PEER REVIEWED PERSPECTIVE

Extracorporeal membrane oxygenation in adults

When life support alone is just not enough

TIFFANY FULDE MB BS; **JEFFREY BREEDING** MN, RN, GradDipEd; **PRIYA NAIR** MB BS, MD, FCICM

Extracorporeal membrane oxygenation (ECMO) is a potentially life-saving rescue strategy for patients with severe, refractory respiratory and/or cardiac failure despite maximal ventilatory, pharmacological and/or mechanical support. Although used relatively widely in paediatric intensive care, its use in adults until almost a decade ago was infrequent. Technological advances and an increase in experience and understanding have resulted in improvements in outcome from ECMO support, leading to wider use of this technology in adult intensive care. There are, however, important considerations in the follow-up care of patients who have had ECMO support.

Key points

- **Extracorporeal membrane oxygenation (ECMO) is a potentially life-saving rescue strategy for patients with severe, refractory respiratory and/or cardiac failure.**
- **Its use in specialised critical care units is becoming more widespread as a result of improved technology and experience.**
- **It remains an invasive and expensive intervention and judicious patient selection is important to ensure good outcomes.**
- **Newer applications of ECMO include isolated carbon dioxide removal and ECMO–CPR to facilitate definitive curative intervention in appropriate patients.**
- **Management of potential complications and long-term sequelae is an area that is receiving increasing attention.**

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Dr Fulde is an Anaesthetic Registrar at St Vincent's Hospital, Sydney. Mr Breeding is a Clinical Nurse Consultant at the Intensive Care Unit, St Vincent's Hospital, Sydney. Dr Nair is a Senior Specialist, Intensive Care Unit at St Vincent's Hospital, Sydney, and Conjoint Senior Lecturer at the University of New South Wales, Sydney, NSW.

Case scenario

Mr GG, a 45-year-old man, was brought to the emergency department by police on a winter morning. He was found in a park unresponsive, very cold and smelling of alcohol. Soon after arrival he had a ventricular fibrillation arrest and his body temperature was 26.7°C. Advanced life support was implemented as per guidelines; however, his ventricular fibrillation remained refractory to conventional therapy. It was decided to institute peripheral veno-arterial extracorporeal membrane oxygenation (V-A ECMO) to provide organ perfusion, restore normothermia, and allow time for the heart to recover and for the next appropriate therapeutic decision to be made. Soon after institution of peripheral V-A ECMO the patient reverted to sinus rhythm and was transported to the intensive care unit (ICU) with inotropic support (see Figure 1). Echocardiography demonstrated biventricular impairment.

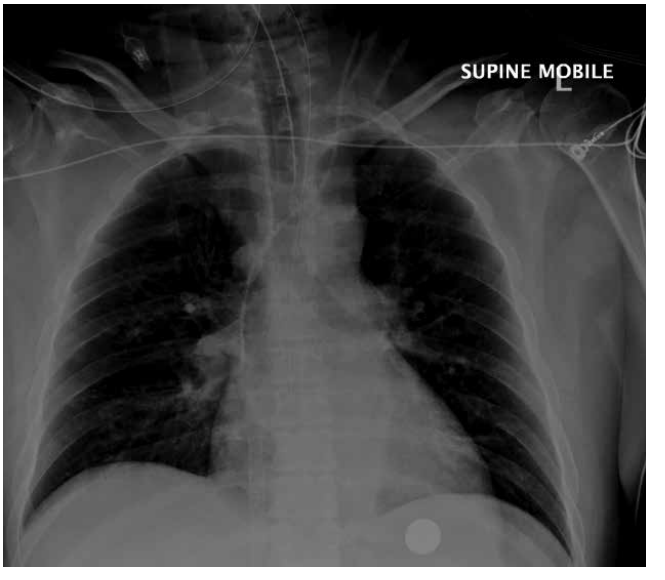

Figure 1. Mr GG's x-ray soon after extracorporeal membrane oxygenation showing the cannula introduced up the inferior vena cava, draining venous blood close to the right atrium.

