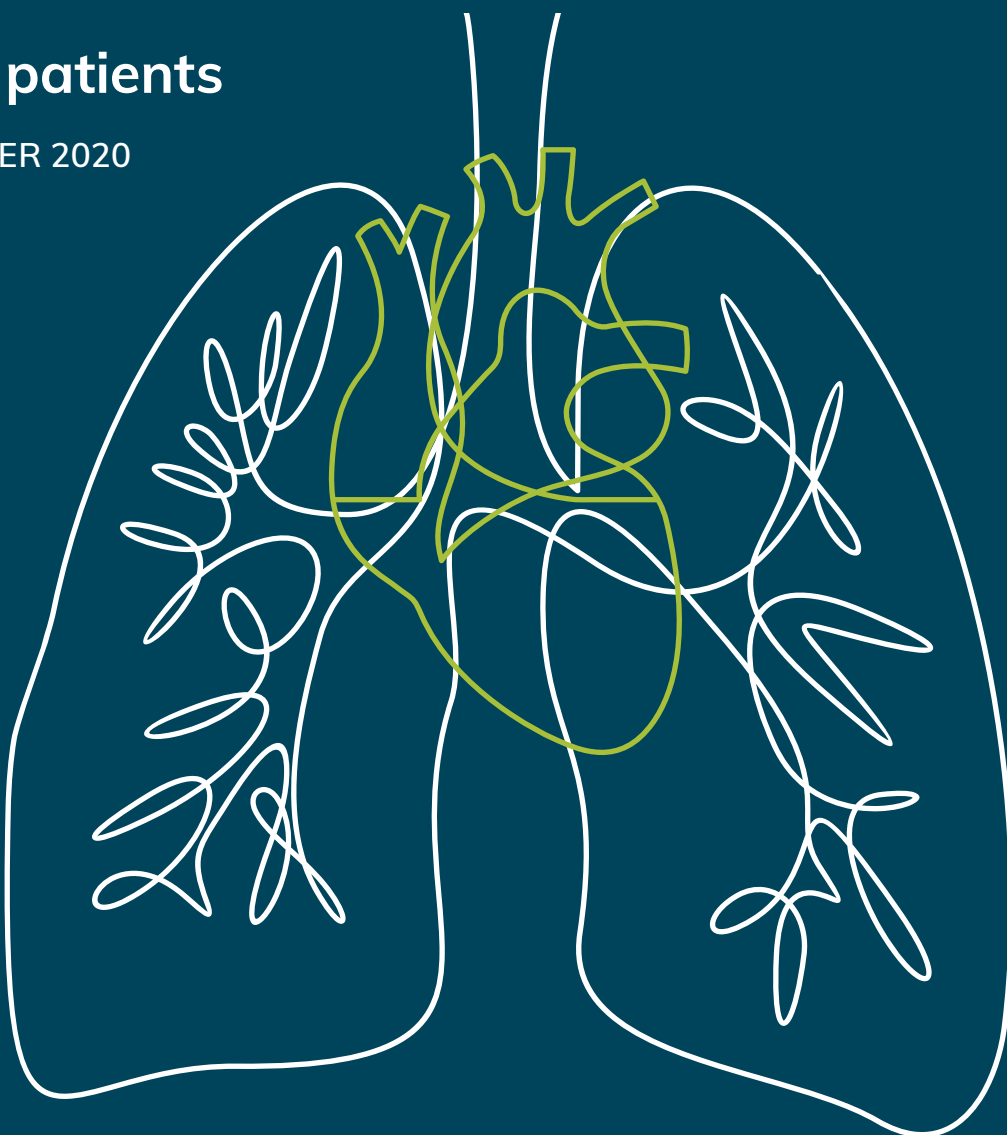


ECMO (extracorporeal membrane oxygenation) services in NSW

Adult patients

NOVEMBER 2020



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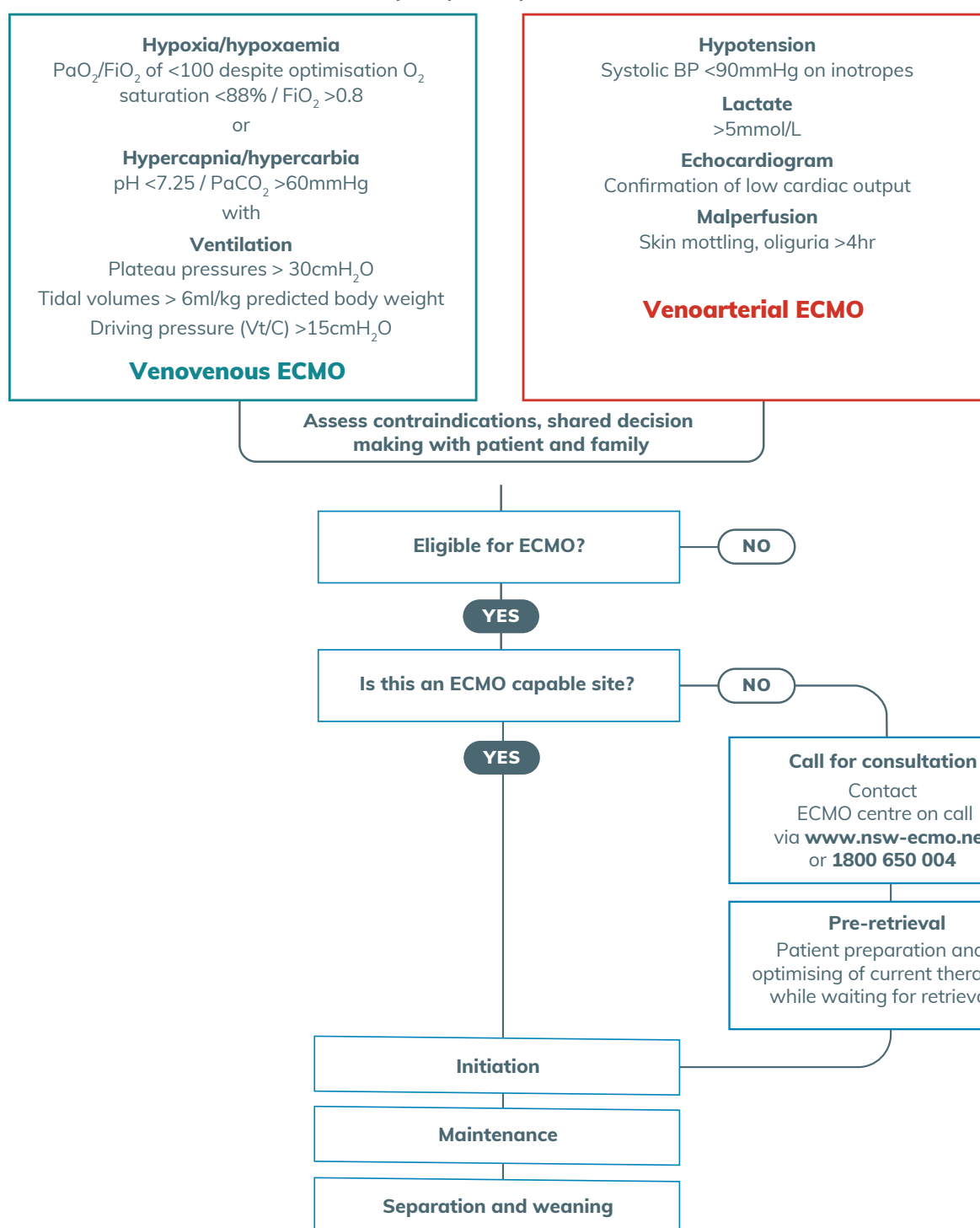
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ECMO (extracorporeal membrane oxygenation) services in NSW

ECMO for adult patients, at a glance

Patients with refractory respiratory or cardiac failure, assess for:



Summary

Extracorporeal membrane oxygenation (ECMO) is an advanced form of life support targeted at the heart and lungs. It may be indicated in cases of acute severe cardiac or pulmonary failure that is potentially reversible and unresponsive to conventional management. ECMO is delivered in an intensive care unit (ICU). There are two main types of ECMO – venovenous and venoarterial. Both provide respiratory support, but only venoarterial ECMO provides haemodynamic support.

Each ECMO episode of care is referred to as a 'run'. In 2018–19, there were 124 ECMO runs in New South Wales (NSW). Eight ICUs currently provide ECMO services. Two sites, the Royal Prince Alfred Hospital and St Vincent's Hospital, manage a retrieval service. Between January 2016 to November 2019, NSW Aeromedical Retrieval Service transferred 100 adult patients for the purpose of receiving ECMO. The NSW case mortality rate was 42% for the five year period from July 2014 to June 2019.

