Extracorporeal support of the respiratory system

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Abstract

In the last 20 years there have been significant advances in extracorporeal support of the respiratory system. What once was a highly complex intervention, undertaken as a salvage procedure in a handful of patients, has become more wide spread, both in terms of availability and underlying indications. We review the principles of equipment; physiological control of oxygenation and decarboxylation; associated complications; and role in clinical practice. The evidence for extracorporeal life support in this rapidly evolving field of organ support is critiqued.

Keywords Acute respiratory distress syndrome; decarboxylation; extracorporeal membrane oxygenation; hemorrhage; respiratory insufficiency; thrombosis

Royal College of Anaesthetists CPD Matrix: 1A01, 2C04, 3C00.

Learning objectives

After reading this article, you should be able to:

- explain the main functional components of an extracorporeal life support circuit for respiratory failure
- describe the physiology of oxygenation and decarboxylation
- identify the complications associated with extracorporeal support
- discuss the role of extracorporeal life support in clinical practice

Principles of extracorporeal support

The principle underpinning extracorporeal support of the respiratory system is the oxygenation and decarboxylation of blood at a point distinct from the native lungs. This allows lung rest and provides a bridge to lung recovery.

Extracorporeal support of respiratory (and cardiac) function is not new; cardiopulmonary bypass machines have been used in this capacity in a perioperative setting since the mid-twentieth century. In the 1960s, this extracorporeal technology was applied in the intensive care unit to support patients with respiratory failure. Early attempts at this so-called extracorporeal life support (ECLS) were typically unsuccessful: complication rates were high, in part due to the inflammatory and coagulation effects of early circuits, and in part due to the tendency for operators to access the arterial circulation.

Over time, technology has advanced, and experience has grown. Circuits and components are more biologically inert and there has been a move away from arterial cannulation to the less complex and lower risk venous approach.

While some variation in practice and in equipment remains, extracorporeal support of the respiratory system consists of four key components: a venous cannula for blood drainage, blood pump, membrane oxygenator and venous cannula for return of blood (Figure 1).

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Equipment

Cannula

Cannulae are made from polyurethane with biocompatible coatings to reduce inflammatory reaction and coagulation. Typically, these are inserted using the Seldinger technique with serial dilation. Blood is drawn from the central venous circulation via a 'drainage' cannula and re-enters the right sided circulation via a 'return' cannula.[1]

Cannulation sites include bifemoral placement (with the drainage cannula in mid-hepatic inferior vena cava and return cannula in right atrium), femoral access with jugular return or use of a bicaval dual lumen cannula into internal jugular vein.

In adults, single lumen cannulae may be in excess of 25Ch diameter, with the length for femoral insertion of up to 60 cm; bicaval cannulae are available up to 31Ch. As described later, high blood flow is an important aspect of some forms of respiratory ECLS and wide bore cannulae are often necessary.

Pump

A centrifugal pump generates flow through the circuit. Blood flow is dependent upon pump speed (revolutions per minute), 'preload' (i.e. the volume of blood available within the venous circulation, and resistance to flow in the drainage limb) and 'afterload' (return resistance and downstream pressure).

Membrane oxygenator

The oxygenator, a gas exchange interface, provides oxygen and removes carbon dioxide from the patient's blood through a capillary network composed of polymethylpentene tubules. Diffusion of CO_2 and O_2 occurs down a concentration gradient with blood and gas (known as sweep gas) in counter-current flow. A heat exchanger can be coupled with the oxygenator for systemic temperature control.