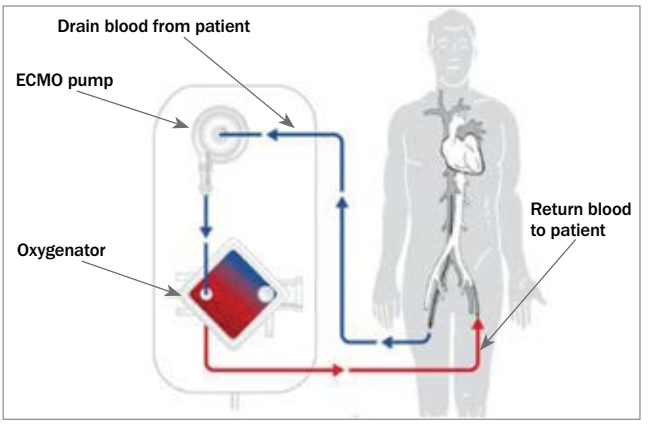

Figure 2a. Diagrammatic representation of extracorporeal membrane oxygenation circuit.

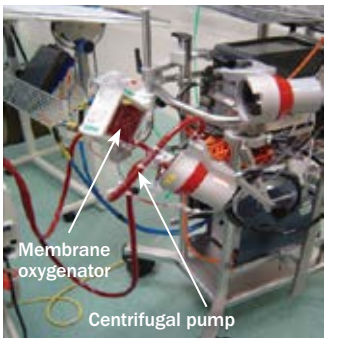

Figure 2b. Extracorporeal membrane oxygenation circuit.

Figure 2c. Portable extracorporeal membrane oxygenation console.

Introduction

ECMO was first used successfully in the 1970s, but following discouraging results from an early randomised trial in adults with respiratory failure, which showed high mortality (above 90%) in both intervention and control groups,[1] it was largely abandoned worldwide. Since then, ECMO technology has greatly improved and the risk of lung injury from high ventilatory volumes and pressure is now better appreciated. Following on from its widespread use in paediatrics with reversible cardiorespiratory failure, there is increasing evidence supporting its use in adults, particularly following the conventional ventilatory support versus ECMO for severe adult respiratory failure (CESAR) trial[2] and the widespread use of ECMO during the 2009 H1N1 pandemic.[3]

What is ECMO?

ECMO consists of a circuit that removes blood via a large vein and transports it to a membrane oxygenator where oxygen is added and carbon dioxide removed (Figures 2a to c). The blood is then returned to the patient either via a large vein (veno-venous [V-V] ECMO) or artery (veno-arterial [V-A] ECMO).

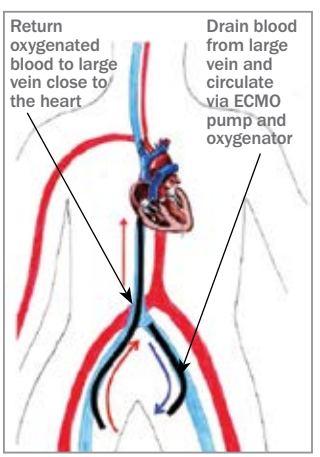

Figure 3a. Veno-venous extracorporeal membrane oxygenation (ECMO).

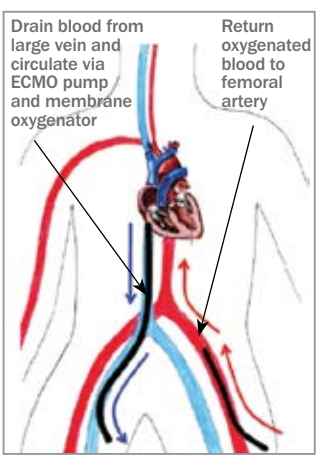

Figure 3b. Peripheral veno-arterial extracorporeal membrane oxygenation (ECMO).

