. Conversely, an initial increase in volume of distribution at the start of ECMO priming solutions such as plasma or saline can affect hydrophilic anti-seizure medications such as gabapentin, leading to subtherapeutic concentrations and potential therapeutic failure (105).

Data are limited on anti-seizure medication dosing for patients with ECMO. When possible, therapeutic drug monitoring should be performed, but medications should also be titrated to seizure suppression. Because of the aforementioned sequestration, it is important to increase maintenance doses of highly lipophilic or highly protein-bound medications such as propofol and midazolam (102, 104). In one study, only 13% of baseline midazolam was detected 24 hours after initiation of ECMO (106). Alternatively, hydrophilic anti-seizure medications may require a higher loading dose (106). One case

report suggested that ECMO had a minimal effect on removal of levetiracetam, which exhibits a small volume of distribution and less protein binding (107). When dose escalations are implemented, clinicians should anticipate the need for dose reductions at the time of ECMO discontinuation given the anticipated decrease in the volume of distribution (105).

USE OF SEDATIVES AND ANALGESICS DURING ECMO

Achieving desired levels of sedation in critically ill adults supported by ECMO is challenging. The Society of Critical Care Medicine's guidelines for the management of pain, agitation, sedation, delirium, immobility, and sleep disruption do not provide recommendations for patients on ECMO (108). According to ELSO, sedation should be titrated to the point of light anesthesia during cannulation and management for the first 12 to 24 hours (75). After 24 hours, in an effort to assess neurologic status, all sedation and opioids should be stopped. But no recommendations are made for long-term sedation. If mechanical ventilation is no longer needed after ECMO initiation, sedation requirements may decrease.

Little is known regarding the optimal sedative or analgesic to use in patients. One study showed that only 3% of an initial fentanyl dose was detectable 24 hours after initiation of ECMO (106). This finding is notable because fentanyl's short half-life makes it the most frequently used sedative in the acute care setting. Given its high clearance rate in ECMO patients, however, it may not be the best choice, as much higher than normal doses are needed. On the other hand, the ECMO circuit does not substantially change concentrations of morphine (low lipophilicity and protein binding) at 24 hours. Therefore, it may be reasonable to use morphine if an opioid is needed for analgesia or sedation in ECMO patients. If renal failure is present, hydromorphone may be preferable. Data are fairly limited regarding ketamine use for sedation of patients on ECMO. Farrokh et al (109) reported that ketamine may provide an adequate level of sedation as an adjunctive therapy. Midazolam may be the preferred benzodiazepine despite the fact that sequestration in the ECMO circuit leads to lower plasma levels (110) because lorazepam causes propylene glycol toxicity. Propofol, which is highly lipophilic, is probably not a good choice, as some studies have reported that 98% of this drug is lost after 40–120 minutes of infusion in patients on ECMO (111, 112). Likewise, one study reported that nearly 93% of dexmedetomidine was lost at 24 hours, not surprising given its high lipophilicity and protein binding (113).

NEUROLOGIC MONITORING DURING ECMO

Bedside neuromonitoring has the potential to influence outcome by enabling early detection and appropriate intervention for a wide range of injuries. A recent prospective study of noninvasive neurologic monitoring (continuous EEG, somatosensory evoked potentials, transcranial Doppler [TCD], and neuroimaging) in patients on ECMO described the standardized neuromonitoring protocol and its impact on diagnosis and prognostication for neurologic outcome (114). The standardized noninvasive neuromonitoring during ECMO was feasible and revealed a high neurologic complication rate (114). However, more studies are needed to determine the specific utility of neuromonitoring in patients on ECMO. For noncomatose "stable" ECMO patients, bedside neurologic examination is fundamental to assessing acute neurologic changes that may occur. Some neuromonitoring tests relevant to ECMO include the following:

TCD Monitoring

TCD detects cerebral hemodynamic changes in real time and is the only method able to detect microembolic signals (MES) in real time. Pathologic findings of particular interest in the ECMO population include cerebral blood flow impairment, which potentially indicates progression to brain death, and microemboli, which lead to cerebral infarction (115). Cerebral infarctions are caused by microemboli in the arterial line during cannulation and decannulation of peripheral arteries, or by thrombosis within the circuit or cannula in both venoarterial and venovenous ECMO (116). Previously published studies have not addressed ECMO circuit clots and their association with TCD signals, especially on the arterial side (117–119). Additionally, these studies did not report MRI scans or cognitive outcomes, which may be more appropriate neurologic outcome measures (117–119). Data are limited on the frequency and duration of TCD monitoring. Few pragmatic TCD monitoring protocols (e.g., every other day routinely or daily if MES-positive) have been reported (113–115). Therefore, research is needed on TCD MES and their relation to brain injury by MRI before recommendations can be made.

NIRS

Cerebral NIRS may be used to measure brain oxygen saturation noninvasively and to monitor cerebral autoregulation continuously; however, the data are limited. NIRS has demonstrated good agreement with a previously validated TCD-based method for assessing cerebral autoregulation in comatose patients (120). One small study of NIRS (bifrontal) during ECMO showed the potential to identify neurologic complications and possibly guide interventions (121).

Neuroimaging

A CT brain study (including portable CT) is recommended for ECMO patients who are comatose or exhibit focal neurologic deficits when assessed off sedation. A CT study can detect cerebral ischemia in the posterior fossa with low sensitivity, and hemorrhage with high sensitivity. Obtaining MRI scans in ECMO patients can be quite challenging. However, a recent case series of patients who underwent MRI after ECMO support revealed diffuse cerebral microbleeds, similar to findings in some patients with LVADs (122, 123).

Biomarkers

The literature is sparse on the use of plasma biomarkers to predict neurologic outcome in adult patients with ECMO. One

biomarker that has been studied is neuron-specific enolase (NSE) (124). The clinical implication of NSE in ECMO is unclear as the NSE measurement is very sensitive to hemolysis, which is common in patients on ECMO (125). Biomarker studies in brain are limited because the complexity of the CNS circuit and its numerous functions make it impossible to predict outcomes based on only one or two proteins. Bembea et al (126) reported that combinations of brain-specific proteins associated with unfavorable outcome increased the sensitivity and specificity for outcome prediction.

Electrophysiology

Bilateral absence of the median somatosensory evoked potential N20 response and malignant EEG patterns in patients after cardiac arrest are reliable prognostic markers of poor functional outcome (127–130). However, little is known about the reliability of the electrophysiologic tests in patients undergoing ECMO. Future studies on the use of continuous EEG in comatose patients supported by ECMO may be helpful in ascertaining the degree of brain injury and monitoring patients for seizures and brain function.

ICP Monitoring

ICP monitoring is rarely used in patients on ECMO owing to the risks associated anticoagulant cessation and ICP monitor placement. Hence, the literature in this area is sparse. In one case report, anticoagulation was maintained with nafamostat mesilate during ICP monitor placement, and cerebral perfusion pressure was maintained at greater than 70 mm Hg based on the values obtained (130). However, placement of an ICP monitor should be considered cautiously, as no data currently suggest that ICP monitoring improves the outcome in patients with ECMO.

CONCLUSIONS

Our review of the current science and best practices for guiding neurologic assessment and management of ECMO patients revealed little or low-quality evidence on this topic. With the overall increase in the use of ECMO, improving outcomes will likely depend on precisely defining the extent and types of neurologic complications. Only then can monitoring protocols and interventions be designed that take into account the dynamic changes in cerebral circulation and the physiologic alterations that occur during ECMO.

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