This clinical guide outlines key areas of ECMO practice. The content draws on consensus statements and recommendations published by the Extracorporeal Life Support Organization (ELSO) and other jurisdictions, supplementary searches of research literature and advice from local experts gathered through structured deliberative processes.

Indications and patient selection

A wide range of underlying diseases have been identified as indications for ECMO. For venovenous ECMO it includes acute respiratory distress syndrome (ARDS). For venoarterial ECMO they include cardiogenic shock, pulmonary embolism with obstructive shock, cardiac failure due to sepsis or anaphylaxis and as a bridge to transplantation.

International guidance recommends that any decision to initiate ECMO be made on a case-by-case basis by a multidisciplinary team. This team should be led by an ECMO intensivist with involvement of other specialists such as a cardiologist or cardiothoracic surgeon, respiratory physician, cardiac perfusion service and nursing staff. The final decision to initiate ECMO is preceded by patient optimisation that includes strategies to optimise organ supports.

Retrieval for ECMO Services

There is some evidence of a volume outcome relationship in ECMO. Patients who received ECMO at hospitals with more annual cases have historically had significantly better outcomes. If patients need ECMO and they are located in a lower-volume hospital, depending on the capabilities of that hospital, they may need to be transferred to a higher-volume hospital.^{1,2}

This supports the use of retrieval services to a limited number of expert centres. Volumes have however been identified as only one contributory factor to good outcomes.

Initiation phase of ECMO

The initiation phase incorporates patient selection, anticoagulation, imaging, cannulation, titration and consideration of patient and family/carer needs. There is not clear agreement on anticoagulation regimens, however cannula site selection is well established and appears to be standardised internationally.

Maintenance phase of ECMO

There are a number of dynamic factors that require monitoring and adjustment during ECMO. These include the circuit, anticoagulation, haemoglobin levels and ventilator settings. Routine patient care and prevention of complications such as pressure injury is also required.

Separating and weaning from ECMO

Weaning strategies are generally based on expert opinion rather than evidence. Venovenous ECMO indications include improvement in pulmonary compliance, oxygenation and CO₂ removal and arterial oxyhaemoglobin saturation. For venoarterial ECMO, measures of improvement in left ventricular cardiac output, such as enhanced aortic pulsatility, are an important indicator of successful weaning.

One or more weaning trials should be performed prior to separation from ECMO.

Complications of ECMO

The morbidity associated with ECMO can be significant. The most common serious complications for ECMO are thrombosis and haemorrhage.

Extracorporeal cardiopulmonary resuscitation (ECPR)

ECPR is the use of venoarterial ECMO to augment resuscitation following cardiac arrest. Observational studies have assessed ECPR in both in-hospital and out-of-hospital settings. Compared to poorer outcomes associated with out-of-hospital cardiac arrest, better outcomes are achieved among in-hospital cardiac arrest patients. Research and evaluation of ECPR are ongoing.

The European Resuscitation Council and the American Heart Association do not recommend the routine use of ECPR in the context of cardiac arrest.

Next steps

Although ECMO is widely acknowledged as an option for acute cardiogenic shock and severe respiratory failure, most developed healthcare systems have taken steps to restrict its use to populations that would derive the most benefit.

The operational model of care to guide the provision of ECMO services in NSW, informed by this clinical guide, is available on the ACI website www.aci.health.nsw.gov.au.

Background

ECMO is a means of providing cardiac and respiratory support to critically ill patients. ECMO can be used for oxygenation, carbon dioxide removal and haemodynamic support. ECMO is based on cardiopulmonary bypass technology. ECMO circuits typically consist of cannulae, tubing coated with an anticoagulant, a centrifugal blood pump, an oxygenator, a temperature control system, monitors and tubing access points.³

There are two main types of ECMO – venovenous and venoarterial. Both provide respiratory support, but only venoarterial ECMO provides haemodynamic support. ECMO is delivered in an intensive care unit (ICU).

Venovenous ECMO (V-V ECMO) involves venous blood from the patient being accessed from the large central veins and returned to the venous system near the right atrium after it has passed through an oxygenator. It provides support for severe respiratory failure when no major cardiac dysfunction exists.

V-V ECMO improves the patient's oxygenation by adding oxygen to blood that then passes through the lung to the systemic circulation. Carbon dioxide is removed from the patient's blood. This also allows the level of ventilatory support to be reduced, which may reduce ventilator-induced lung injury.

Venoarterial ECMO (V-A ECMO) involves venous blood from the patient being accessed from the large central veins and returned to a major artery after it has passed through the oxygenator. It provides support for severe cardiac failure (sometimes with associated respiratory failure), most commonly after cardiac surgery. Extra corporeal cardiopulmonary resuscitation (ECPR) is a specific type of time critical V-A ECMO performed on patients in cardiac arrest.

ECMO is a multidisciplinary service involving a wide range of specialists.

Source: Health Information Exchange, NSW Ministry of Health

Method

A rapid literature review of the peer reviewed and grey literature (2015 onwards) used the following search terms:

- "Extracorporeal Membrane Oxygenation/ standards"[MAJR]
- "Extracorporeal Membrane Oxygenation: OR ECMO [tiab] AND systematic review
- ("extra corporeal cardiopulmonary resuscitation" OR ECPR) AND (out-of-hospital OR OHCA)
- ECMO AND volume AND mortality AND adult.

Current ECMO services in NSW

In NSW there are 38 adult intensive care units. Of these, eight currently provide ECMO services, with seven ECMO centres in metropolitan Sydney and one in Newcastle. Two Sydney hospitals, Royal Prince Alfred and St Vincent's, provide clinical advice on the management of adults with severe respiratory and/or severe cardiac failure via a roster system. These two centres also work with NSW Aeromedical Retrieval Service to manage ECMO retrieval services for hospitals without ECMO capability. This is a supra LHD service covered by NSW Health Service Agreements and described by PD2018_011 NSW Critical Care Tertiary Referral Networks and Transfer of Care (ADULTS).⁴

In NSW there were 643 ECMO runs over a five year period between July 2014 – June 2019. Of these, 273 (42%) patients died in hospital during their ECMO admission. In 2018-19 there were 124 ECMO runs in NSW, of which 11 runs (9%) were for Aboriginal patients. In comparison, there were a total of 563 ECMO runs in Victoria in 2012–2017.

The Agency for Clinical Innovation (ACI) developed this clinical guide by drawing on the evidence base, consulting with clinical experts and reviewing arrangements in other jurisdictions. It outlines key elements of ECMO care:

- indications
- retrieval
- initiation
- maintenance
- separation and weaning
- complications
- the use of ECPR.

Clinical criteria

Venovenous ECMO indications

- Refractory hypoxia and/or hypercapnia despite optimal ventilation strategies
- Unsafe non-protective ventilation settings required to support gas exchange (with or without barotrauma)
- Air leaks or bronchopleural fistulas (e.g. due to trauma).

Clinical criteria	Indicator ranges
Hypoxaemia	$\text{PaO}_2/\text{FiO}_2$ of <100 despite optimisation of ventilator settings (including the tidal volume)*
Hypercapnia	$\text{pH} < 7.25$ [40] with $\text{PaCO}_2 > 60\text{mmHg}$
Ventilation	Plateau pressures $> 30\text{cmH}_2\text{O}$ Tidal volumes $> 6\text{ml/kg}$ predicted body weight Driving pressure (peak pressure OR Pplat-PEEP) $> 15\text{cmH}_2\text{O}$

* $\text{PaO}_2/\text{FiO}_2$ in ELSO is <100 on $\text{FiO}_2 > 90\%$, whereas figures as low as $\text{PaO}_2:\text{FiO}_2 < 50$ were used for defined time periods in three studies, <70 , <80 and <100 retrospectively.⁵⁻⁸

Severe respiratory failure defined as $(\text{PaO}_2/\text{FiO}_2 < 70)$.⁹

Adapted from Safer Care Victoria.¹⁰

Venoarterial ECMO indications

A persistent low cardiac output state despite adequate support.

Clinical criteria	Indicator ranges
Hypotension	Systolic BP <90mmHg on inotropes*
Lactate	>5mmol/L
Echocardiogram	Confirmation of low cardiac output
Malperfusion	Skin mottling, oliguria >4hr

* Maximal inotrope vasopressor threshold for ECMO initiation: adrenaline >0.2mcg/kg/min; dobutamine >5mcg/kg/min; milrinone >0.5mcg/kg/min; noradrenaline >0.5mcg/kg/min; vasopressin >2 units/hr. ECMO may be commenced before these limits are reached. Continuing haemodynamic deterioration or shock despite inotrope vasopressor treatment are strong indications for venoarterial ECMO, with an emphasis on early consideration prior to development of multi-organ failure.

