CASE REPORT

Feasibility of Performing Apnea Test in a Brain Dead Patient on Veno-Venous Extracorporeal Membrane Oxygenation (ECMO)

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Introduction: Extracorporeal membrane oxygenation (ECMO) is being increasingly used to provide support in patients with refractory cardiopulmonary distress syndromes. Neurological sequelae, either from the ECMO or the hypoxic/hypotensive event leading to ECMO, are common. We present a patient requiring veno-venous (V-V) ECMO for an acute respiratory distress syndrome (ARDS) following cardiopulmonary arrest who suffered an irreversible brain injury. Eventually she required an evaluation for death by neurological criteria while on V-V ECMO making apnea testing challenging. We report the ability to safely perform apnea testing in a patient with a devastating brain injury requiring V-V ECMO.
Case: A 33-year-old female initially presented with flu-like symptoms. Following admission, she suffered a cardiac arrest with return of spontaneous circulation, but developed severe ARDS requiring V-V ECMO. Computed tomography (CT) of the head showed effacement of basal cisterns and cortical sulci consistent with a global cerebral edema. Continuous electroencephalography (cEEG) showed background suppression. After addressing confounding factors, her physical exam confirmed complete absence of brainstem reflexes. Apnea testing was performed by adjusting the sweep rate to provide a hemodynamically stable increase in PaCO2.
Conclusion: Apnea testing in patients on V-V ECMO can be safely performed by adjusting the sweep rate. The adjustment should be individualized for the patient.

Keywords: Extracorporeal membrane oxygenation (ECMO), brain death, apnea test, continuous electroencephalography (CEEG)

INTRODUCTION

Extracorporeal membrane oxygenation (ECMO) is being increasingly used to provide support in patients with refractory cardiopulmonary distress.[1] It can be delivered by two methods: veno-venous (V-V) or veno-arterial (V-A). The determination of the method to be used depends on the patient's cardiac function.[2]

V-V ECMO provides a lung bypass for hypoxia relief, and V-A ECMO provides a cardiopulmonary bypass for a refractory cardiogenic shock[2].

Neurological sequelae, either from the ECMO or the hypoxic or hypotensive event necessitating ECMO, have been shown to occur in up to 50% of patients.[3] Up to 28% of non-survivors on ECMO may suffer severe brain injury that may progress to brain death.[4] While physical exam can be performed in such patients, performing an apnea test may be challenging. A requisite for supporting the diagnosis of brain death is the apnea test, which is considered positive if there are no respiratory movements as blood carbon dioxide (PaCO2) is allowed to increase by 20 mmHg over a baseline PaCO2 or reach levels greater than 60 mmHg.[5,6] We report here the feasibility of performing an apnea test in a patient with a devastating brain injury requiring V-V ECMO.

CASE REPORT

A 33-year-old female with a past medical history of diabetes mellitus type 2, hypertension, and alcohol abuse presented to the emergency department (ED) with flu-like symptoms. While in the ED, she became unresponsive and pulseless. Cardiopulmonary resuscitation (CPR) was initiated for pulseless electrical activity (PEA) reverting to ventricular fibrillation (VFib) after receiving epinephrine 1 mg. She received one shock along with bicarbonate, dextrose, calcium, and amiodarone with return of spontaneous circulation (ROSC) after 6 minutes. She remained in a coma, and targeted hypothermia for a goal of 32-34^{o}C was started. She developed hypotension, and in order to keep mean arterial pressure (MAP) > 65mmHg she required norepinephrine, dopamine, phenylephrine, and vasopressin. She was started on broad-spectrum antibiotics including: vancomycin, cefepime, and metronidazole.

Ongoing refractory hypotension and hypoxia (oxygen saturations in mid to low 80%) continued requiring manual bag mask valve ventilation and an epinephrine infusion. Further course was complicated by symptomatic bradycardia requiring atropine, which progressed to PEA and again required CPR. She received epinephrine 1 mg with resulting rhythm showing VFib. She then received one shock before ROSC. Her infectious disease coverage was broadened to vancomycin, cefepime, metronidazole, ampicillin, oseltamivir, and tobramycin.

She continued to have refractory hypoxia despite adjustments to the mechanical ventilation, anticoagulation for suspected pulmonary embolus, and inhaled nitric oxide. Her oxygen saturation improved to 90% with a recurrent decline requiring prone ventilation for an acute respiratory distress syndrome (ARDS). With no improvement, V-V ECMO was initiated emergently with cannulation via the right internal jugular vein. She remained on the ventilator with a FiO2 of 50%, tidal volume (Tv) of 200 cc, positive end expiratory pressure (PEEP) of 5 cmH20, and a respiratory rate (RR) of 20/min. She was rewarmed after 24 hours of cooling.

