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Early Mobilisation in Patients Undergoing Extracorporeal Membrane Oxygenation

Extracorporeal membrane oxygenation is a resource that is accessible in hospitals and intensive care units all over the world. In serious situations, ECMO therapy is intended to provide haemodynamic and/or ventilatory support. Because of this, many people refer to the ECMO patient as "the most critical patient." As a result, there is a very high likelihood that a critical disease will result in physical disabilities. A well-timed commencement to overcome such problems is crucial, as is a rehabilitation team that is well-trained and experienced.

Introduction

The critically ill patient is at high risk of developing functional alterations derived from the severity of the disease. The usage of drugs needed in critical illness, prolonged immobility and other factors directly impact muscle health (Martínez-Camacho et al. 2020). The muscle is an organ that can be severely affected in the intensive care unit (ICU) in various ways, such as fatty infiltrates, necrosis, ion channel alterations, mitochondria involvement and denervation. Together they manifest as generalised muscle weakness, usually symmetrical and that has no other explanation apart from critical pathology. This is known as ICU-acquired weakness (ICUAW) (Calixto-Mejía et al. 2020).

Currently, with the advancement in technology, life support measures have increased the therapeutic arsenal for critically ill patients and extracorporeal assistance is a reality in most units around the world. Among these devices, extracorporeal membrane oxygenation (ECMO) stands out, which, depending on the configuration, can provide pulmonary support (VV-ECMO) or haemodynamic support (VA-ECMO)(Combes et al. 2020; Shah et al. 2021). One of the most used indications for VV-ECMO is severe acute respiratory distress syndrome (ARDS) that does not respond to conventional management (protective mechanical ventilation, prone position, and neuromuscular blockade). An adequate selection of ECMO candidate patients is crucial to obtain favourable results.

ECMO and Physiotherapy

Before connecting the patient to ECMO, a management plan must be established, and the purpose of extracorporeal therapy must be determined. Nevertheless, ECMO can work as a bridge-to-resolution, bridge-to-transplantation or gain some time while the problem that conditioned the patient to require assistance can be resolved. Given the characteristics of the patients, it is possible to keep them hospitalised for a prolonged period in the ICU (Hayes et al. 2021). This puts these patients at a higher risk of developing relevant functional sequelae, post-intensive care syndrome, difficulty in weaning from mechanical ventilation, etc. Early mobilisation (EM) is a widely used strategy for the prevention of ICU-acquired weakness (ICUAW) in critically ill patients, and patients undergoing ECMO therapy are no exception.

Studies currently support the safety of the implementation of EM in this group of patients, with low adverse effects and many functional benefits (Hogdson et al. 2014; Cameron et al. 2015; Hayes et al. 2021). To carry out an EM programme, it is necessary to implement a highly trained rehabilitation team due to the special characteristics of this group of patients.

Identifying several situations in patient care before carrying out the exercise in patients on ECMO is crucial. For instance, the ECMO configuration, the type of support provided and the type of cannulation (**Table 1**). In addition, it is necessary to inspect the extraction and drainage cannula visually (Wieruszewski et al. 2023; Combes et al. 2020) (**Figure 1**). This can alert us to a malfunction of the membrane. The normal colouration in the extraction cannula is dark red and in the return cannula bright red. This is due to the blood characteristics (deoxygenated and oxygen-rich blood respectively). Also, the inspection of the cannula entry site to identify bleeding, displacement, or infection is crucial for the prevention of adverse effects (Mossadegh et al. 2016). Special care must be taken when moving the cannulas, especially in the lower limbs, since they can be bent and thus increase resistance, in addition to reducing the extraction flow; this is prevented by avoiding hip flexion >90° (Raurell-Torredà et al. 2021). It is recommended to fix the cannulas during the mobilisation of the patient to avoid any adverse event.

