Surgery: Current Research

Interaction between Renal Replacement Therapy and Extracorporeal Membrane Oxygenation Support

Thiago Gomes Romano*

Assistant Teaching Professor for the Discipline of Nephrology, ABC Medical School Medical Intensivist at Hospital, Sírio-Libanês, Brazil

Abstract

Extracorporeal Membrane Oxygenation (ECMO) is one of the designations used for extracorporeal circuits capable of oxygenation, carbon dioxide removal and, eventually, circulatory support. Acute respiratory distress syndrome with severe hypoxemia or acidemia with high carbon dioxide levels in a scenario of low pulmonary tidal volume is its mainly indication. Acute Kidney Injury (AKI) and its complications such as volume overload and azotemia are common in this situation; some epidemiological studies have shown that around 78% of the patients demanding ECMO therapy develop AKI. Therefore, renal replacement therapy is required in about 50% of those cases. This papers aims to explain the concept of the ECMO circuit and the ways continuous renal replacement therapy (CRRT) can be instituted in critical ill patients who need ECMO.

Keywords: ECMO; Renal replacement therapy; Dialysis

Introduction

Extracorporeal Membrane Oxygenation (ECMO) is one of the designations used for extracorporeal circuits capable of oxygenation, carbon dioxide (CO_2) removal and, eventually, circulatory support.

Extracorporeal techniques did not yield encouraging results when they were first used in the late 1970s [1,2], but interest in the technique has spread in recent years following the publication of a case series in Australia and New Zealand on the use of ECMO for severe respiratory distress syndrome during the influenza A (H1N1) pandemic in 2009 and the publication of the Conventional Ventilation or ECMO for Severe Adult Respiratory Failure Trial (CESAR trial) in the same year. The first publication reported a 71% survival rate for patients with severe acute respiratory distress syndrome (ARDS) [3] (average PaO_2/FiO_2 of 56) associated with H1N1 who were treated with ECMO [4], and a second publication reported a 37% mortality or severe sequelae rate for patients who underwent this procedure versus a 53% rate for patients who underwent conventional therapy [5].

The indication for this therapy is based on cases of potentially reversible respiratory and cardiac insufficiency that are unresponsive to conventional therapy and do not have contraindications to the procedure. Potential candidates include patients with: PaO_2/FiO_2<80 with optimized ventilation therapy for at least 6 hours, decompensated hypercapnia with acidosis (pH <7.15) despite optimized ventilation and a *plateau* pressure of >35-45 cm despite low tidal volume ventilation. The main contraindications include a clinical picture characterized as irreversible, metastatic neoplastic disease, a poor prognosis due to the underlying disease or any situation in which anticoagulation is not possible [6].

To understand the interaction between the renal replacement therapy (RRT) circuit and the ECMO system, which is the main objective of this chapter, it is important to understand some concepts about the circuit and the epidemiology of Acute Kidney Injury (AKI)/ volume overload in these patients.

The ECMO circuit

The ECMO circuit is composed of six basic components: a cannula, connecting lines, a pump, an oxygenation membrane, a heater and an oxygen "sweeper".

The cannulation position depends on the indication for therapy. If it is intended for ventilatory and circulatory support [Venoarterial (VA) ECMO], the most frequent option is a drainage cannula placed in the internal jugular or femoral vein with the return placed in the femoral artery. Additionally, a jugular-carotid cannulation is one option despite the potential for neurological injury. In cases exclusively intended for ventilatory support [venovenous (VV) ECMO], cannulation can be placed femoro-jugular, jugular-femoral or femoral-femoral depending on the patient characteristics or the choice of center. Another option is the cannulation with a double-lumen catheter with two venous drainage sites (superior and inferior vena cava) and one return site (right atrium).

The diameter, length and placement of the cannulae are important for the effectiveness of the therapy and the success in coupling the circuit to the RRT system. Several cannula diameters are available, ranging from 8 to 31 French, with lengths up to 50 cm. The capacity to generate blood flow through the drainage cannula is inversely proportional to its length and is directly proportional to its diameter.

Traditionally, when a VV ECMO is selected, the drainage cannula is placed using the Seldinger technique in the femoral vein with the tip of the cannula located at the junction of the inferior vena cava with the right atrium, and the cannula return is placed in the internal jugular vein with its tip in the entrance of the right atrium. However, some services with extensive experience in ECMO, such as the Karolinska Institute in Stockholm, Sweden, have opted to drain blood via the jugular vein and return it via the femoral vein.