Adapted from Safer Care Victoria.¹⁰

Eligibility for venovenous ECMO

Contraindications

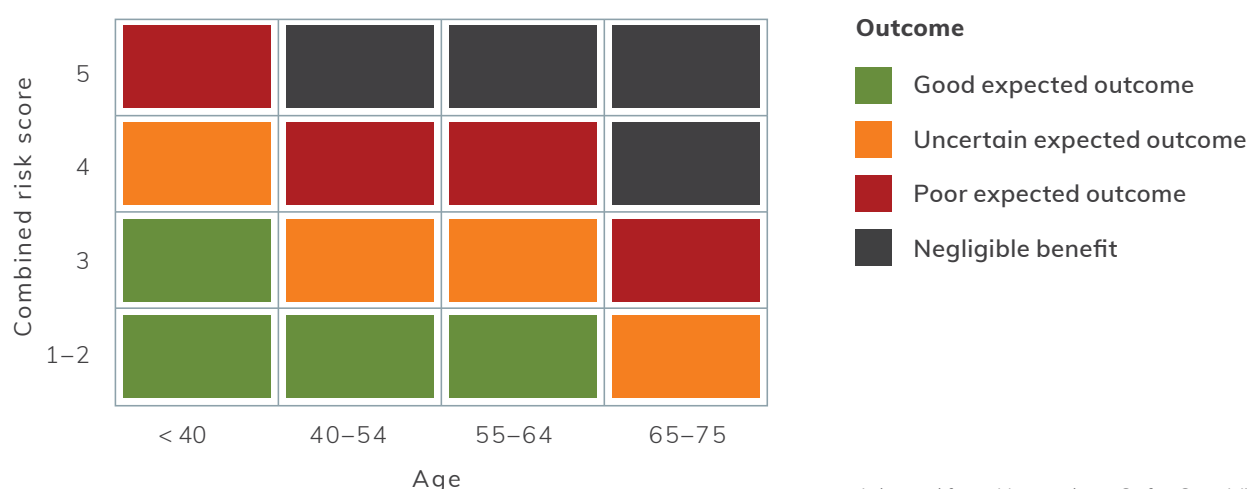
ECMO is unlikely to be successful for patients with:

- non-recoverable respiratory failure, who are not candidates for transplantation
- pre-existing conditions incompatible with recovery (severe neurologic injury, end-stage malignancy)
- relative contraindications to therapeutic anticoagulation (such as active bleeding)
- pre-existing severe multi-organ failure
- allogeneic stem cell transplantation
- advanced age
- prolonged pre-ECMO mechanical ventilation.^{3, 11}

The decision to initiate ECMO is made on a case-by-case basis, usually following consideration by two ECMO consultants in conjunction with specialists from other disciplines.

The risk matrix has been adapted from Safer Care Victoria for NSW clinician use. It should be used to help clinicians inform their decision about initiation of ECMO for patients with severe respiratory or cardiac failure. While this matrix has not been validated in NSW, it provides guidance for decision making. Initiation of ECMO should always be assessed on a case-by-case basis by an experienced ECMO consultant as part of a multidisciplinary discussion. The matrix matches a risk score with acute and chronic modifiers (see Figure 1) and age to determine an expected outcome.

Figure 1: Risk matrix to aid decision making about ECMO



Adapted from Up-to-date, Safer Care Victoria.¹⁰

Steps

1. Determine base risk score (score = 1, 2 or 3), see next page.
2. Determine presence/absence of modifying acute (score = +1) and chronic illness (score = +1), see next page.
3. Calculate combined risk score (1-5).
4. Make sure there are no absolute contraindications.
5. Use chart to observe expected outcome from ECMO.

Determining venovenous ECMO base risk score to use with matrix

Favourable (base risk score =1)	High risk (base risk score =2)	Unfavourable (base risk score =3)
Community acquired pneumonia	Necrotising pneumonia	ARDS from non-pulmonary cause (e.g. pancreatitis)
Status asthmaticus	Pulmonary vasculitis	Invasive aspergillosis
Aspiration pneumonitis	Lung transplant recipient	Pneumocystis jirovecii pneumonia
Primary graft dysfunction following lung transplant within 7 days	Traumatic injuries	Lung transplant recipients >30 days and suitable for retransplantation
Acute respiratory distress syndrome (ARDS) for primary pulmonary pathologies (excluding trauma)	Moderate traumatic brain injury (TBI), hypoxia from chest injury	
	Bronchial tear with air leak and hypoxia	
	ARDS from direct chest trauma	

** Adapted from Safer Care Victoria.¹⁰

Determining clinical modifiers to use with matrix

Acute clinical conditions +1 to base risk score	Chronic clinical conditions +1 to base risk score
Lactate >5 mmol/L (type A lactic acidosis despite resuscitation)	Known ischaemic heart disease or prior revascularisation
Noradrenaline (norepinephrine) >0.3 mcg/kg/min and/or adrenaline (epinephrine) ≥0.1mcg/kg/hr	Peripheral vascular disease (symptomatic or requiring interventions)
Acute liver dysfunction (bilirubin ≥33µmol; or AST/ALT ≥70 IU/L)	Hypertension and dyslipidaemia
Acute kidney injury (creatinine ≥133µmol – with or without renal replacement therapy)	Moderate COPD (GOLD stage II, FEV1 50-80%)
Cardiac arrest prior to ECMO with uncertain neurologic status	Chronic renal failure (stage 3 or 4 CKD eGFR <60)
Prolonged unsafe mechanical ventilation for 7 days (plateau pressures >30cmH ₂ O; driving pressures >15 cm/H ₂ O)	Chronic liver disease
	Chronic immunosuppression (≥7.5mg prednisolone for >3 months, or equivalent)
	Advanced frailty (e.g. Charlson comorbidity score ≥3)

Adapted from Up-to-date, Safer Care Victoria.¹⁰

Eligibility for venoarterial ECMO

Contraindications

ECMO is unlikely to be successful for patients with:

- non-recoverable cardiac or respiratory failure, who are not candidates for transplantation
- pre-existing conditions incompatible with recovery (severe neurologic injury, end-stage malignancy)
- contraindications to therapeutic anticoagulation (such as active bleeding)
- severe peripheral arterial disease, severe aortic regurgitation and aortic dissection
- pre-existing severe multi-organ failure
- out-of-hospital cardiac arrest with prolonged low blood flow
- refractory septic shock with preserved left ventricular function³
- advanced age.

V-A ECMO is indicated in patients with cardiac failure (often in conjunction with respiratory failure). The matrix used is the same as that for V-V ECMO however, the descriptors for base risk scores and acute and chronic modifiers are different (see Figure 1).

Determining venoarterial ECMO base risk score to use with matrix

Favourable (base risk score =1)	High risk (base risk score =2)	Unfavourable (base risk score =3)
Fulminant myocarditis	Acute myocardial infarction (AMI) complicated by cardiogenic shock including vasospasm	Chronic cardiomyopathy (ejection fraction $\leq 40\%$) without the prospect of ventricular assist device/ transplant
Pulmonary embolism with cardiogenic shock	Ischaemic ventricular septal defect or papillary muscle rupture post AMI	Septic shock without left ventricular dysfunction
First presentation acute cardiomyopathy	Failure to wean off cardiopulmonary bypass	
Primary arrhythmogenic cardiomyopathy (e.g. ventricular tachycardia storm)	Heart transplant recipient with chronic rejection suitable for ventricular assist/ device transplant	
Drug overdose with cardiac depression and no long term sequelae		
Primary graft dysfunction post-heart transplant		

Adapted from Up-to-date, Safer Care Victoria.¹⁰

Determining clinical modifiers to use with matrix

Acute clinical conditions +1 to base risk score	Chronic clinical conditions +1 to base risk score
Lactate >10 (type A lactic acidosis despite resuscitation)	Known ischaemic heart disease or prior revascularisation
Adrenaline (epinephrine) $\geq 0.5\text{mcg/kg/h}$ (or equivalent inotrope dose)	Peripheral vascular disease (symptomatic or requiring interventions)
Ischaemic hepatitis (AST/ALT >1000 , or INR >2.0)	Prior valve surgery, coronary artery bypass graft or aortic surgery
Acute kidney injury (creatinine $\geq 133\mu\text{mol}$ – with or without renal replacement therapy)	Moderate COPD (GOLD stage II, FEV1 50-80%)
Onset of shock $>12\text{h}$ Intubation $>30\text{h}$ prior to ECMO	Chronic renal failure (stage 3 or 4 CKD eGFR <60)
Cardiac arrest prior to ECMO with uncertain neurological status	Chronic liver disease
CNS dysfunction (neurotrauma, stroke, encephalopathy, seizure syndromes)	Chronic immunosuppression ($\geq 7.5\text{mg}$ prednisolone for $>3\text{months}$, or equivalent)
	Advanced frailty (e.g. Charlson comorbidity score ≥ 3)

Adapted from Safer Care Victoria.¹⁰

Retrieval for ECMO services

If optimal patient management strategies cannot be provided locally, patients may need to be retrieved to an ECMO capable centre.