Within the general monitoring of the patient on ECMO, a DO2/VO2 ratio of at least 3:1 must be guaranteed to consider clinical stability (Lorusso et al. 2021). For this reason, it is essential to maintain SpO_2 >90% and SvO_2 >60%, which may have a direct correlation. On the other hand, a haemoglobin level >10 g/d is recommended; however, in some cases values >8g/dL, fibrinogen >150 mg/dL and platelets >80,000/mcL may be considered. If available, rotational thromboelastography can help in haematological monitoring. Haemodynamic stability must be continuously monitored at the patient's bedside, verifying perfusion windows, blood pressure, echocardiography and, if required, advanced invasive monitoring. The measurement of cardiac output is important for the termination of the flow and the revolutions per minute (rpm) in ECMO VV, recommending that it be close to 80% or 60 ml/Kg/Hr (Tonna et al. 2021; Ki et al. 2019; Shekar et al. 2020). It should be taken into account that exercise, especially active exercise, can increase oxygen consumption and the need for increased cardiac output, so it may be necessary to modify some parameters such as rpm, flow, FiO_2 or sweep gas, as well as the monitoring of ECMO pressures, which in the face of their alteration, rehabilitation should be temporarily suspended until resolution (**Table 2**) (Mossadegh et al. 2016).

VV	Inferior vena cava	Superior vena cava	• ARDS
VPa	Right atrium	pulmonary artery	• Right heart failure
VA	Right atrium	Common iliac artery	• Cardiogenic shock • Extracorporeal resuscitation
VAV	Inferior vena cava	Common iliac artery Superior vena cava	• Respiratory failure during VA ECMO • Cardiogenic shock during VV ECMO

Table 1. ECMO configurations and indications

Considerations to Mobilise VV ECMO Patients

Currently, the main indication for VV ECMO is severe ARDS, which entails some specific challenges for mobilisation in this population (Abrams et al. 2014; Pruijsten et al. 2014; Haji et al. 2021) These patients

Parameter	Relationship with EM during ECMO
Extraction pressure (P1) (mmHg)	It is the negative pressure generated by the centrifuge (cone) with which the patient's blood is extracted. At this point, it has not yet passed through the membrane (low O_2 level). A sudden change with or without movement of the cannula (wobble or whipping) requires further evaluation (volume requirement, bent cannula, cannula attached to the vein wall or pneumothorax). Hip flexion > 90º can generate a change in this pressure and compromise ECMO extraction, which is why it becomes one of the most important pressures to monitor during the mobilisation of these patients. Like the rest of the pressures (P2, P3, ΔP), the parameters may vary due to equipment and console, as well as the diameter of the cannulas. The medical staff should then be consulted about the trends and values of each patient to determine an alteration.
Pre-membrane pressure (P2) (mmHg)	It is the pressure taken between the centrifuge and the membrane; at this point the pressure becomes positive. The blood in this area is still low in oxygen. Its alteration may indicate a problem in the membrane such as the presence of a thrombus. For this reason, it is important to explore it with a flashlight in addition to evaluating ΔP.
Post-membrane pressure (P3) (mmHg)	It is the pressure taken after the blood passes through the membrane, because of this the pressure drops with respect to P2. At this point the visualisation of the cannula that is directed back to the patient (return) becomes important. Occlusion of the return cannula or increase in preload can increase its values.
Δ Pressure pre-post membrane (mmHg) (ΔP)	The pressure difference between P2 and P3 must be monitored on a recurring basis. A sudden increase would make us suspect an event that compromises the function of the membrane (e.g. thrombi). If membrane dysfunction is suspected due to a significant increase in Δ pressure pre-post membrane, a pre and post membrane gasometrical evaluation is recommended to confirm its integrity and function.

Sweep (l/min)	It is part of the mixture of gases that go to the ECMO membrane, which is in the blender. From the point of view of physiotherapy, it is the main parameter that allows us to regulate the CO_2 of the patient. It can directly influence the respiratory drive in awake patients (increased CO_2 levels in the blood increase the respiratory drive). Care must be taken with the repercussion of CO_2 at the level of cerebral perfusion. CO_2 levels depend on the sweep and the ventilation of the native lung, the corroboration of $PaCO_2$ is important. Capnography is not recommended in VV ECMO since all values and monitoring are done through arterial gases.
FiO2 of ECMO (0.21 to 1)	Quantity of oxygen that is provided to ECMO, usually kept at 100% during most part of de therapy. Prior to consider ECMO decannulation, it needs to be as low as 21%. We shall remember that SpO_2 and PaO_2 on the VV ECMO patient rely on both ECMO and native lung subjected to mechanical airway assistance.
Flow (l/min)	It is the amount of blood mobilised in one minute by the machine. The flow may be increased during exercise to improve tolerance. The flow (dependent variable) is the consequence of the revolutions per minute (independent variable).
Revolutions per minute (rpm)	It is the number of times that the centrifuge cone rotates per minute. Flow in adjustments are made through the rpm. In other words, to increase the flow, the rpm must be increased or vice versa.