She remained comatose and was noted to have bilateral, nonreactive pupils of 4 mm and a generalized myoclonus. She was started on levetiracetam. A computed tomography (CT) of the head did not show any acute intracranial process. Continuous electroencephalography (cEEG) showed burst suppression pattern (Figure 1A). Over the next 48 hours, her myoclonus resolved. cEEG showed evolution from burst suppression to generalized periodic discharges to background suppression (<2 uV) without bursts (Figure 1A-D). Her neurological examination worsened to

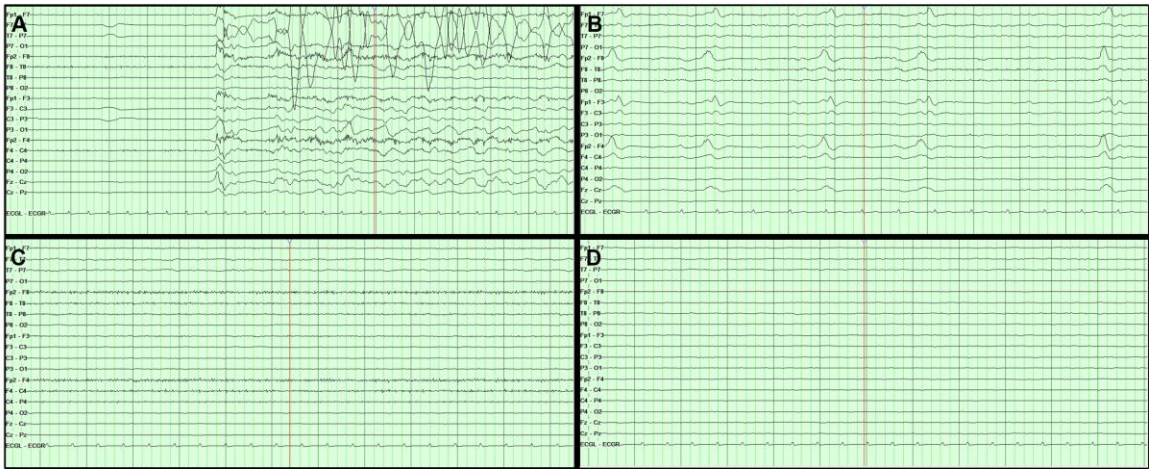

Figure 1. Evolution of continuous electroencephalography (cEEG) in a Patient on ECMO. (A) Burst suppression pattern. (B) Generalized periodic pattern. (C) Background suppression (<10uV) with low amplitude muscle artifact. (D) Background suppression (<10uV). These changes occurred over 48 hours. Bipolar montage. LFF=1Hz, HFF=70Hz, Notch 60Hz, sensitivity 10uV/mm.

absent brainstem reflexes. Repeat CT of the head showed diffuse cerebral edema with effacement of the basal cisterns and cortical sulci (Figure 2A-D). Given her neurological examination and findings on head CT, evaluation for death by neurological criteria was initiated after ensuring normothermia and excluding confounders such as sedatives, paralytics and/or metabolic derangements. Her systolic blood pressure was >100 mmHg. Her neurological examination showed coma. There was no grimace or changes in vitals to peripheral or central noxious stimulation. There was no eye opening upon painful stimulation. Pupils were 4 mm and nonreactive bilaterally. She did not have a corneal reflex or reflexive eye movement to head turning or to cold caloric stimulation. There was no gag reflex to tonsillar stimulation or cough reflex to deep endotracheal stimulation. Her motor examination showed flaccid quadriparesis with no movement to noxious stimulation. She was areflexic.

Her ECMO settings were notable for a sweep speed of 3210 rpm, a flow of 3.17 LPM, an air/oxygen mixer of 80%, and a sweep rate of 2L O2/min with SVO2 of 71%. In preparation for apnea testing, ventilator settings were kept the same (Tv = 200 cc, PEEP = 5 cmH2O, RR = 20/min), but the FiO2 was increased to 100%. She had a temperature of 37.1ºC. To keep systolic blood pressure >100 mmHg she remained on pressor support including phenylephrine, epinephrine, and vasopressin. An arterial blood gas (ABG) at the start of testing showed a baseline PaCO2 of 41 mmHg and a PaO2 of 186 mmHg. The sweep rate on the ECMO was changed to 0L O2/min. She was disconnected from the ventilator. A catheter was advanced through the endotracheal tube to the level of the carina and delivered 4L/min of 100% oxygen. She was monitored with arterial line and pulse oximetry. After 5 minutes of monitoring, her oxygen saturation quickly dropped to 62% saturation. She was placed back on the ventilator and the ECMO sweep was dialed to 2L O2/min. She was preoxygenated again for ~20 minutes. A repeat baseline ABG was obtained showing a pH of 7.4, a PaCO2 of 43 mmHg, and a PaO2 of 212 mmHg. She was again disconnected from the ventilator. The ECMO sweep was decreased to 900 mL