There are three types of retrieval:

- patient retrieval to ECMO capable centre prior to ECMO cannulation and initiation
- ECMO cannulation and initiation at referring site and retrieval to ECMO capable centre on ECMO (known as primary transport)
- on ECMO and transferring to another ECMO site (secondary transport).

Patients who are retrieved to a high-volume ECMO capable centre prior to cannulation and initiation have better outcomes.^{1, 12-15} While this is often feasible for patients requiring respiratory support via venovenous ECMO, patients in cardiac failure require immediate intervention. This means patients are sometimes retrieved while on ECMO. International studies have shown no worse outcomes for these patients when compared to those cannulated and initiated at high-volume ECMO capable centres.¹⁰

The decision to transfer a patient on ECMO is informed by clinical factors, as well as the availability of additional staff resources and time to coordinate and manage an ECMO retrieval. A lack of adequate resources may prevent a patient retrieval.¹⁰

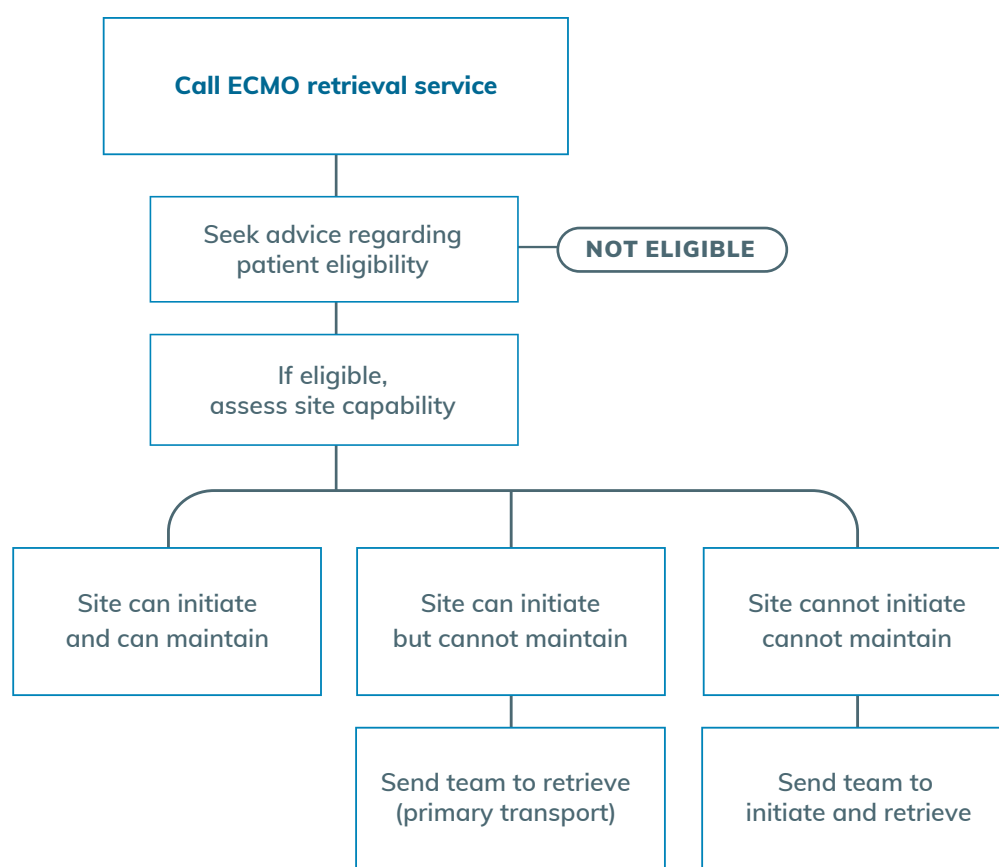
In NSW, the decision to support a referred patient with ECMO is made by the ECMO consultant in charge and is based on a risk/benefit assessment. Alternative treatment options may be recommended, which may be undertaken at the referring hospital or an ECMO capable centre (Figure 1).

Should a decision to transfer occur, ELSO recommends that the retrieval team is self-sufficient, having spare parts for all components, a variety of cannulae and sizes, operating instruments and medications.

In preparation for the arrival of the retrieval team, the referral hospital should arrange:

- appropriate access for the retrieval team
- family details and signed consent
- availability of blood, platelets and plasma
- an operating room, if necessary.

Figure 1: The decision to transfer



Optimising pre-ECMO patient management

If optimal patient management cannot be provided locally, patients may need to be transferred to an ECMO capable centre.

At an ECMO capable centre

Vessel cannulation for ECMO and connection to the ECMO circuit may be performed by a medical officer who has undergone comprehensive training.

Primary transport preparation

In preparation for retrieval, a patient preparation protocol ensures timely transfer and care delivery (Box 1).

Box 1: Primary transport preparation

Patient preparation protocol prior to retrieval team arrival

- Inform the patient, their family and carer of the retrieval and preferably have them available to discuss consent.
- Insert a RIGHT radial arterial line if ECMO is required for cardiac support.
- Pregnancy test for all women aged 12–60 years.
- Leave central venous catheter (CVC) in place (these may be required for ECMO cannulation). If right internal jugular (IJV) vein or femoral vein is occupied, insert a 4 or 5 lumen CVC to LEFT IJV and transfer all infusions.
- Attach a pump set (with crystalloid) to a large bore intravenous access device.
- All notes, charts and imaging photocopied or transferred electronically to receiving hospital.

Organise the ICU or operating theatres

- ICU bed space capable of accommodating surgical trolleys.
- Procedural vascular ultrasound machine.
- Transoesophageal echocardiogram (TOE) probe and ultrasound machine (if available).

At a non ECMO capable centre

If an appropriately trained clinician is not available to perform ECMO cannulation, the NSW ECMO retrieval service may decide to cannulate the patient at the local site before retrieval to an ECMO capable centre. Early identification, timing and retrieval of individual patients requiring ECMO is important. Outcomes are better if patients are retrieved while they are in a relatively stable condition.

- A theatre scrub nurse to assist with cannulation.
- Two large empty surgical trolleys with drapes to create a sterile field for cannulation.
- One small empty trolley to hold the ECMO pump.

Current Investigations

- Full blood count, electrolytes, creatinine, liver function tests, lactate, C-reactive protein (CRP).
- Activated partial thromboplastin time (APTT), international normalised ratio (INR), fibrinogen, D-dimer, lactate dehydrogenase (LDH).
- Chest x-ray, electrocardiogram (ECG), echocardiogram (if possible).
- Current microbiology.

Blood Bank

- Pretransfusion compatibility testing, i.e. group and hold.
- Crossmatch 2 units packed red cells if haemoglobin <100g/L.
- Crossmatch platelets if platelet count <100x10⁹/L.
- Crossmatch 2 units of fresh frozen plasma (FFP) if INR >1.5iu or APTT > 60 seconds.

Source: An amalgamation of clinician developed local policies and protocols.

Secondary transport preparation

Where a patient on ECMO has been deemed by the ECMO consultant and multidisciplinary team to require transfer to another ECMO capable centre (interhospital) or another department within the existing hospital (intrahospital) for ongoing care. This is referred to as secondary transport. Protocols can facilitate preparations prior to transferring the patient (Box 2).

All hospitals should develop protocols and procedures to mitigate risk of patient transfers between and within hospital departments.

Box 2: Secondary transport preparation protocol for intrahospital transfers on ECMO

When planning an intrahospital transfer the following should be considered.

- The patient is physiologically stable for transport.
- The ECMO machine battery is fully charged and the hand crank is available for the pump.
- Portable ventilation and suction is available and in working order.
- Two oxygen cylinders, for gas sweep and emergency use, are full.
- Portable ECG, blood pressure and peripheral oxygen saturation (SpO₂) monitoring in-situ.
- Emergency airway equipment, ECMO clamps and emergency drugs (typical cardiac arrest drugs, muscle relaxant, sedation, intravenous fluid are available).
- The patient's intravenous access has been rationalised to provide a clear route of administration of emergency drugs, should this be required.
- The logistics of the route to the destination have been considered e.g., hallways are clear, elevators can be controlled and the receiving destination is ready.
- Role allocation of the transfer team has occurred to assign one team member to the ECMO machine and another team member to the ECMO cannulae during transit to reduce risk of disconnection.¹⁶

Source: An amalgamation of clinician developed local policies and protocols.