Types of ECMO

V-V ECMO is generally used for patients with isolated respiratory failure without major cardiac failure and assumes the function of the patient's lungs. There may be a degree of cardiac impairment secondary to hypoxia and hypercarbia, which often improves following initiation of V-V ECMO. The ECMO cannulae are usually placed percutaneously into the femoral or internal jugular veins, with oxygenated blood returned near or into the right atrium, and then pumped through the pulmonary and systemic circulation by the native heart (Figure 3a).

V-V ECMO may use two cannulae (access and return cannulae in two different veins [for adults, generally French sizes 21 to 25]) or a single dual-lumen cannula (for adults, generally French size 27 or 31), which is capable of draining venous blood as well as returning oxygenated blood to the right atrium.

V-A ECMO is primarily used for patients with cardiac failure with or without coexisting respiratory failure. V-A ECMO assumes the function of the patient's heart and lungs, draining venous blood, bypassing the heart and returning oxygenated blood into the patient's ascending aorta (central V-A ECMO) or peripheral artery (e.g. femoral peripheral V-A ECMO). It therefore decreases pulmonary artery pressure and increases arterial oxygen, as well as supports systemic perfusion by delivering blood under pressure to the arterial circulation (Figure 3b). It is used in patients with reversible left and/or right ventricular failure.

V-V ECMO and V-A ECMO are occasionally used as a bridge to lung or heart transplant (or ventricular assist device), respectively, in a select group of patients in good general health and with no other organ dysfunction. In more recent times, there is a growing interest in providing V-A ECMO support in cardiac arrest situations (ECMO-cardiopulmonary resuscitation [ECMO-CPR or E-CPR]) when there is a likely reversible pathology, such as acute coronary syndrome or pulmonary embolism, while definitive therapy is undertaken. Currently, this can only be provided in designated ECMO centres and requires careful patient selection and specialised ongoing management to result in favourable outcomes. Another area of growing interest is the use of low-flow ECMO, achieved with a smaller size cannula, purely for carbon dioxide removal in isolated hypercarbic respiratory failure without hypoxia. This is known as extracorporeal CO_2 removal (ECCOR).

Benefits and indications

ECMO itself is not a cure, but supports the patient while the underlying causes are identified, treated or resolved. Recent evidence points to increased survival with the use of ECMO (Table 1).[4]

Early initiation of ECMO has been associated with better outcomes in some observational studies. The CESAR trial, the only randomised control trial in this area from the UK from 2001 to 2006, showed that transfer of patients with severe respiratory failure to a single specialist ECMO centre significantly reduced the risk of death or severe disability at six months, compared with conventional mechanical ventilation management in multiple ICUs without ECMO capabilities.[2]

The 2009 H1N1 influenza pandemic provided valuable experience in the use of ECMO in the management of patients with acute respiratory distress syndrome. A cohort study of patients supported with ECMO from Australia and New Zealand was published early in the pandemic. A total of 68 patients were managed in 15 ICUs across the two nations over a three-month period. The median duration of ECMO support was 10 days and favourable outcomes were noted, with a 71% survival rate to ICU discharge and a relatively low rate of severe complications.[3]

Broadly, there are two categories of patients who may benefit from V-V ECMO.

Table 1. International survival rates from the Extracorporeal Life Support Organization registry report (2014)[4]

Adult ECMO	Total patients	Survived extracorporeal life support	Survived to discharge or transfer
Respiratory	5146	3317 (64%)	2905 (56%)
Cardiac	4042	2255 (56%)	1636 (40%)
ECMO–CPR	1238	476 (38%)	355 (29%)
Total	10426	6048 (58 %)	4896 (47%)