Physiology

Control of oxygenation

In a normally functioning oxygenator blood returning to the patient will be fully saturated. The contribution of the returning oxygenated blood makes to systemic oxygenation is dependent upon the extracorporeal blood flow relative to the patient's cardiac output. Blood returning from the extracorporeal circuit

Venoarterial and venovenous ECMO

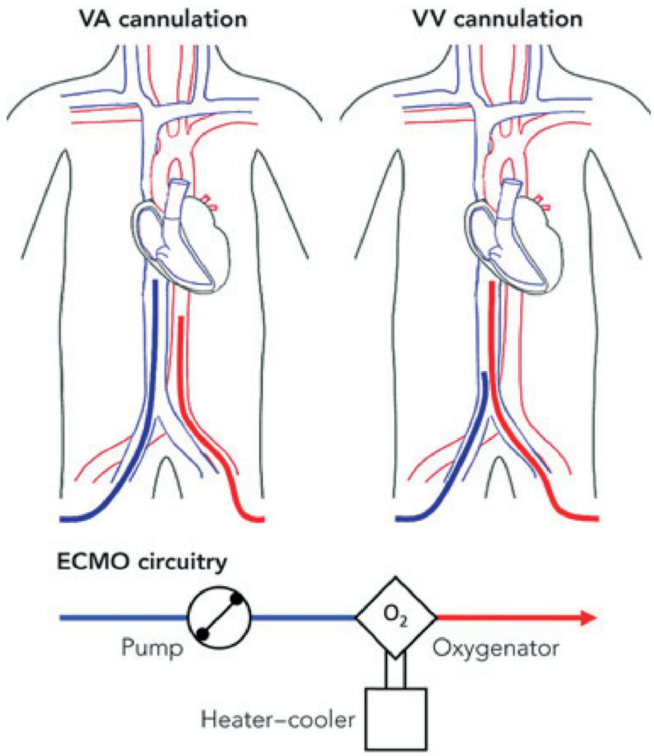

Figure 1 Examples of venovenous (VV) and venoarterial (VA) extracorporeal membrane oxygenation (ECMO) and circuitry used for both In both modalities blood is drained from the venous system (blue). In VA ECMO it is returned (red) to the arterial system and in VV ECMO it is returned to the venous system. Direction of blood flow in the circuit is indicated by the arrow. *Reproduced from Medical Journal Australia, 191, Lindstrom* et al. *'Extracorporeal Membrane oxygenation' pp178-182. Copyright (2009) with permission from John Wiley and Sons.*

mixes with deoxygenated venous return – which has not passed through the extracorporeal circuit – in the right atrium. The closer the extracorporeal blood flow to cardiac output (and therefore venous return), the greater the proportion of blood entering the pulmonary artery which has been oxygenated, and the higher the oxygen content of the mixed blood.

If the pulmonary pathology is so severe that the lungs make no contribution to gas exchange, the oxygen content in the left-sided circulation will be the same as that in the pulmonary artery; as the lungs recover, native pulmonary gas exchange will have an additive effect to oxygen content.

Oxygen transfer of the membrane is affected by recirculation, membrane efficiency, blood flow and haemoglobin concentration.

Control of decarboxylation

CO_2 removal is directly related to sweep gas flow (SGF) and is efficient even at low blood flow rates. The contribution of the extracorporeal circuit and native lungs are additive in the removal of CO_2. Extracorporeal removal of CO_2 allows maintenance of acceptable acid–base status despite significant reduction in ventilator tidal volume, alveolar pressure and frequency: the potentially injurious effects of mechanical ventilation are thus mitigated.

ECLS allows rapid correction of CO_2 and SGF should be titrated to ensure slow correction of arterial CO_2 in the initial phase due to vasoactive changes and risk of intracranial haemorrhage.[2]

Complications

The most common complications while on ECLS relate to coagulation. Both thrombosis and haemorrhage and can co-exist. Circulation of blood through an extracorporeal circuit triggers an inflammatory response and initiates the coagulation and fibrinolytic pathway.[3] This can be further exacerbated by the inflammatory stimulus of the underlying disease process (e.g. sepsis) creating a challenging balance of risks between bleeding and thrombosis.

