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# Respiratory ECMO

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**Introduction:** The H1N1 epidemic in 2009 caused a significant increase in the utilization of respiratory extracorporeal membrane oxygenation (ECMO) therapy for severe respiratory failure (SRF) patients who failed to improve following conventional ventilation therapy. Its use was linked to a high patient survival rate (more than 70%) reported from Australian and New Zealand[1] as well as Canadian ECMO[2] registries. It eventually led to the CESAR randomized controlled trial[3] that clearly showed mortality benefits for adult patients with, potentially reversible, severe respiratory failure who were treated in ECMO centers. In that study, more than 63% of the referred patients survived and 75% of them received ECMO therapy, whereas in the conventional treatment arm, the survival rate was only 47%.

The significant change in the outcome, compared with old data, is related to several factors, such as advances in ECMO technologies, the use of veno-venous (VV) ECMO instead of veno-arterial (VA) ECMO, advances in the tubing and the membrane that are currently used, better understanding of lung and patient management during ECMO therapy, and early deployment of the rescue therapy.

In this review, we are going to discuss the physiology of oxygenation and the overall management strategy on ECMO during early course of active inflammation, all the way through to weaning during the healing phase of the lung injury.

**$O_2$ is a perfusion-limited gas:** This means that $O_2$ depends not only on its ability to diffuse through the membrane, which is 25 times less than $CO_2$, but also on perfusion capacity of the area being oxygenated. To explain that in a simple way, we will assume that $O_2$ is a gas that cannot swim in the blood, and if it is left alone it will sink and cause free radical injury.

It needs a carrier, such as the hemoglobin, and flow, which is the cardiac output or ECMO flow to push that carrier. If the transport capability of the blood is saturated, additional oxygen will be left out and

will not be transported to the rest of the body.
The perfusion limitation concept is very important to understand the shunt physiology. For example, if a patient with complete consolidation of both lungs has a cardiac output of 10 L/min and is on a 5 L/min ECMO flow, only 50% of the patient cardiac output is getting exposed to the gas exchange area and 50% is shunting through the diseased lung. When they mix together, 50% of the blood will be de-oxygenated, which will cause severe persistent hypoxemia.
To solve this problem, we either recruit more lung units or decrease the overall patient cardiac output to decrease the intrapulmonary shunt. Adding more oxygen to either disease obstructed alveoli or the ECMO membrane will not solve the problem.[4]
**Carbon dioxide is a diffusion-limited gas:** $CO_2$ does not have the same problem as oxygen. It can ride on the hemoglobin, the albumin, and can also swim in the $CO_2 - HCO_3$ buffer. The only limitation of $CO_2$ is the flow of fresh air, whether it is minute ventilation or ECMO sweep gas flow, and this is related to the very low concentration of $CO_2$ in room air and its ability to diffuse through the membrane 25 times more than oxygen. $CO_2$ clearance on ECMO can be controlled by increasing the sweep gas flow.
**The difference between membrane lung and artificial membrane:** Despite the significant advances in technologies, the artificial lung development remains in its infancy and far from complete for various reasons: The total surface area of a normal human lung is about 70 $m^2$, whereas the best artificial lung membrane has a maximum equivalent of 4 $m^2$. The thickness of a normal human lung is about 0.5 μm, whereas an artificial membrane is 300 times thicker, with an average thickness of 150 μm. Important factors affecting the diffusion and the uptake of oxygen are:

A – The red blood cell (RBC) transient time, which is 0.4 – 1 second in a normal lung and much shorter in the artificial membrane lung.
B – The way that RBC cross the normal capillary is almost one cell at the time, compared with the membrane lung capillary where red blood cells cross in clusters. For all the above reasons, the maximum oxygen transfer capability of the artificial membrane (400 – 600 mL $O_2$/min) is much less than the normal human lung (> 2000 mL $O_2$/min).

**Lung periods during ECMO run:** It is of crucial importance to differentiate between the early course and the late course on ECMO therapy for severe ARDS.
**Early course:** It can last from a few days to a couple of weeks depending on the nature of the pathogen that is causing the lung injury and whether it is associated with a multi-organ dysfunction syndrome and shock or not. This period is characterized by severe lung inflammation and systemic inflammation with increased $O_2$ consumption and decreased $O_2$ delivery, with non- or minimally recruitable alveoli.
The focuses in this phase are:

1 – Maximizing ECMO flow as the patient depends almost 100% on the ECMO for oxygenation to maximize $O_2$ delivery;
2 – Resting the lung and switching the focus of ventilation from enhancing lung recruitment to preventing the de-recruitment of whatever is left of the lung tissue.
3 – Full patient rest to decrease $O_2$ consumption, which will also decrease the cardiac output appropriately and hence decrease intra-pulmonary shunt. This is usually achieved by sedation, paralysis, temperature control, and sometimes adding beta blockade.
4 – Optimizing the native lung function by early diagnosis and treatment of the underlying condition, negative fluid balance if tolerated by the ECMO flow and secretion mobilization usually with bronchoscopies rather than just physiotherapy, as the patient is usually deeply sedated.