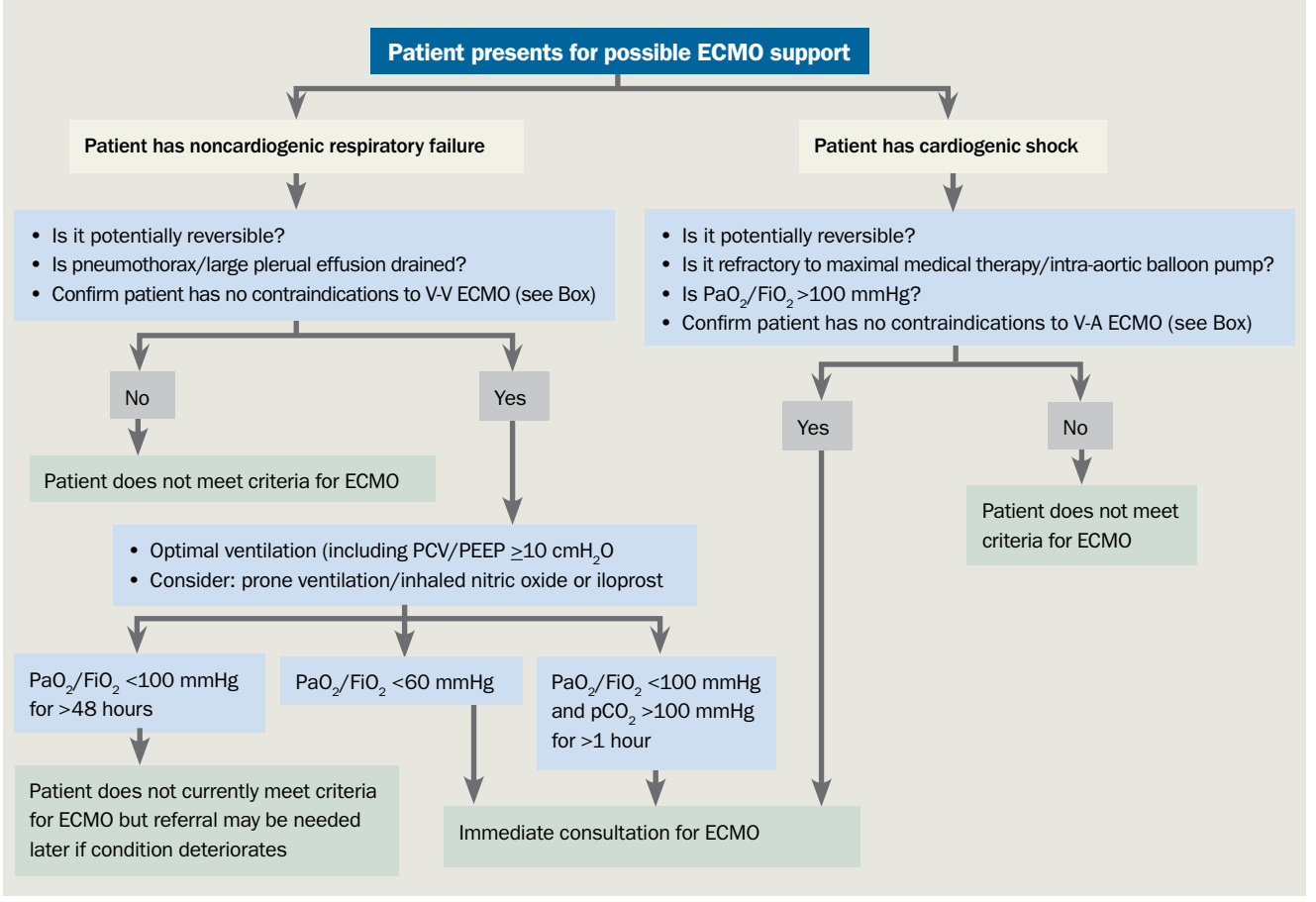

Figure 4. Indications for extracorporeal membrane oxygenation therapy and referral of patients (based on guidelines developed by Extracorporeal Life Support Organization).[5]

Modified from Ministry of Health, NSW, Critical Care Tertiary Referral Networks and Transfer of Care (Adults), Policy Directive PD2010_021, 30 March 2010.

