Mechanical support of the circulation

Mok YH, Chan YH

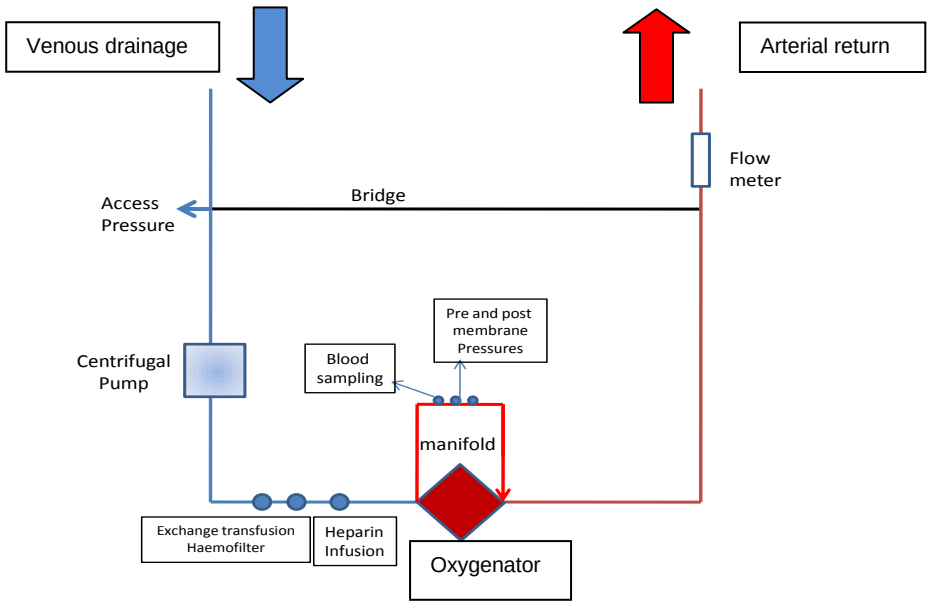
Extra-Corporeal Membrane Oxygenation (ECMO) uses modified cardiopulmonary bypass technology to provide respiratory or cardio-respiratory support in the ICU for prolonged periods. It is indicated when the patient has a potentially reversible condition and conventional ICU support of the cardiopulmonary system is failing.

There are 2 basic techniques of ECMO:

- Veno-venous (V-V): used for respiratory support when there is adequate cardiac function.
- Veno-arterial (V-A): used for cardio-respiratory support when there is inadequate cardiac function. Arterial access is via central sternotomy or via carotid or femoral artery cannulation (beware distal limb ischaemia with femoral arterial cannulation).

ECMO Circuit

The circuit consists of a pump, oxygenator, heat exchanger, pressure monitors, venous line saturation monitor and bridge to connect arterial return and venous drainage lines.



V-A ECMO

V-A ECMO provides near total cardiopulmonary support. It allows control of the cardiac output through the flow rate generated by the ECMO pump. This mode of support allows time for the heart and/or the lungs to rest as a bridge to recovery. Flow rates are approximately 100 ml/kg/min (but may need higher flows in hyper-dynamic shock states such as septic shock) or to achieve flows approximating a cardiac index of 2.4-3.6L/m^2/min.

V-V ECMO

V-V ECMO introduces oxygen and removes carbon dioxide from the venous blood. Oxygenated blood is then returned to the venous system. It does not provide circulatory support.

Indications

1. Neonatal respiratory failure

- Oxygen Index [*where OI = [Mean Arterial Pressure xFiO$_2$ x100)/PaO$_2$]*
  - ≥ 20 consider ECMO
  - = 40 ECMO indicated
- Contraindications
  - Lethal chromosomal disorder
  - Irreversible brain damage
  - Grade III or greater intraventricular haemorrhage (IVH)
- Relative contraindications
  - Irreversible organ damage (unless considered for organ transplant)
  - < 2 kilograms
  - < 34 weeks post-menstrual age because of the increased incidence of intracranial haemorrhage
  - Disease states with a high probability of a poor prognosis