In the cannulation process, the use of ultrasound-guided punctures is essential because it provides additional safety for the process [7] and allows for the direct measurement of the vein diameter and, consequently, the choice of the cannula to be used. Importantly, there is an additional need for distal cannulation in cases of VA ECMO, given the demand for ipsilateral limb perfusion to the femoral artery cannulation.

*Corresponding author: Thiago Gomes Romano, Assistant Teaching Professor for the Discipline of Nephrology, ABC Medical School Medical Intensivist at Hospital, Sírio-Libanês, Brazil, Tel: 55-11-994128065; E-mail: thromano25@hotmail.com

The pump generating the flow that is currently used in almost all cases is a centrifugal pump, which generates a blood flow through a system that is magnetically coupled with a motor, and the venous drainage is dependent on the suction generated by this system. Such systems can generate negative pressures that can range from -50 to -700 mmHg. After the blood flows through the pump, the pressure in the system becomes positive at levels of up to 400 mmHg when the blood passes by the oxygenation membrane. The blood then returns to the patient at an average pressure of 300 mmHg depending on the characteristics of the cannula's location, diameter and length and the presence of clots in the system. Therefore, the circuit can be divided into regions of negative and positive pressure (pre- and post-pump).

The oxygenation membranes are generally made of solid or micro porous polypropylene or polymethylpentene (PMP) fibers, in which the surface and characteristics of the fiber determine its oxygenation capacity. During the oxidation/CO_2 removal process, the membrane is heated via a water bath that circulates through an external heating system that has a target temperature of approximately 37°C. Thus, the thermal control of the patient is effectively maintained given the blood flow rate to which the system is exposed.

The so-called "sweeper" is the tool used to supply oxygen (O_2) to the membrane; it generally contains 100% O_2 or 5% CO_2 and 95% O_2, and the quantity of O_2 supplied is controlled by a flow meter. Some systems have the capacity to control the fraction of O_2 in contact with the membrane. In general, the flow determined by the "sweeper" is responsible for the removal of CO_2, whereas the blood flow generated by the pump and the membrane characteristics determine the oxygenation capacity of the system [8].

Anticoagulation system

Although the ECMO circuit allows for high blood flow rates and is coated with heparin, it is still necessary to use systemic anticoagulation. Anticoagulation is started during the cannulation process with a 50-100 U/Kg bolus of unfractionated heparin followed by a continuous infusion that targets an activated partial thromboplastin time (APTT) near the lower anticoagulation limit, or approximately 1.5 times the normal time. Thus, the hemodialysis circuit does not require additional anticoagulation.

The anticoagulation process for ECMO patients is a fine balance between the patency of the circuit and the risk of bleeding, which is a major complication for this method. Thus, the process should be individualized for each patient, and several parameters should be considered, including the levels of fibrinogen, D-dimer, platelets and antithrombin III; the anticoagulation time; and the prothrombin activity.

Acute kidney injury and ECMO

As in critically ill patients who have not used ECMO supportive therapy, AKI and fluid overload are also associated with worse outcomes for patients on ECMO [9,10]. Despite the importance of managing these conditions in these individuals, the procedural recommendations are based solely on isolated data from centers that have experience in managing these patients.

In recent years, epidemiological studies on AKI have undergone extensive changes, resulting from the standardized diagnosis for AKI that was initially proposed by the RIFLE system (risk, injury, failure, loss and end-stage). Studies published after RIFLE systems have reported AKI incidences of approximately 78% in patients with respiratory failure [11] and 81% in post-cardiotomy patients among adults on ECMO [12]. Chang et al. have shown that AKI following weaning from ECMO is an important prognostic tool for mortality [13,14].

The etiology of AKI in these patients is almost always due to multiple factors, including sepsis, low cardiac output syndrome, exposure to nephrotoxic antimicrobials and high intrathoracic pressures. One peculiarity is the potential patients undergoing VA ECMO have for renal injuries caused by ischemia/reperfusion [15] and the renal injury induced by hemoglobinuria because different degrees of hemolysis occur in the extracorporeal circuit.

Approximately 50% of the patients on ECMO require RRT. Given the degree of hemodynamic instability and the need for better water balance throughout therapy, almost all patients receive continuous therapy [16].

The first initiative to standardize RRT and ECMO data has come from the KIDMO group (Kidney Intervention During Extracorporeal Membrane Oxygenation Group). Based on the analysis of data from 65 centers with experience performing ECMO, the current overall picture of the use of RRT in ECMO has been established.

The most frequent indications for RRT included addressing fluid overload (43%) or even preventing it (16%), and AKI led to the decision to commence dialysis in 35% of cases. The main mode used was continuous venovenous hemofiltration (CVVHF), and interaction between the dialysis machine and the ECMO circuit was used in 47% of centers. Of these cases, 42% were connected to the venous portion (negative pressure), and 33% were connected to the pre-oxygenation positive pressure portion. Some centers (21%) use the so-called series connection of dialysis membrane, using a conventional pump to control the ultra filtrate [17].