Table 2. Principal parameters and their relationship with early mobilisation during ECMO

usually have significant lung parenchyma damage or inflammation that requires specific measures such as ultraprotective mechanical ventilation, neuromuscular blockade, and deep sedation. One of the most complex situations in the rehabilitation of a patient with ARDS in ECMO is to determine when they are ready for functional progression.

One of the main limitations is the need for deep sedation and neuromuscular blockade. There are some cases where it is necessary to combine ECMO with prone ventilation to reach oxygenation goals (Combes et al. 2020; Tonna et al. 2021). Oxygenation depends mainly on the membrane and the native lung; the latter being severely affected. As in most critically ill patients, sedation withdrawal is recommended as soon as possible to minimise deleterious effects. Early tracheostomy (as in the first seven days after intubation) can help in the rehabilitation process for better airway management, and a higher level of mobility, in addition to reducing swallowing and phonation complications derived from prolonged intubation (Nukiwa et al. 2022; DiChiacchio et al. 2020; Shaw et al. 2015).

Thus far, there is no evidence to mobilise patients in prone position; clinical stability will be the main priority in decision-making (Hogdson et al. 2014; Gómez et al. 2022). The approach can begin with passive interventions such as passive mobilisation, positioning, stretching, and neuromuscular electrostimulation (NMES) to maintain range of motion, joint health, and muscle preservation; however, priority should always be given to the extent of those possible from active muscle contraction and resisted exercise in and out of bed. Verticalisation can be useful starting with sitting in bed and continuing at the edge of it, depending on haemodynamic stability. Later, when the patient can overcome gravity with the lower extremities and the ability to support the trunk, standing or walking can be considered. If the patient is not cooperative, an alternative can be using hoists, cranes or verticalisation tables. All interventions should be aimed at improving functionality and activities of daily living (Haji et al. 2021). It is extremely important to establish therapeutic objectives based on functional scales applied in ECMO such as the ICU-Mobility Scale (IMS) or its adaptation for patients with ECMO (IMS-ECMO) (Abrams et al. 2021) (**Figure 2**).

One of the main concerns with physical exercise in patients with ARDS, especially on ECMO, is the possibility of generating patient self-inflicted lung injury (PSILI). So far, there is no evidence of the impact of exercise on lung injury in this population (Langer et al. 2016). As a precautionary measure, some parameters such as P0.1,

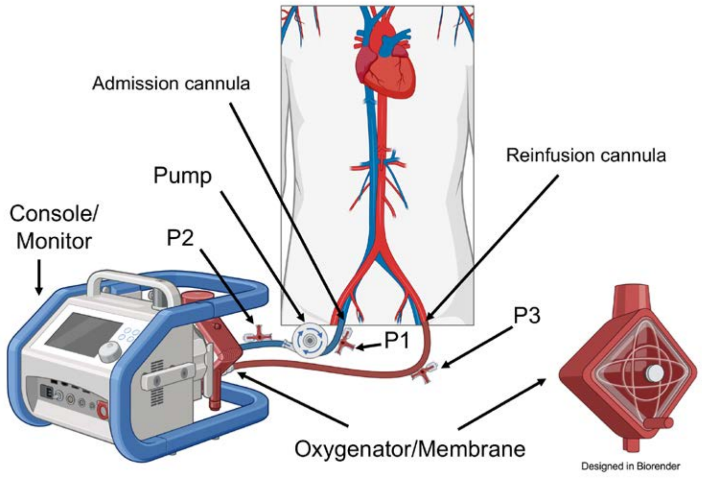

Figure 1. Anatomy of ECMO devices

muscle pressure (Pmus), muscle pressure index (MPI) or dynamic transpulmonary driving pressure (ΔPL) can be evaluated to monitor mechanical ventilation in spontaneous modes, which is recommended in patients who are already awake and who are in an active rehabilitation programme (Pavez et al. 2022). On the other hand, continuous monitoring of tidal volume and respiratory rate could be sufficient during the rehabilitation session, in addition to respiratory and haemodynamic stability. As previously mentioned, it may be necessary to modify some of the ECMO parameters to improve exercise resistance; increasing pressure support or FiO_2 on the ventilator can contribute to this objective.