2. Paediatric respiratory failure

- Indications:
  - no absolute indicators are known, but consider ECMO if Oxygen index (OI) is > 40 on 2 or more arterial blood gases
  - consideration for ECMO is best done within the first 7 days of mechanical ventilation at high levels of support
  - Conditions that may be amenable to ECMO include pneumonia or ARDS of various causes, severe RSV bronchiolitis or asthma
- Contraindications:
  - Recent neurosurgical procedures or intracranial bleeding (within 10 days)
  - Recent surgery or trauma: increased risk of bleeding
  - Patients with severe neurologic compromise, genetic abnormalities (not including Trisomy 21)
- Relative contraindications:
  - endstage hepatic failure, renal failure
  - primary pulmonary hypertension
  - respiratory failure as a result of a primary respiratory disease with no bridge to lung transplant (eg. alveolar-capillary dysplasia, severe primary surfactant deficiency, bronchiolitis obliterans)

3. Cardiac failure

- Failure to wean from CPB in the operating theatre (*post cardiotomy ECMO*)
- Severe post-operative cardiac failure defined by pressor and inotropic requirement, metabolic acidosis, and decreased urine output for 6 hours
- Witnessed cardiac arrest with response to CPR but still unstable OR no response to CPR and direct massage underway for 5 minutes *(ECPR*)
- Myocardial failure unrelated to operation eg. myocarditis, cardiomyopathy (as a bridge to transplant) or toxic drug overdose.
- Failure to oxygenate a patient with cyanotic heart disease (eg. blocked BT shunt, poor mixing in TGA, obstructed TAPVD), usually better on V-V ECMO

4. Sepsis

Historically, ECMO was considered a contraindication in patients with septic shock as the risk of bleeding complications were higher, there was a risk of bacteraemia with vascular catheters and the development of a systemic inflammatory response from exposure to foreign membranes could possibly lead to a worse haemodynamic profile. However, there is emerging data on successful outcomes in fluid and catecholamine-resistant septic patients in case series and ELSO registry data.

ECMO can be considered in patients with catecholamine-resistant septic shock after discussion with intensive care specialist.

5. Extracorporeal Cardiopulmonary Resuscitation (ECPR)

ECMO should only be considered for children in cardiac arrest refractory to standard resuscitation attempts. Cardiac arrest should be witnessed with response to CPR but still unstable or where there is no response to CPR and direct massage underway for 5 minutes *(ECPR*). ECPR may be applied in the setting of a witnessed in-hospital cardiopulmonary arrest with effective resuscitation instituted without delay. The cause of the arrest must be deemed to be potentially reversible and ECMO provided as a bridge to recovery. The decision for ECPR is a joint one made by the NICU or the PICU consultant with the cardiothoracic surgeons and/or cardiologists. In such circumstances, ECMO code will be activated in the respective ICU.

General Contraindications

- Recent neurosurgical procedures or intracranial bleeding (within 10 days). Grade II or III intracranial haemorrhage is a general contraindication
- Recent surgery or trauma with increased risk of bleeding
    - ECMO has been performed successfully in these patients and the use of heparinized circuits and/or oxygenators may limit bleeding initially. Care to maintain adequate coagulation factors, platelet counts and use of low ACTs (160-180 seconds) may be helpful
- Patients with severe neurologic compromise or genetic abnormalities for which the underlying condition has guarded prognosis

Relative contraindications

- Inability to tolerate heparinisation
- Moribund patient with established organ failure (especially brain injury)
- Underlying chronic condition with poor prognosis (eg. primary immunodeficiency in septic shock with multi-organ failure, oncological patient with failed BMT)
- Inadequate cardiac repair (either technical failure, or because substrate does not allow for adequate repair)
- No avenue for transplant if unable to come off ECMO
- Pre-existing active intracranial bleeding

There are no absolute parameters that define the indications for ECMO support and the decision to place a patient on ECMO combines both numerical data and clinical setting.

Initiation

Contact

- Intensive care specialist (if not already present)
- Cardiac surgeon
- Anaesthetist and scrub nurse
- Perfusionist/ ECMO nurse specialist
- Blood bank
- Cardiologist

Equipment and Procedures

The following equipment should ready and procedures performed:

- ECG monitor
- Airway secured and ventilation initiated
- NG tube and urinary catheter inserted PRIOR to ECMO cannulation
- Cranial ultrasound completed for neonates (except for emergency ECMO)
- Establish lines (central venous line, peripheral intravenous cannula, intra-arterial line)
- Remove unnecessary lines
- Emergency cart
- ECMO cart

- Bedside 2D echo
- GXM,FBC,ABG, PT/PTT, ACT

Blood products

- Blood products used in ECMO should preferably be leuco-reduced and less than 7 days old.
- Irradiated or washed blood may be requested for neonates if ECMO is anticipated and cannulation is expected in >4 hours.
- 1 unit of fresh frozen plasma (AB+) and 1 unit each of apheresed paediatric platelets (A+ and B+) are available at KKH Blood Bank.
- Requests for FFP and platelets are based on individual indications and the requisition process is as per KK Hospital protocol.