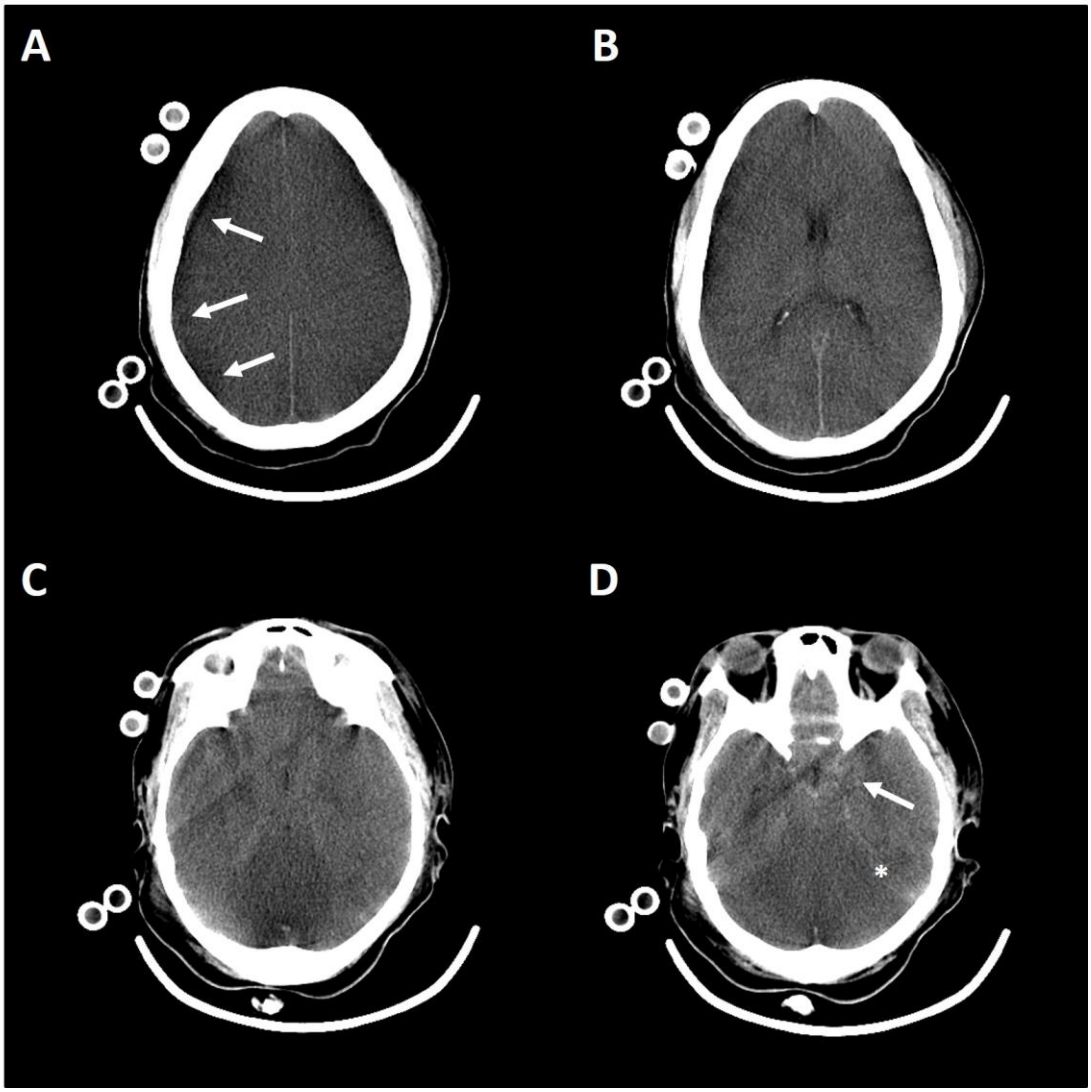

Figure 2. Computed tomography (CT) of the Head Showing Diffuse Cerebral Edema. Complete effacement of sulci (A; arrows) and basal cisterns with uncal herniation (D; arrow) and "pseudo-subarachnoid" hemorrhage (D; asterisk) are seen.

O2/min. She was again monitored with an arterial line and pulse oximetry. Serial ABGs were obtained every five minutes. The PaCO2 increased to 62 mmHg by 37 minutes of apnea testing. Her PaO2 was 220 mmHg and the pH was 7.26. Her oxygen saturation throughout the testing remained at a 100%. Her systolic blood pressure remained >100 mmHg without the need to adjust vasopressors. She showed no respiratory movement during the examination. The apnea test was determined to be positive, and she was pronounced dead by the neurologic criteria.