Thrombosis

Contact between the extracorporeal circuit and blood leads to activation of coagulation and consequently there is a tendency for clot formation within the circuit, particularly within the oxygenator. Thrombosis within the oxygenator degrades gas exchange and causes a rise in the trans-membrane pressure. Furthermore, extracorporeal thrombus may precipitate intrinsic haematological problems, with a picture of thrombocytopenia, hypofibrinoginaemia and elevated D-dimer, not dissimilar to disseminated intravascular coagulation (DIC).

In addition, there is a high rate of in vivo venous thrombosis in ECLS survivors with an incidence of 8.1 per 1,000 cannula days reported.[4]

To prevent thrombosis – and prolong circuit life – the patient is typically anticoagulated with intravenous unfractionated heparin for the duration of their ELCS run. This is often withheld if the haemorrhagic issues described below arise.

Haemorrhage

The pathological, pharmacological and mechanical impact upon clotting places the ECLS patient at risk of life-threatening haemorrhage which may be precipitated by minor procedures or occur spontaneously.

In one retrospective study, 60% of ECLS runs were complicated by haemorrhage. The most common bleeding source being the cannulation site. Bleeding incidence was independently associated with severity of illness, higher activated partial thromboplastin time and recent surgery, resulting in an increased risk of death.[5]

Spontaneous intracranial haemorrhage (ICH) is a recognized complication of ECLS with an incidence of 16.4%.[2] The underlying mechanism is uncertain and not exclusively related to extracorporeal support: a significant proportion of severe respiratory failure patients exhibit ICH without ECLS exposure. If active screening for ICH is undertaken for patients on ECLS, and heparin withheld if haemorrhage detected, survival is comparable to the general ECLS population.[2]

Mechanical issues

The insertion of large intravenous cannulae into patients with life-threatening organ dysfunction carries inherent risk; however, the reported incidence of significant complications is low.[6]

For the patient established on ECLS, several potential mechanical issues exist, which are outlined in Table 1. In a robust system these issues are rare but can be immediately life

Mechanical issues of ECLS

Problem	Cause	Management
Air embolism	Can be catastrophic to circuit function Air entering circuit eg leaving caps off, intravascular devices or inadequate infusion de-airing	De-air circuit Find source ± circuit change
Membrane failure	Thrombus (usually) Hypertriglyceridaemia (propofol,TPN)	Circuit change Change propofol to midazolam
Console failure	Loss of power Issue with pump (rare)	Alternative driver New console
Unplanned decannulation	Partial or complete removal of cannula from vessel due to inadequate fixation or inappropriate tension on line	Partially removed – reinsert till side holes covered. Manage haemorrhage + de-air circuit Complete – clamp return line, turn off pump, establish emergency ventilation + replace volume

Table 1

threatening. Frequent skill training for prevention and management should therefore occur.

Role of extracorporeal support

Acute respiratory distress syndrome (ARDS)

ARDS is a syndrome precipitated by local or systemic inflammatory insult which manifests clinically as reduced lung compliance and impaired gas exchange. Severe ARDS (P:F ratio <100 mmHg) has a high risk of death: a recent international epidemiological study reporting short term mortality of 46%.[7]

ECLS offers two broad theoretical benefits in the ARDS population.

Firstly, for those with life threatening hypoxia and hypercapnia despite optimal mechanical respiratory support, ECLS offers an alternative means of gas exchange as a bridge to lung recovery. The use of ECLS in this population has been explored in recent years with two randomized controlled trials and a number of quasi-experimental propensity matched studies (Table 2).[8–10]

The second potential role for ECLS in ARDS is to facilitate lung protective ventilation in patients with moderate to severe ARDS. Lowering tidal volume (Vt) and trans-alveolar pressure will reduce the mechanical energy applied to the inflamed lung, and may reduce the risk of ventilator induced lung injury.