Interaction between the RRT and ECMO circuit

The use of a hemodialysis circuit connected to an ECMO is not approved by the FDA (Food and Drug Administration), the United States health care regulation institution. Therefore, its use is considered "off label" and cannot be recommended as a more ideal therapy than another therapy.

In essence, three different methods can be used to introduce hemodialysis to patients on ECMO. First, a double-lumen catheter can be used to connect the RRT circuit to part of the ECMO circuit. Second, a series circuit can be used. Third, a connection can be made between the RRT machine and the ECMO circuit.

The second option described above involves the incorporation of a hemofilter into the ECMO circuit, typically through the arterial route of the RRT circuit in the region with the most positive pressure (post-pump and pre-oxygenator), with the return route placed in a negative pressure region (pre-pump). Using this configuration, a Slow Continuous Ultrafiltration (SCUF) can be installed, and a medication infusion pump can be used to control the rate of ultrafiltrate per hour or diffusive therapy with the dialysate running countercurrent by the blood controlled by simple infusion pumps, in which the dialysis dose is limited to the flow of the pump, which is generally approximately 1 L/h. If such a strategy is selected, the use of an infusion pump to control the ultrafiltrate is mandatory because a hemofilter has a very large ultrafiltration potential (high efficacy). This option has some questionable points. First, if an ultrasonic probe is not placed to measure the flow, the blood flow through the hemofilter will remain unknown. Second, the infusion pumps are not accurate when they are used to prevent fluid loss in a high-pressure system [18,19] and can generate a large discrepancy between the desired and actual ultrafiltrate volumes.

The third option involves the use of a dialysis machine that is connected to the circuit. The locations of the arterial and venous line connections are still controversial, but there is more mutual agreement that post-oxygenator installation leads to additional risk for embolism. However, a pre-pump (negative pressure) or post-pump (positive pressure) connection will depend on the machine being used and the settings allowed for each system. Some machines, such as the Gambro Prismaflex and the Braun Diapact, will allow these settings to be changed. If we choose to connect both lines into the negative pressure region, the return line may have alarm problems on certain machines, such as the Fresenius 2008K and the Gambro Prisma. One way of facilitating such a condition is to use some flow restriction mechanism, such as an external restrictor, for the line. A connection in the pre-oxygenator positive pressure region seems to be an attractive option given that, on some machines, the software can tolerate returning pressures of to 350 mmHg. In this region, the mean pressures are 300 mmHg, depending on the blood flow used.

Santiago et al. reported that this last option is safe and effective in controlling both nitrogenous waste and the water balance without incurring any additional risks to the patient [19,20].

My personal impression is that the connection from the dialysis circuit to the ECMO has not been formalized. However, the advantages offered by central catheterization combined with systemic anticoagulation in reducing both the patient's risks and the risk of infection should be taken into account. Among the two options for circuit connection, the use of a hemodialysis machine appears to be the more attractive option because it will allow for more control over the blood and ultrafiltrate flow rates. The decision to connect into negative or pre-oxygenator positive pressure portions will depend on the machine that is available in each clinical department.

Conclusion

AKI is extremely prevalent in patients on ECMO, and just as in the critically ill population that is not on ECMO therapy, it is a factor in increased morbidity and mortality. Approximately half of patients on ECMO require RRT, and continuous therapies may offer better blood volume control and hemodynamic stability.

Coupling the RRT circuit to ECMO has not been officially recognized; the recommendations for this coupled therapy come from centers that have experience performing these procedures. The use of a hemodialysis machine has become a safer option than the use of a hemofilter in series, and the locations of the lines connecting the RRT circuit will depend on the equipment available in each clinical department; however, post-oxygenator connections are highly discouraged.

There are very few studies in the medical literature on AKI in patients on ECMO and on questions concerning the timing, dose and method of RRT in these patients. However, this field of research is quickly expanding.

References

1. Zapol WM, Snider MT, Hill JD, Fallat RJ, Bartlett RH, et al. (1979) Extracorporeal membrane oxygenation in severe acute respiratory failure. A randomized prospective study. JAMA 242: 2193-2196.

2. Morris AH, Wallace CJ, Menlove RL, Clemmer TP, Orme JF Jr, et al. (1994) Randomized clinical trial of pressure-controlled inverse ratio ventilation and extracorporeal CO2 removal for adult respiratory distress syndrome. Am J RespirCrit Care Med 149: 295-305.