DISCUSSION

We present a case of a devastating neurological injury progressing to brain death in a patient on V-V ECMO. This case highlights an approach to safely perform apnea testing in a patient on V-V ECMO.

Brain death is the irreversible cessation of function of the whole brain,

including the brainstem, with sustained systemic perfusion.[5] The rest of the organs may be supported by mechanical ventilation, medications, and other devices, such as ECMO, making it challenging to perform clinical testing in some circumstances. As a pre-requisite to diagnosing brain death, an irreversible and proximate cause of coma must be present.[5] Thus, neuroimaging to support a catastrophic brain injury leading to brain death is necessary, and the final pathway for brain death is cerebral circulatory arrest from intracranial hypertension.

An apnea test is a key component for brainstem areflexia assessment and requires a methodical approach[5]. Factors such as hypothermia that deters PaCO2 production and prevents the requisite rise in PaCO2 must be corrected prior to apnea testing.[5] During the testing, accumulation of PaCO2 results in an acidosis causing a predictable drop in blood pressure.[5] Thus, pressor support may be necessary.

While monitoring for any spontaneous respiratory effort during the apnea testing, it is recommended to detach the patient from the ventilator and provide oxygen via the endotracheal tube at 4-6 L/min using a suction catheter attached to the wall oxygen. If higher oxygen flow rate is used, it may wash out the PaCO2 and ultimately prevent accumulation in the blood.[7] It is recommended to continue testing for a minimum of 10 minutes since the slowest rise in PaCO2 in euthermia is 2 mmHg/min.[7] However, in patients on ECMO, these guidelines may need to be modified.

ECMO is a method to directly oxygenate the blood and remove carbon dioxide from the blood.[2] There are two types of ECMO: V-V and V-A ECMO. [2] The choice of ECMO is based on organ failure.[2] If the primary problem is lung failure, for example an acute respiratory distress syndrome like in our case, V-V ECMO is used as the salvage therapy.[2] In V-V ECMO, blood is withdrawn from the vein into the extracorporeal membrane by a mechanical pump. It then enters the oxygenator. A blood-gas interface is present across a membrane allowing for diffusion of gas. This blood gas interface is created from fresh gas known as the sweep gas. The composition of the gas is adjusted by a blender allowing for the determination of the fraction of delivered oxygen. The removal of carbon dioxide is controlled by adjusting the flow rate of the sweep gas. By decreasing the sweep flow rate, less carbon dioxide is removed. The oxygenated extracorporeal blood is then returned to the central venous system.[8]

The appropriate ventilator strategy with a patient on ECMO is individualized while employing lung protective ventilator strategy. This approach may include using low tidal volumes (less than 4 cc/kg of predicted body weight), higher PEEP (10-15 cmH20), peak inspiratory pressure of 20-25 cmH20, respiratory rate of 10 bpm, and a FiO2 of 30%. Oxygenation is provided by ECMO.[2]

Unfortunately, several neurological complications have been observed in patients on ECMO.[9] These events may be from the insult that led to the ECMO or a result of the ECMO procedure itself and may occur up to 50% of patients on ECMO.[3,9,10] A retrospective study of the Extracorporeal Life Support Organization registry found neurological complications to be common and include: cerebral infarction (3.6%), seizure (1.8%), intracerebral hemorrhage (1.8%), and brain death (7.9%).[9] Presence of central nervous system (CNS) complications predicted higher mortality (89%) compared to 57% in patients without CNS complications.[9] This highlights the importance of monitoring and controlling for these devastating events.

If a patient is suspected to have progressed to brain death, apnea testing can be challenging while on ECMO, but can be performed safely.[11] Different approaches have been recommended in literature including avoiding apnea testing altogether.[11-14] We report that apnea testing can be performed safely with sweep flow rate kept above zero to maintain normoxemia. This finding is in contrast to the case report by Shah et al. (2015).[14] Additionally, we show that there was no need for oxygenation through the endotracheal tube. Patients on ECMO are not relying on the alveolar gradient allowing for the diffusion of oxygen to maintain normoxemia. The purpose of mechanical ventilation while on ECMO is to prevent further lung injury, not to provide oxygenation. We arbitrarily chose a sweep rate of 900 cc/min. It took approximately 37 minutes before PaCO2 rose above 60 mmHg. Lower sweep rates may be considered to allow for a quicker rise in PaCO2, but may lead to hemodynamic instability. It is recommended to use the lowest sweep rate possible to prevent desaturation and to maintain hemodynamic stability.

In conclusion, we demonstrate the feasibility and safety of performing the apnea test in a patient with devastating brain injury on V-V ECMO.

Notes

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