The ECMO rehabilitation programme can be very extensive in these patients because ARDS tends to evolve slowly compared to other respiratory pathologies. In addition, in some cases the patient must be kept mechanically ventilated until a lung transplant is available, which can take considerable time. The importance of rehabilitation in critically ill patients has been demonstrated, as well as the patient undergoing ECMO therapy. Therefore, a well-trained team is needed to mobilise a severely ill patient such as those assisted through extracorporeal machines in order to increase the chances of recovery and improve its long-term prognosis.

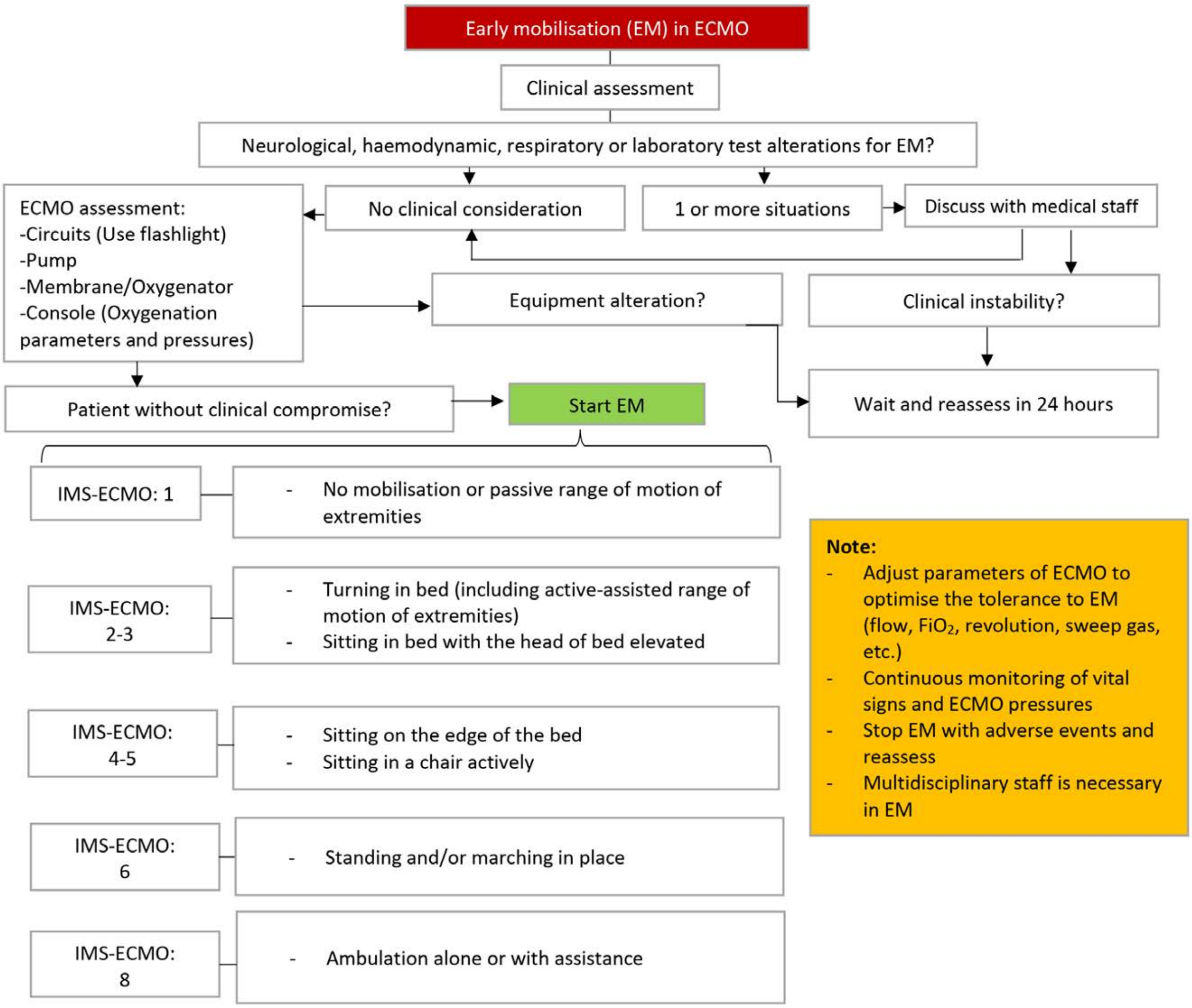

Figure 2. Algorithm early mobilisation in ECMO

Conflict of Interest

None. ■

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