Abbreviations: FiO_2 = fraction of inspired oxygen; PaO_2 = partial pressure of oxygen in arterial blood. pCO_2 = partial pressure of carbon dioxide in blood; PCV = pressure control ventilation; PEEP = positive end-expiratory pressure; V-A ECMO = veno-arterial extracorporeal membrane oxygenation; V-V ECMO = veno-venous extracorporeal membrane oxygenation.

Contraindications to ECMO therapy[5]

Absolute contraindications to all forms of ECMO
- Significant pre-existing comorbidity, such as irreversible neurological condition, cirrhosis with ascites, encephalopathy, history of variceal bleeding, active malignancy with predicted limited survival, HIV infection
- Weight above 120 kg

Relative contraindications to all forms of ECMO
- Age over 65 years
- Multiple trauma with uncontrolled haemorrhage
- Multiple organ failure

Absolute contraindications to veno-venous ECMO (for respiratory failure)
- Pulmonary hypertension (mPAP >50 mmHg)
- Severe right or left heart failure (EF <25%)
- Cardiac arrest

Relative contraindications to veno-venous ECMO
- High pressure, high FiO_2 IPPV for >1 week

Absolute contraindication to veno-arterial ECMO (for cardiac failure)
- Severe aortic valve regurgitation
- Aortic dissection

Relative contraindication to veno-arterial ECMO
- Severe peripheral vascular disease

Abbreviations: ECMO = extracorporeal membrane oxygenation; EF = ejection fraction; FiO_2 = fraction of inspired oxygen; IPPV = intermittent positive pressure ventilation; mPAP = mean pulmonary artery pressure.

Reproduced from Ministry of Health, NSW, Critical Care Tertiary Referral Networks and Transfer of Care (Adults), Policy Directive PD2010_021, 30 March 2010.

- Patients who are unable to be supported with maximal positive pressure ventilation due to hypoxic (type I) or hypercarbic (type 2) respiratory failure.
- Patients who could be sustained by positive pressure ventilation, but at the expense of the damaging effects of excessively high pressures resulting in ventilator associated lung injury. In these patients, ECMO enables the use of lung-protective ventilator settings, which deliver lower tidal volumes, thereby lowering the airway pressures and delivered oxygen concentrations, thus preventing volutrauma, barotrauma and oxygen-toxicity while maintaining acceptable gas exchange.

Patients may benefit from V-A ECMO when cardiogenic shock persists despite adequate volume resuscitation and pharmacological and/or other interventions, including inotropic and vasopressor support and other devices such as intra-aortic balloon pump.

The potential benefits of ECMO must be carefully weighed against the risks to the patient and resources used. Relative contraindications include conditions that are associated with a poor outcome or which will impair the patient's quality of life (including the primary illness and pre-existing conditions) and futility (patients who are unlikely to increase their overall survival due to a fatal diagnosis, or who are too unwell or deconditioned).

The NSW critical care tertiary referral network have developed guidelines that outline the indications for ECMO therapy and when to refer patients to an ECMO centre (see Figure 4 and the Box).[5]

Complications

Patients requiring ECMO support are a very heterogeneous group, with a variety of indications for ECMO and a wide spectrum of underlying disease severity and comorbidities. Therefore the potential complications these patients can develop, both short and long term, relate to the severity of illness as well as the ECMO support itself. ECMO-related complications, which can be acutely life-threatening, include circuit-related and patient-related complications (Table 2). A high level of staff training and close monitoring is required to manage these complex patients.