Ultra-protective lung ventilation (with Vt 3ml kg^{-1} and plateau pressure ≤ 25 cmH_2O^{-1}) may reduce mortality in moderate to severe ARDS.[12] The use of low blood flow ECLS (often referred to as extracorporeal CO_2 removal ($ECCO_2R$) as the blood flow is insufficient to provide meaningful oxygenation) has been shown to be a feasible means of achieving this ultra-lung protective strategy.[11] The REST trial, which is in progress, seeks to test whether the use of $ECCO_2R$ in this context reduces mortality.[12]

Summary of evidence

Study	Intervention	Outcome	Caveat
CESAR (Peek 2008)[8]	Severe ARDS patients retrieved to expert centre for ECLS consideration versus managed locally	Increased disability free survival in intervention arm at 6 months (63% vs 47%; RR 0.69; 95% CI 0.05 –0.97, p = 0.03)	75% intervention arm received ECLS Is a study of benefit of transfer to expert centre capable of ECLS (rather than ECLS therapy)
EOLIA (Coombs 2018)[9]	Severe respiratory failure patients ECLS vs conventional therapy	No statistically significant mortality benefit at 60 days (35% ECMO group vs 46% control group; RR 0.76; 95% CI 0.55–1.04; p = 0.09)	28% control patients received ECLS as rescue therapy Possible type 2 error Re-analysis using Bayesian theorem suggested mortality benefit with ECLS
Meta-analysis (Munshi 2019)[10]	Included propensity matched trials, EOLIA + CESAR	Significant mortality benefit with ECMO at 60 days (34% vs 47%; RR 0·73; 95% CI 0·58–0·92; p = 0·008)	

Table 2

Severe respiratory failure indications for ECLS

Criteria
Lung injury Score >3 (includes PF ratio, consolidation on CXR, PEEP and compliance)
Uncompensated hypercapnia with pH<7.20
Reversible pathology
No underlying life limiting comorbidity leading to dependency on ECMO

Table 3

Patient selection

In the United Kingdom, extracorporeal respiratory support is delivered through a national network. Patients are accepted if they meet criteria in Table 3. Analysis of this approach demonstrated a 72.1% survival in those selected for ECLS.[13]

Novel uses of respiratory ECLS

Refractory shock

In selected patients with severe respiratory failure and significant haemodynamic instability, respiratory ECLS may offer cardiovascular benefits. The increased oxygen delivery and carbon dioxide clearance, reduction in intrathoracic pressures and improved acid base status may improve myocardial contractility. It is not uncommon for initiation of respiratory ECLS to be followed by a significant reduction in cardiovascular support requirements.

In cases in which myocardial function remains impaired despite correction of oxygenation and acid base, respiratory ECLS can be adapted to a hybrid mode of extracorporeal support. By inserting a further cannula into the arterial system, the return blood flow may be split between right and left circulations, thereby providing both respiratory and cardiac support.

Perioperative ECMO

ECLS as an adjunct to complex airway or thoracic surgery allows prolonged periods of apnoea (and thus optimization of the surgical field), reduction in mechanical ventilatory pressures and extubation (reducing strain on suture lines). This approach, however, exposes the patient to the risks described above, and in particular, bleeding. ECLS as a bridge to lung transplant in select patients is controversial but favourable outcomes have been reported.

Extracorporeal carbon dioxide removal ($ECCO_2R$)

Chronic obstructive pulmonary disease (COPD)

Exacerbation of COPD resulting in hypercapnic respiratory failure can require non-invasive or invasive ventilation which is associated with increased mortality and often prolonged weaning. The use of $ECCO_2R$ in this patient group to facilitate early extubation or prevention of intubation is an appealing prospect. A randomized clinical trial is currently examining the use of $ECCO_2R$ upon physiology and outcomes in this context.[14]

Conclusion

The role of extracorporeal support for severe respiratory failure continues to increase with improving survival. The research database is expanding with several pivotal studies awaited that could change the future of this therapy in modern day intensive care medicine. ◆

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