Pre-ECMO patient management

Once a decision has been made to proceed with ECMO, multi-organ-system management to optimise the patient in the pre-ECMO period is required.

Prior to initiating ECMO, the treating clinicians should:

- complete appropriate investigations to confirm patient eligibility for ECMO referral, e.g. pathology testing and imaging including vascular ultrasound
- support optimal patient management, primarily of those with severe respiratory failure or refractory cardiogenic shock.

Severe respiratory failure management

Lung protective ventilation strategies

Lung protection is based on maintaining low volume and pressure states within the lung while preventing alveolar collapse through the use of high end expiratory pressure. Strategies include:

- low volume/low pressure. Aim for tidal volumes 4-6ml/kg ideal body weight (IBW)¹⁷
- Plateau pressure (P_{plat}) of ≤ 30 cm H₂O, peripheral oxygen saturation (SpO₂) 88–93% or partial pressure of oxygen (PaO₂) 55–80mmHg
- optimise inspiration: expiration (I:E) ratio
- optimise positive end expiratory pressure (PEEP)
- alveolar recruitment manoeuvres using controlled PEEP
- avoidance of mechanical ventilator disconnection
- optimise pH = 7.30–7.45 accepting permissive hypercapnia if this is not achievable.

Inhaled pulmonary vasodilators

Although there is little evidence supporting its use, inhaled Nitric Oxide (iNO) and epoprostenol (inhaled prostacyclin) may be considered in certain circumstances to decrease pulmonary vascular resistance, decrease pulmonary artery pressure and improve ventilation/perfusion mismatch.¹⁸

Prone positioning

Prone positioning may help to minimise collapse of dorsal lung segments in patients with adult respiratory distress syndrome (ARDS) and when initiated early has been associated with reduced mortality.¹⁹ To avoid complications associated with prone positioning, local sites require appropriate resources and capability regarding safe turning and managing a patient on ECMO in the prone position.⁵

- Prone ventilation should be considered for all patients with moderate-severe ARDS with arterial oxygen partial pressure to fractional inspired oxygen (P/F) ratio <150.
- Target duration of prone positioning should be for 16+ hours, with consideration of staffing logistics for timing of manoeuvres.
- Prone ventilation should be continued for a target of five consecutive days unless complications or dramatic clinical improvement occur.

Sedation and neuromuscular blockade

Deep sedation and/or neuromuscular blockade may initially be needed to inhibit respiratory movement to facilitate severe respiratory failure management.

Restrictive fluid strategy

Fluid balance should be monitored closely in patients with severe respiratory failure. A restrictive fluid strategy should be employed and cumulative positive fluid balance avoided.

Refractory cardiogenic shock management

Profound depression of myocardial contractility is a hallmark feature of cardiogenic shock. The following strategies may assist in supporting myocardial function, implemented in conjunction with general intensive care measures:

- reverse aetiology if possible e.g. coronary reperfusion, pericardial tamponade, drug overdose
- optimise intravascular volume to achieve adequate tissue perfusion
- provide catecholamine support
- correct metabolic and electrolyte imbalances
- manage arrhythmias
- maximise ventilation
- consider mechanical circulatory support e.g. intra-aortic balloon counterpulsation, if appropriate.

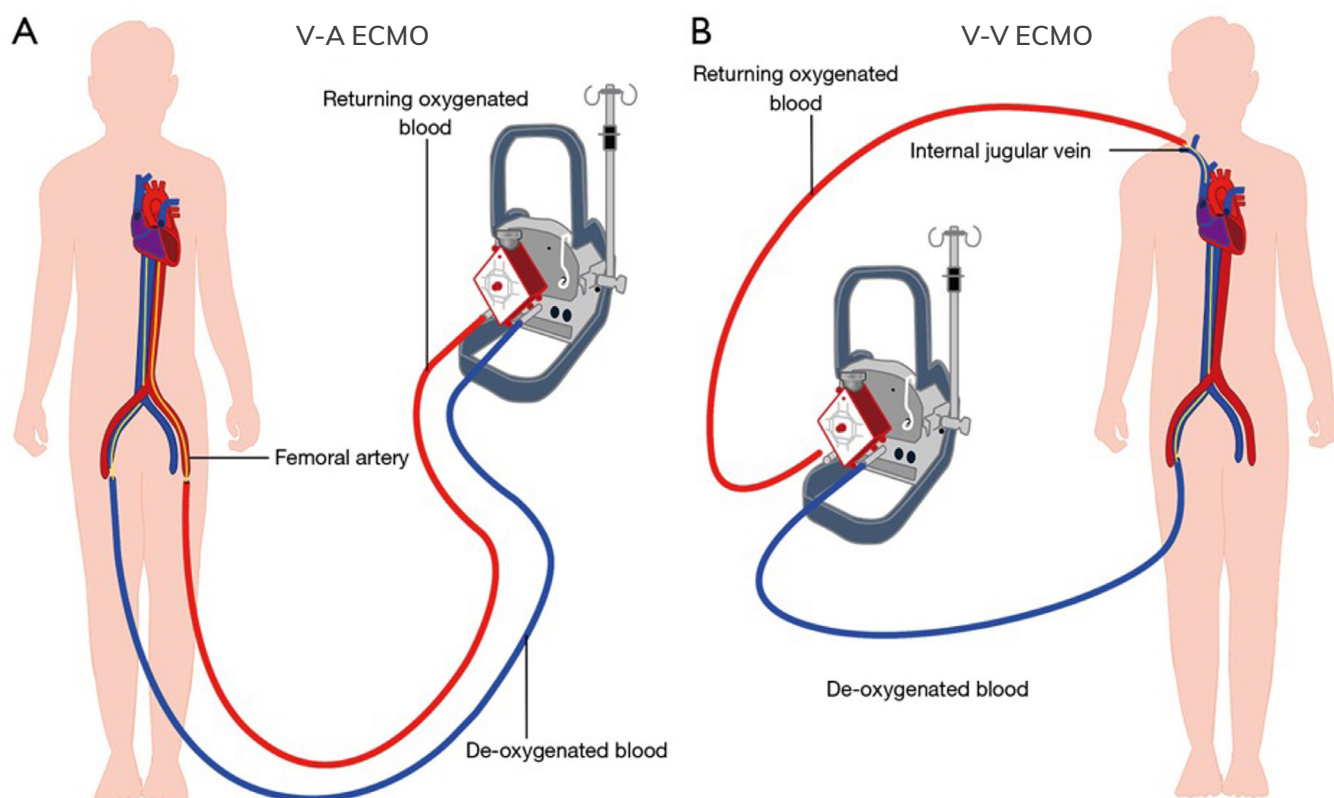
Initiation phase of ECMO

Following the decision to initiate ECMO, the patient is anticoagulated typically with a bolus of intravenous heparin at 50–100 units per kilogram and the ECMO cannulae are inserted (Figure 2).⁹

Venovenous cannulation

For V-V ECMO, venous cannulae are most commonly placed in the right or left femoral vein for drainage and right internal jugular vein for infusion. The femoral cannula tip lies at the junction of the inferior vena cava and right atrium and the internal jugular cannula tip lies at the junction of the superior vena cava and right atrium. A double lumen cannula may be used as an alternative, which is large enough to accommodate 4-5L/min of blood flow. This reduces the risk of recirculation.⁹

Figure 2: Circuit configuration for venovenous and venoarterial ECMO



Pillai AK, Bhatti Z, Bosserman AJ, Mathew MC, Vaidehi K, Kalva SP. Management of vascular complications of extra-corporeal membrane oxygenation. *Cardiovasc Diagn Ther* 2018;8(3):372-377. doi: 10.21037/cdt.2018.01.11.²⁰

Venoarterial cannulation

For V-A ECMO, a venous cannula is placed in the inferior vena cava or right atrium for drainage while an arterial cannula is placed in the right femoral artery for infusion. Femoral access is preferred. There is a risk of ischaemia of the ipsilateral lower extremity that can be managed by inserting an additional arterial cannula distal to the femoral artery cannula, which redirects a portion of the infused blood to the additional cannula. Alternatively, a cannula can be inserted into the posterior tibial artery.⁹

Occasionally, the femoral vessels are unsuitable for cannulation for V-A ECMO and the subclavian artery can be used. Use of the subclavian artery offers the advantage of allowing patients on ECMO to ambulate.⁹

For post-cardiotomy ECMO, the cannulas employed for cardiopulmonary bypass can be transferred from the heart lung machine to the ECMO circuit, with blood drained from the right atrium and reinfused into the ascending aorta.