3. Hecker M, Seeger W, Mayer K (2012) [The Berlin Definition: novel criteria and classification of ARDS]. Med KlinIntensivmedNotfmed 107: 488-490.

4. Australia and New Zealand Extracorporeal Membrane Oxygenation (ANZ ECMO) Influenza Investigators, Davies A, Jones D, Bailey M, Beca J, et al. (2009) Extracorporeal Membrane Oxygenation for 2009 Influenza A(H1N1) Acute Respiratory Distress Syndrome. JAMA 302: 1888-1895.

5. Peek GJ, Mugford M, Tiruvoipati R, Wilson A, Allen E, et al. (2009) Efficacy and economic assessment of conventional ventilatory support versus extracorporeal membrane oxygenation for severe adult respiratory failure (CESAR): a multicentre randomised controlled trial. Lancet 374: 1351-1363.

6. Brodie D, Bacchetta M (2011) Extracorporeal membrane oxygenation for ARDS in adults. N Engl J Med 365: 1905-1914.

7. Moore CL, Copel JA (2011) Point-of-care ultrasonography. N Engl J Med 364: 749-757.

8. Park M, Costa EL, Maciel AT, Silva DP, Friedrich N, et al. (2013) Determinants of oxygen and carbon dioxide transfer during extracorporeal membrane oxygenation in an experimental model of multiple organ dysfunction syndrome. PLoS One 8: e54954. Sell LL, Cullen ML, Whittlesey GC, Lerner GR, Klein MD (1987) Experience with renal failure during extracorporeal membrane oxygenation: treatment with continuous hemofiltration. J PediatrSurg 22: 600-602.

9. Askenazi DJ, Ambalavanan N, Hamilton K, Cutter G, Laney D, et al. (2011) Acute kidney injury and renal replacement therapy independently predict mortality in neonatal and pediatricnoncardiac patients on extracorporeal membrane oxygenation. PediatrCrit Care Med 12: e1-6.

10. Lin CY, Chen YC, Tsai FC, Tian YC, Jenq CC, et al. (2006) RIFLE classification is predictive of short-term prognosis in critically ill patients with acute renal failure supported by extracorporeal membrane oxygenation. Nephrol Dial Transplant 21: 2867-2873.

11. Yan X, Jia S, Meng X, Dong P, Jia M, et al. (2010) Acute kidney injury in adult postcardiotomy patients with extracorporeal membrane oxygenation: evaluation of the RIFLE classification and the Acute Kidney Injury Network criteria. Eur J CardiothoracSurg 37: 334-338.

12. Chang WW, Tsai FC, Tsai TY, Chang CH, Jenq CC, et al. (2012) Predictors of mortality in patients successfully weaned from extracorporeal membrane oxygenation. PLoS One 7: e42687.

13. Chen YC, Tsai FC, Chang CH, Lin CY, Jenq CC, et al. (2011) Prognosis of patients on extracorporeal membrane oxygenation: the impact of acute kidney injury on mortality. Ann ThoracSurg 91: 137-142.

14. Keckler SJ, Laituri CA, Ostlie DJ, St Peter SD (2010) A review of venovenous and venoarterial extracorporeal membrane oxygenation in neonates and children. Eur J PediatrSurg 20: 1-4.

15. Cavagnaro F, Kattan J, Godoy L, Gonzáles A, Vogel A, et al. (2007) Continuous renal replacement therapy in neonates and young infants during extracorporeal membrane oxygenation. Int J Artif Organs 30: 220-226.

16. Fleming GM, Askenazi DJ, Bridges BC, Cooper DS, Paden ML, et al. (2012) A multicenter international survey of renal supportive therapy during ECMO: the Kidney Intervention During Extracorporeal Membrane Oxygenation (KIDMO) group. ASAIO J 58: 407-414.

17. Jenkins R, Harrison H, Chen B, Arnold D, Funk J (1992) Accuracy of intravenous infusion pumps in continuous renal replacement therapies. ASAIO J 38: 808-810.

18. Murphy RS, Wilcox SJ (2010) The link between intravenous multiple pump flow errors and infusion system mechanical compliance. AnesthAnalg 110: 1297-1302.

19. Santiago MJ, Sánchez A, López-Herce J, Pérez R, del Castillo J, et al. (2009) The use of continuous renal replacement therapy in series with extracorporeal membrane oxygenation. Kidney Int 76: 1289-1292.

20. Maki DG, Kluger DM, Crnich CJ (2006) The risk of bloodstream infection in adults with different intravascular devices: a systematic review of 200 published prospective studies. Mayo Clin Proc 81: 1159-1171.