ECMO weaning and decannulation

Clinical improvement is measured against the initial indication for commencing ECMO. In V-V ECMO, improvements in gas exchange and oxygenation (reflected on arterial blood gas), lung compliance and chest radiology are signs of recovery. ECMO support is weaned and the patient reassessed prior to decannulation. Similarly, suitability for weaning from V-A ECMO is assessed by looking for improvement in cardiac contractility and ejection fraction on echocardiography and improvement in clinical parameters.

Considerations in follow-up care

In addition to the potential sequelae of long-term critical illness, such as pressure areas, neuropraxias, altered taste sensation and slow muscle recovery from deconditioning, patients who have had ECMO therapy require specific additional considerations in follow-up care with surveillance for specific complications. These include infection, lymphocoeles and aneurysm formation of the femoral vessels. The development of post-traumatic stress disorder (PTSD) is an important concern that may require specific attention.

In a local, single-centre follow-up study of 56 patients who received ECMO over a two-year period, 75% survived to hospital discharge, six died prior to follow up and 15 were lost to follow up.[6] Of the 21 survivors contacted, four patients declined consent and 17 patients completed a quality of life (Short Form-36) survey with a median follow-up time of 19.5 months. Overall, moderately reduced scores were noted in the domains of physical function, which was more pronounced in patients who received VA-ECMO, possibly reflecting their overall severity of illness. However, scores across the mental health domains were relatively preserved. Despite not being part of the SF-36 questionnaire, a number of patients voluntarily reported features of PTSD.[6]

Patients may experience ongoing respiratory or cardiac impairment, which may impact their physical functioning; however, ECMO follow-up studies have shown that patient quality of life is comparable or even better than their counterparts who have similar underlying disease severity but have not received ECMO, therefore reflecting the disease process rather than ECMO therapy itself.

Table 2. Complications of extracorporeal membrane oxygenation (ECMO)

ECMO-related complication	Clinical significance	Preventative measures/prescription
Thrombus formation, particularly in oxygenator	Circuit failure Systemic embolisation e.g. cerebrovascular accident	Systemic anticoagulation, most commonly unfractionated heparin
Loss of cardiac pulsatility leading to intraventricular thrombus formation	Systemic embolisation	As above, echocardiographic surveillance
Haemorrhage – Anticoagulation, haemostatic changes, platelet dysfunction, consumptive coagulopathy	Minor local bleeding to catastrophic intracranial or gastrointestinal haemorrhage Complications of transfusion	Close monitoring of coagulation state and targeted therapies
Red cell injury	Haemolysis	Monitoring/early intervention
Air in the circuit, disconnection or circuit rupture	Air embolus	Inbuilt alarms, careful surveillance
Limb ischaemia, lymphocoele or pseudoaneurysm with veno-arterial ECMO	Compartment syndrome, limb loss	Backflow perfusion cannula to perfuse lower limb
Hospital-acquired infections	Cannulation site infections, blood stream infections	Surveillance and appropriate therapy
Altered pharmacokinetics of administered drugs due to circuit	Risk of underdosing, particularly antimicrobials	Therapeutic drug monitoring
High sedation requirements to optimise circuit function	Risks of immobility-pressure areas, deep vein thrombosis, infections, muscle wasting, critical illness polyneuropathy, delirium, post-traumatic stress disorder	Minimise the use of sedative agents, including 'awake ECMO', active physiotherapy and early rehabilitation

Case continued

Mr GG's vasoactive drugs were able to be weaned rapidly as his cardiac function improved. After two days, he was weaned and decannulated from ECMO, and subsequently from the ventilator. He spent a total of four days in the ICU. Repeat echocardiography showed normal left and right ventricular size and function. He was well on the ward, although malnourished and deconditioned. He had multiple social and psychological issues, which required attention. He was discharged home after 20 days in hospital.

Conclusion

ECMO technology and understanding is evolving, leading to improving outcomes for patients with refractory respiratory and/or cardiac failure. The application of this intervention may consequently expand. Appropriate management of potential complications and long-term sequelae is an area that is receiving increasing attention. CT

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Further reading

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