Most commonly, cannulae are placed percutaneously (using the Seldinger technique). A transoesophageal echocardiogram (TOE) is used to guide cannulation. The largest cannulae that can be placed in the arteries are used (range 16F–23F).^{9, 21}

Establishing ECMO flows

Immediately following cannulation, the procedures below establish V-V ECMO and V-A ECMO flows.

- ☐ Ensure fresh gas flow is connected to oxygenator. Gas flow of 100% O₂ should be commenced at 1–3 L/min and then titrated.
- ☐ Sterile extracorporeal circuit is opened and taken by the cannulating clinician.
- ☐ Extracorporeal circuit is connected to cannulae ensuring no air is introduced.
- ☐ Clamps removed as circuit flows are gradually increased.
- ☐ Target flow rates are determined by the cannulating clinician (Box 3).
- ☐ Check APTT is within local laboratory range and if there is no contraindication to full dose heparin.

For V-V ECMO, target flows must provide adequate arterial oxygenation.

For venoarterial V-A ECMO, target flows must provide adequate oxygen delivery.

- ☐ Check patient and circuit arterial blood gases.
- ☐ Reduce ventilator settings as indicated.
- ☐ Establish baseline anticoagulation sampling times.²¹

Box 3: Titration⁹

ECMO support is initiated once the cannulae are connected to the appropriate limbs of the circuit. Blood flow is increased until respiratory and hemodynamic parameters are satisfactory.

Reasonable targets include:

- arterial oxyhemoglobin saturation of >85% for V-V ECMO or right hand SpO₂ >90% for V-A ECMO
- venous oxyhemoglobin saturation 20–25% lower than the arterial saturation, measured on the venous line if possible
- adequate tissue perfusion, as determined by the arterial blood pressure, venous oxygen saturation and blood lactate level.

As ECMO flows are established,

a significant amount of blood volume will be drained from the patient toward the extracorporeal circuit and will be replaced by the priming fluid of the circuit. This leads to:

- haemodilution of the blood volume
- severe hypoxia
- brief but significant hypotension requiring further vasopressors or a fluid bolus.

In addition, as bolus heparin doses are often administered during cannulation, the bleeding risk may be increased at this point.

Once ECMO flow has been established, oxygenated blood is delivered to the patient. Ventilator settings may be altered to allow enforcement of lung protective strategies that cause:

- a reduction in intrathoracic pressure
- improved preload and right ventricle afterload
- correction of severe respiratory acidosis (note rapid reversal or over correction of respiratory acidosis may be detrimental in some settings such as spontaneously breathing patients or suspected brain injury), although this may necessitate an increase in gas flow in association with a reduction in minute volume.²²

Maintenance phase of ECMO

Once respiratory and haemodynamic goals have been achieved, ECMO blood flow is maintained at that rate. Constant monitoring of blood flow, the need for diuresis and in the case of V-A ECMO, left ventricular function, is required (Table 1).

Frequent assessment and adjustments are facilitated by continuous venous oximetry, which directly measures the oxyhaemoglobin saturation of the blood in the venous limb of the ECMO circuit.

If the venous oxyhaemoglobin saturation is below target, options include:

- increase blood flow, intravascular volume, or haemoglobin concentration
- decrease the systemic oxygen uptake by reducing body temperature and increasing sedation and muscle relaxation.⁹

Anticoagulation

Anticoagulation is necessary to prevent activation of the clotting cascade and thrombosis of the circuit although there is no clear evidence on optimal therapeutic targets for anticoagulation.²³

It is possible to run ECMO without anticoagulation but this significantly increases the risk of thrombosis, particularly in the context of arterial cannulation.

A thrombus formation within the extracorporeal circuit can be devastating.⁹ Most experts recommend a continuous infusion of unfractionated heparin or a direct thrombin inhibitor titrated to coagulation targets according to local laboratory values, such as:

- an activated partial thromboplastin time (APTT)
- drug specific anti-Xa activity
- D-dimer
- fibrinogen
- lactate dehydrogenase (LDH).

However anticoagulation brings the risk of haemorrhage and one centre in Germany reported that 61 patients on venovenous V-V ECMO were successfully managed with only prophylactic low molecular weight heparin.²⁴

Clinicians should address the risk/benefit ratio of anticoagulation on a case-by-case basis.

Table 1: Considerations for maintenance of ECMO⁹

Venovenous ECMO
<p>Blood flow Near maximum flow rates may be necessary during V-V ECMO to optimise oxygen delivery.</p> <p>Diuresis Aggressive diuresis once the patient is stable on ECMO. Consider adding ultrafiltration to circuit.</p>
Venoarterial ECMO
<p>Blood flow Flow rate high enough to provide adequate perfusion pressure and venous oxyhemoglobin saturation (measured on drainage blood), but low enough to avoid excessive afterload that will stop left ventricular ejection.</p> <p>Diuresis Aggressive diuresis once the patient is stable on ECMO. Consider adding ultrafiltration to circuit.</p> <p>Left ventricular monitoring Closely monitor by identifying pulsatility in the waveform of the arterial line and frequent echocardiography.</p> <p>Interventions to improve left ventricular output include inotropes and intra-aortic balloon counterpulsation. Immediate left ventricular decompression is essential to avoid pulmonary haemorrhage if left ventricular ejection cannot be maintained despite intra-aortic balloon counterpulsation and inotropic agents. Decompression can be achieved by transatrial balloon septostomy or insertion of a left atrial or ventricular drainage catheter.</p>

Platelets are continuously consumed during ECMO because they are activated by exposure to the foreign surface area of the ECMO circuit. Thrombocytopaenia is therefore a common problem and platelet counts should be maintained greater than 50,000/microliter, which may require platelet transfusion to reduce the risk of bleeding.²⁵

Heparin induced thrombocytopaenia is a potential complication, requiring expert haematological input to guide management of anticoagulation as diagnosis can be very complex.¹

Ventilator

Ventilator settings are reduced during ECMO in order to avoid barotrauma, volutrauma (i.e. ventilator-induced lung injury) and oxygen toxicity.

Plateau airway pressures should be maintained less than 25cm H₂O and FiO₂ less than 0.6. Reduction of ventilator support is usually accompanied by increased venous return which improves cardiac output.⁹

Tracheostomy

Early tracheostomy can improve patient comfort. Patients typically require light sedation during ECMO, although many centres maintain patients awake, extubated and breathing spontaneously once stabilised.

Nursing Care

Nursing care is complex and varied (Box 4). Nursing levels of care should be appropriate to accommodate patient acuity especially during initial stages of treatment and times of instability.

Box 4: Nursing care in maintenance phase²⁶

Local policies and protocols should guide individual facilities on nursing care.

- Safety checks – to ensure the ECMO cannulae and circuit are working appropriately, alarms are set and emergency equipment is readily available.
- ECMO observations – to observe patient status, monitor trends and predict complications.
- Circuit management – to observe oxygenator and blood pump function.
- Respiratory management – to achieve adequate oxygenation.
- Haematological management – to prevent clot formation.
- Temperature management – to accomplish normothermia.
- Daily investigations – to monitor progress, including chest imaging and blood pathology.
- Doppler examination – to monitor lower limb perfusion.

Patients should be nursed in the supine position.

- Head of bed should be elevated 30 degrees.
- Pressure relieving mattress, heel pressure should be offloaded.
- If the patient needs to be moved, a designated person must take responsibility for ensuring cannulae, tubing and flow rates do not move or change.
- A Jordan frame should be deployed when moving patients. They can be log rolled if not contra indicated.
- Neurological and pupillary assessment must be attended hourly (patient is at increased risk of intracranial bleed).
- Pain scores with CPOT (Critical Pain Observation Tool) and sedation scores with RASS (Richmond Agitation Sedation Score) should be attended two hourly.
- Daily sedation vacations are attended to assess underlying neurological assessment.

Separation and weaning from ECMO

Separation from ECMO occurs when a patient either:

- clinically improves and weaning from ECMO can begin, or
- clinically deteriorates and the decision to cease ECMO is made.

All decisions are made in consultation with the patient (if possible), family members, carers and the multidisciplinary team. A simple pathway to illustrate the process is shown in Figure 3.

Differences in weaning strategies are generally based on expert opinion rather than evidence.²⁷

Indications that patients are ready for weaning from ECMO include:

- in respiratory failure, improvement in radiographic appearance, pulmonary compliance and arterial oxyhemoglobin saturation
- in cardiac failure, enhanced aortic pulsatility correlated with improved left ventricular output

One or more weaning trials should be performed prior to discontinuing ECMO permanently (Table 2).