**Late course:** It usually starts when the systemic and lung inflammation is decreasing, and when the exhaled tidal volume of the diseased lung and dead space fraction start to improve. The period can last from several days to couple of weeks depending on all the factors mentioned above.
The focuses in this phase are:

1 – Starting to wean ECMO flow and sweep gas flow to allow the stimulation of the native lung.
2 – Focusing on lung recruitment and diaphragmatic muscle dysfunction prevention using various ventilation modes such as neutrally adjusted ventilatory assist (NAVA), pressure support ventilation (PSV), and others, and also early extubation on ECMO is warranted.
3 – Weaning of all sedatives and paralytics, management of delirium, and most

importantly, aggressive physiotherapy on ECMO.

4 – Continuing to optimize native lung function with aggressive chest physiotherapy; however, fluid strategy could be liberal at this stage to facilitate sedation weaning without affecting the ECMO flow.

**Fluid management and ECMO access insufficiency during early versus late course on ECMO:** One of the most common problems that is faced during an ECMO run is access insufficiency, and if it is left untreated it could progress to cease the ECMO flow which could lead to severe hypoxemia and pulseless electrical activity (PEA) if the patient is depending on ECMO. The access pressure depends on several factors, such as cannula size and position, intra-abdominal pressure if the cannula is in the inferior vena cava (IVC), swing in intra-thoracic pressure which usually can be controlled by sedation and paralysis, and most importantly, the volume status of the patient. The default step to treat this condition is to push fluid to correct the access pressure. Repeated episodes of access insufficiency might lead to several liters of positive fluid balance which will certainly delay the weaning from ECMO. The general rule, especially in the early course of ECMO, is to keep the patient in negative fluid balance to expedite lung recovery, ensure upfront the right size and secured position of the cannula, manage elevated intra-abdominal pressure vigorously, and decrease the swing in intra-thoracic pressure by taking full ventilator control of the lung. If despite that the access insufficiency is recurrent or the patient hemodynamic status is compromised, it is very important to evaluate the volume responsiveness status of the patient. Unfortunately, many of the tools that are generally used for regular ICU patients to assess volume responsiveness, such as PICCO and LiDCO monitors, are not very reliable for ECMO patients, but ECHO-guided assessment is generally acceptable in VV ECMO, such as passive leg raising test with aortic blood flow monitoring.[5]

Later in the course, as discussed earlier, the goal is to wean sedation and paralysis, and to ensure spontaneous ventilation to decrease the risk of ventilator-induced diaphragmatic muscle dysfunction. During this period, the access insufficiency occurrence might increase and controlling the access will be by fluid boluses in the expense of weaning the sedatives and paralytics.

**Summary:** The use of respiratory ECMO has been continuously increasing for SRF patients globally. Despite significant advances in technologies, the artificial membrane lung still has significant limitations in comparison to the normal human lung. Given that oxygen is a perfusion-limited gas, maximizing the ECMO flow to match the patient's cardiac output is essential to overcome the membrane limitation. The management strategy during an ECMO run is different from the early inflammatory course to the late recovery course, not only on the diseased lung, but also on the entire body system, and this has to be considered during therapy on VV ECMO. Fluid management in particular has to be carefully evaluated using different tools such as ECHO-guided assessment for volume responsiveness.

Keywords: ARDS, ECMO, gas exchange, shunt physiology, severe respiratory failure, extracorporeal membrane oxygenation, SRF

## REFERENCES

1. Davies A, Jones D, Bailey M, Beca J, Bellomo R, Blackwell N, Forrest P, Gattas D, Granger E, Herkes R, Jackson A. Extracorporeal membrane oxygenation for influenza A (H1N1) acute respiratory distress syndrome. *JAMA*. 2009;302(17):1888 – 1895.
2. Kumar A, Zyarychanski R, Pinto R, Cook DJ, Marshall J, Lacroix J, Stelfox T, Bagshaw S, Choong K, Lamontagne F, Turgeon AF, Lapinsky S, Ahern SP, Smith O, Siddiqui F, Jouvet P, Khwaja K, McIntyre L, Menon K, Hutchison J, Hornstein D, Joffe A, Lauzier F, Singh J, Karachi T, Wiebe K, Olafson K, Ramsey C, Sharma S, Dodek P, Meade M, Hall R, Fowler RA. Canadian Critical Care Trials Group H1N1 Collaborative. Critically ill patients with influenza A (H1N1) infection in Canada. *JAMA*. 2009;302(17):1872 – 1879.
3. Peek GJ, Mugford M, Tiruvoipati R, Wilson A, Allen E, Thalanany MM, Hibbert CL, Truesdale A, Clemens F, Cooper N, Firmin RK, Elbourne D, CESAR Trial Collaboration. Efficacy and economic assessment of conventional ventilatory support versus extracorporeal membrane oxygenation for severe adult respiratory failure (CESAR): A multicentre randomised controlled

trial. *Lancet*. 2009;374(9698):1351 – 1363. DOI:10.1016/S0140-6736(09)61069-2.

4. Montisci A, Maj G, Zangrillo A, Winterton D, Pappalardo F. Management of refractory hypoxemia during venovenous extracorporeal membrane oxygenation for ARDS. *ASAIO J.* 2015;61(3):227 – 236. DOI:10.1097/MAT.

5. Guinot PG, Zogheib E, Detave M, Moubarak M, Hubert V, Badoux L, Bernard E, Besserve P, Caus T, Dupont H. Passive leg raising can predict fluid responsiveness in patients placed on venovenous extracorporeal membrane oxygenation. *Crit Care*. 2011;15(5):R216. DOI:10.1186/cc10451.