- **V-V ECMO** weaning trials are performed by eliminating all countercurrent sweep gas through the oxygenator. Extracorporeal blood flow remains constant but gas transfer does not occur. Patients are observed for several hours, during which the ventilator settings that are necessary to maintain adequate oxygenation and ventilation are determined.
- **V-A ECMO** weaning trials can be performed by clamping both the drainage and infusion lines, while allowing the ECMO circuit to circulate through a bridge between the arterial and venous limbs. This prevents thrombosis of stagnant blood within the ECMO circuit. In addition, the arterial and venous lines are either flushed continuously with heparinised saline; or intermittently with

heparinised blood from the circuit. V-A ECMO weaning can also occur with assessment of sonographic LV function with low pump flows. Left ventricular outflow tract (LVOT) velocity time integral (VTI) >10–12 can predict successful weaning.

V-A ECMO weaning trials are generally shorter in duration than V-V ECMO weaning trials because of the higher risk of thrombus formation.⁹

Table 2: Weaning guide²¹

Venovenous ECMO
<input type="checkbox"/> Maintain ECMO flow rate <input type="checkbox"/> Re-establish patient on mechanical ventilation <input type="checkbox"/> Turn off O ₂ to oxygenator <input type="checkbox"/> 6hr stability then decannulation
Venoarterial ECMO
<input type="checkbox"/> Heparin so ACT >400 to decrease risk clotting <input type="checkbox"/> Decrease pump flow to 1 litre while assessing ventricular function by TOE <input type="checkbox"/> Period of low flow ECMO before decannulation <input type="checkbox"/> If respiratory function is a concern, as an alternative weaning strategy, turn off gas flow (only at circuit flows <1.5L/min) and assess oxygenation achieved using the ventilator exclusively. Note: in this situation the circuit flow acts as a right-to-left shunt. If adequate oxygenation and CO ₂ removal can be maintained in the presence of this shunt it is likely that respiratory failure can be managed without ECMO <input type="checkbox"/> If O ₂ is good and CO ₂ is managed by ventilation, consider decannulation

Removal of ECMO cannulae

- Removal of arterial ECMO cannulae should always be performed as an 'open' surgical procedure and be accompanied by vessel wall repair.
- Venous cannula can be removed and pressure applied to the site for 20 minutes.

Post-decannulation doppler

- Lower limb venous doppler studies must be performed following decannulation as prolonged femoral venous cannulation promotes distal deep vein thrombosis formation.²⁸
- Internal jugular veins should be imaged after jugular cannulation for evidence of thrombi.

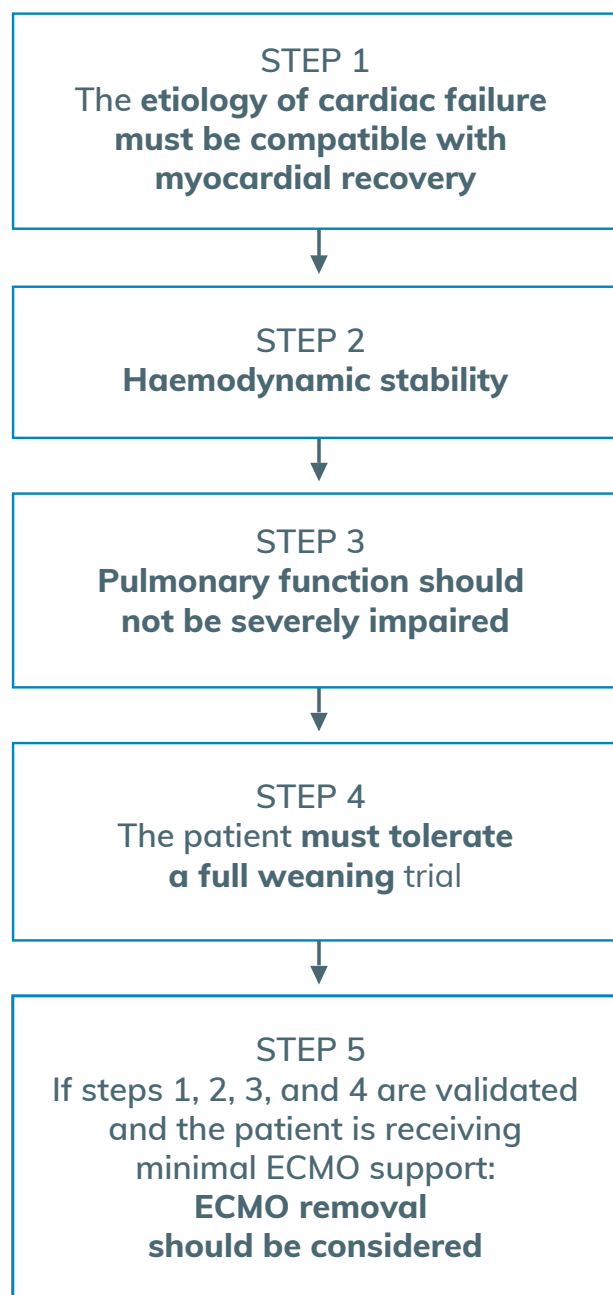
It is the responsibility of the decannulating ECMO intensivist to ensure vascular imaging and any suture removals are planned and undertaken.

Decision to cease ECMO

In the following circumstances the decision to discontinue ECMO may occur.

- ECMO is discussed but withheld.²²
- ECMO is commenced and there is a decision to withdraw because ongoing treatment is considered futile.⁷
- Patient was commenced on ECMO as a bridge to decision about transplantation but is no longer a candidate for transplantation.^{22, 23}
- Patient dies before or while on ECMO.
- Patient has died and may be considered for potential organ donation.^{24, 25}

Figure 3: Separation and weaning flow chart



Source: Ortuno et al, 2019.²⁹

Complications of ECMO

The morbidity associated with ECMO is significant. The most common serious complications of ECMO are thrombosis and haemorrhage.

Thrombosis

There are multiple contributory factors including blood contact with foreign surfaces, blood stasis in cardiac chambers and disseminated intravascular coagulation. Consequently, patients must be therapeutically anticoagulated to prevent development of thrombosis within the circuit, which can affect function of the circuit and/or in V-A ECMO, embolise to the systemic circulation.

A recent single site study that used computed tomography scans to assess thrombotic complications reported pulmonary embolism in 16% cases and deep venous thrombosis in 70%.³⁰

The risk of thrombosis is managed by anticoagulation and observation of the circuit for signs of clot formation. Routine inspection of all connectors and monitoring of the pressure gradient across the oxygenator is recommended. A sudden change in the pressure gradient is suggestive of a clot. Large or mobile clots require immediate circuit or component exchange. Having a primed circuit available facilitates urgent exchange, if necessary.

Haemorrhage

Significant bleeding occurs in 30–50% of patients who receive ECMO and can be life threatening.^{23, 31} The requirement for anticoagulation, the consumption of coagulation factors and platelets and in some cases, heparin-induced thrombocytopenia, all heighten the risk of haemorrhage, which can occur in any organ.

Bleeding is often seen at the cannulation sites.

Meticulous surgical technique, maintaining platelet counts greater than 50,000/mm³ and maintaining an activated partial thromboplastin time (APTT) target all reduce the likelihood of haemorrhage.

Infective complications are often related to the cannulation sites and strict aseptic technique is required when handling the cannulae.

Mechanical equipment failure is very uncommon with modern systems but can be catastrophic.

Neurological complications are generally related to thrombosis with infarction, or haemorrhage. Recent studies have found that around 11% of ECMO patients have neurologic complications such as seizure, stroke and intracranial haemorrhage.³² Intracranial haemorrhage in particular is associated with higher rates of mortality.

Cannulation-related complications such as vessel perforation with haemorrhage, arterial dissection, distal ischemia and incorrect location (e.g. venous cannula within the artery) are relatively rare (<5%).⁹

Complications specific to venoarterial ECMO

A meta analysis of studies of ECMO for treatment of cardiogenic shock or cardiac arrest in adult patients identified a significant complication burden.³³ This study highlighted rates of acute kidney injury (AKI) of over 50%, although it may be debated that AKI was most likely a marker of underlying cardiac dysfunction rather than attributable to ECMO itself (Table 3).

Reviews have identified other specific complications, including:

- pulmonary oedema and haemorrhage in patients with no left ventricular output. Oedema occurs when the left atrial pressure exceeds 25mmHg
- coronary or cerebral hypoxia due to preferential perfusion of oxygenated blood to the lower extremities and the abdominal viscera. Cardiac and cerebral hypoxia may exist and be unrecognised if oxygenation is monitored using only blood from the lower extremity.⁹

Table 3: Complication rates of cardiac extracorporeal membrane oxygenation³³

Complication	Incidence (%)
Acute kidney injury	55.6
Renal replacement therapy	46.0
Re-thoractomy for bleeding or tamponade in postcardiotomy patients	41.9
Major or significant bleeding	40.8
Significant infection	30.4
Lower extremity ischemia	16.9
Neurological complications	13.9
Fasciotomy or compartment syndrome	10.3
Stroke	5.9
Lower extremity amputation	4.7

Modified from Cheng, et al.³³

Extracorporeal cardiopulmonary resuscitation (ECPR)

Extracorporeal cardiopulmonary resuscitation (ECPR) refers to the use of V-A ECMO during ongoing resuscitation attempts in cardiac arrest.³⁴

Observational studies have assessed ECPR in both in-hospital and out-of-hospital arrests (Table 4).³⁵ A number of randomised controlled trials are underway.

Studies report rates of survival to discharge range from 28–60% for in-hospital cardiac arrests and as low as 8% for refractory out of hospital cardiac arrests (OHCA). However, another study demonstrated that if immediate critical care strategies were available to augment the use of ECMO in refractory OHCA, a much higher rate (48%) of meaningful survival could be achieved (Table 4).

The European Resuscitation Council and the American Heart Association on CPR do not currently recommend the routine use of ECPR for patients with cardiac arrest.³⁶

It is anticipated that there may be a rise in ECPR procedures in the near future, despite equivocal success rates so far. International and domestic observational studies show rates of survival to

discharge of about 30–60% for in-hospital cardiac arrests and around 10–50% for out-of-hospital cardiac arrests.

Selection criteria and procedure techniques differ across hospitals, however a recent consensus statement has outlined some standard criteria for ECPR, see next page. A primary determinant of successful clinical outcomes is the interval between collapse and onset of ECPR. The statement distinguishes between 'no-flow time' (the interval between collapse and onset of external chest compressions) and 'low-flow time' (the interval between external chest compressions and onset of ECPR).

Inclusion and exclusion criteria are not standardised across NSW in all ECMO capable sites. It is generally agreed that cannulation for ECMO in a patient during a cardiac arrest confers a much higher risk of complications than in situations where there is not the same time pressure. In light of this, experience in cannulation in non-cardiac arrest situations is vital before embarking on the provision of such a service during emergency situations.

Table 4: Published outcomes with ECPR³⁵

	Cardiac arrest cohort included	Number of patients	Survival to discharge (%)
ELSO Registry, 2017	In-hospital predominantly	3485	28
Chen et al, 2008	In-hospital	59	29
Shin et al, 2013	In-hospital	85	35 (28 day)
Bartos et al, 2018	Out-of-hospital	100	48
Stub et al, 2015	In-hospital	15	60
Stub et al, 2015	Out-of-hospital	9	33
Bougouin et al, 2019	Out-of-hospital	525	8

Adapted from Maclaren et al.³⁵ (Published ELSO data has been used where data in the referenced study could not be verified).³⁷

Uptake of this treatment option is occurring at a rate greater than available evidence. It is important that in centres where ECPR is being used, that all ECPR cases should only be used in the context of a clinical trial and that there is robust data collection and quality assurance processes to monitor complications and outcomes. As with ECMO for other indications, there will be benefit from a centralised data submission such that there can be ongoing evaluation of this highly specialised treatment modality.

ECMO in the context of cardiopulmonary resuscitation (CPR)

There has been an emergence of the use of mechanical devices to deliver external chest compressions during CPR in hospital settings. Studies have not shown these devices to be superior to manual compressions, however there are recognised benefits. These include freeing staff to perform other roles and allowing patients to be transported to other areas of the hospital such as angiography suites, whilst having ongoing external chest compressions.

The increase in use of the mechanical devices has also allowed for consideration of the establishment of ECMO to support patients during cardiac arrest by initiating extracorporeal cardiopulmonary resuscitation (ECPR). The decision to initiate ECPR in these patients should be made following a multidisciplinary discussion involving intensive care specialists and the primary treating physician or emergency department. Essential prerequisites to perform ECPR in a hospital setting broadly include:²⁶

- resuscitation team present and on-site
- early alert system to notify hospital ECMO team
- ECMO team ready within 15 minutes at the site of ECPR
- 24/7 available preassembled ECMO equipment and perfusionist/specialist

- ability to transport a patient with ongoing mechanical CPR in the hospital
- ability to cannulate and perform ongoing invasive procedures under ongoing mechanical CPR
- readily available echocardiography, vascular ultrasound, cardiac catheterisation laboratory, basic laboratory examinations, with optional monitoring of cerebral tissue saturation.

Careful selection of patients for ECPR is crucial and hence decisions should adhere to agreed inclusion and exclusion criteria.²⁶

Inclusion criteria

- Suspected acute coronary syndrome, refractory to standard advanced cardiac life support (ACLS) with a likely reversible cause
- Patients undergoing cardiac catheterisation, who are not immediately responsive to standard ACLS
- Suspected massive pulmonary embolism
- Patients who arrive at hospital within 60 minutes of collapse
- Commencement of CPR within 10 minutes of the patient's collapse
- Patient's initial rhythm which is VT/VF or PEA with a significant End-Tidal CO₂ or other signs of life
- Any other cause with a likely reversible underlying condition if ECMO can be provided
- Age under 70 years – individual, case-by-case consideration.

Exclusion criteria

- Unwitnessed arrest
- Severe active bleeding
- No realistic prospect of reversal of underlying cause
- No realistic prospect of bridge to cardiac assist device or transplantation
- Advanced age precludes prolonged intensive care and mechanical support.

Patient, family and carer support

Patients (if able) and their families and carers need to be kept informed and supported throughout the ECMO process. Every effort should be taken by members of the multidisciplinary team to support them, ensuring they are updated about the ECMO process at regular intervals.

When retrieval is necessary

The referring hospital medical officer should discuss the need for retrieval, covering:

- the reason and timing of retrieval
- mode of transport, approximate travel time and estimated time of arrival
- treatment that may be required during retrieval.

Written information regarding the destination hospital, including directions of how to get there and contact details of key staff, should be given to the family and carers. Family and carers should be informed at the outset that there are circumstances that prevent them being able to accompany the patient during retrieval, e.g. limited space in ambulance, weight restrictions on aircraft.

Relocating patients away from where they live can cause stress, particularly for families identifying as Aboriginal or Torres Strait Islander. Where possible, a senior elder should be included in discussions and an Aboriginal liaison officer engaged at both the referring and receiving hospital.

In addition, clear communication and information should be provided, particularly when plans for ECMO change, including:

- ECMO is discussed but withheld³⁸
- ECMO is commenced and then withdrawn because of an inability to meet the goals of care¹⁶
- ECMO is commenced as a bridge to transplantation but the patient is no longer a candidate for transplantation^{38, 39}
- the patient died before or while on ECMO
- following death, the patient may be considered for potential organ donation.^{40, 41}

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Glossary

ARDS	Acute respiratory distress syndrome
CPR	Cardio-pulmonary resuscitation
CO ₂	Carbon dioxide
ECMO	Extracorporeal membrane oxygenation
ECLS	Extracorporeal life support
ELSO	Extracorporeal Life Support Organization
ECPR	Extracorporeal Cardio-pulmonary resuscitation needs to be added
IHCA	In-hospital cardiac arrest
ICU	Intensive care unit
Low-flow time	Duration between commencement of CPR until ECMO has reached full flow support
MOF	Multi-organ failure
No-flow time	The time between the moment a person collapses until CPR commences
OOHCA	Out-of-hospital cardiac arrest
PaO ₂	Partial pressure of oxygen
PaCO ₂	Partial pressure of carbon dioxide
PEA	Pulseless electrical activity
ROSC	Return of spontaneous circulation
V-A ECMO	Venoarterial Extracorporeal membrane oxygenation
VF	Ventricular fibrillation
VT	Ventricular tachycardia
V-V ECMO	Venovenous Extracorporeal membrane oxygenation.

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The Agency for Clinical Innovation (ACI) is the lead agency for innovation in clinical care.

We bring consumers, clinicians and healthcare managers together to support the design, assessment and implementation of clinical innovations across the NSW public health system to change the way that care is delivered.

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- evidence-based
- value-driven.

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AGENCY FOR
**CLINICAL
INNOVATION**

*Our vision is to create the future of healthcare,
and healthier futures for the people of NSW.*