Weight of patient	**<10kg**	**10-35 kg**
ECMO Pack	**Neonatal**	**Paediatric**
Packed red blood cells (leucodepleted, <7 days old) for circuit priming	2 adult units	2 adult units
Packed red blood cells (Cross matched, not leuodepleted) for procedure. Leucocyte filter will be provided.	0 unit	1 unit

Drugs

Prepare the following drugs for ECMO cannulation:

- 1% lignocaine without adrenaline
- Rocuronium 0.5-1 mg/kg/dose
- Morphine 0.1mg/kg X 2 doses OR fentanyl 10mcg/kg/dose
- Heparin 50-100 units /kg to be given immediately prior to cannulation, once hemostasis has been achieved and vessels identified- the surgeon will tell you when
- Heparin infusion at 10-40 units/kg/hr after flows have been established
- “Resuscitation” drugs including Adrenaline 1:10,000 boluses and adrenaline infusion
- “Volume” as 5% albumin and normal saline aliquots
- Phenylephrine 2-10 mcg/kg/dose (dilution: 10mcg/ml for neonates <5kg, 100mcg/ml for paediatric patients >5kg)
- Prophylactic antibiotics according to unit protocol

Post-Cannulation

The correct positioning of cannulae are checked with 2DE immediately following cannulation:

- tip of the arterial cannula at the aortic arch (rib 3)
- venous catheter must be inserted so that the tip of the cannula lies in the right atrial-IVC junction or in right atrium (rib 8-9)

Echocardiogram is also an effective way of assessing the direction of blood flow in veno-venous ECMO using colour flow Doppler.

A plain chest X-ray is also performed immediately following cannulation. This serves as a guide to the cannulae position after echocardiogram confirmation with subsequent follow up chest X-rays.

Straighten the child’s head where possible after cannulation to aid left sided cerebral venous drainage. Incorrect cannula position usually causes blood flow problems (although not always immediately). Likewise apparently ‘good’ cannula positioning which does not permit full flows must be fully investigated. The surgical team is present until optimal flow is achieved.

Continuous renal replacement therapy (CRRT) while on ECMO

Continuous Renal Replacement Therapy (CRRT) is the filtration of blood through a hollow fiber, semi permeable membrane outside of the body (extracorporeal circuit). CRRT is a slow, continuous therapy and is indicated for solute and/or fluid removal. The different modes of CRRT used are:

- slow continuous ultrafiltration (SCUF)
- continuous venovenous haemodialysis (CVVHD)
- continuous venovenous haemofiltration (CVVH)
- continuous venovenous haemodiafiltration (CVVHDF)

The indications for CRRT are:

- Fluid overload resistant to diuretic therapy
- Solute removal in acute kidney injury Eg. hyperkalaemia, acidosis, hyperphosphataemia, uraemia
- intoxication with dialyzable toxins
- hyperammonaemia

CRRT during ECMO is done by creating a shunt from the ECMO to the PrismaFlex machine via the manifold. The guidelines for CRRT is as per our hospital's CRRT Policies and Procedures.

Slow continuous ultrafiltration

Fluid can be removed by ultrafiltration through a haemofilter attached to the ECMO circuit. In ultrafiltration, minimal solute is removed. The fluid removal rate is to be determined by the volume status of the child. The actual amount of fluid removed should be manually measured per hour.

Continuous veno-venous haemodialysis

Solute is removed by diffusion from the blood (higher concentration) to the dialysis solution (lower concentration) that runs countercurrent to the blood flow.

Continuous veno-venous haemofiltration

Solute is removed via a convective process through solvent drag.

Continuous veno-venous haemodiafiltration

In this process, solute removal is by both diffusive and convective process. Both dialysis and replacement solutions are required.

ECMO management goals

In general, patients on V-A ECMO should maintain ECMO perfusion flows at levels that achieve adequate tissue oxygen delivery as evidenced by:

- Mixed venous oxygen saturation of > 65%
  - Once the SvO_2 is > 65%, adjust the blood pressure by manipulating the systemic vascular resistance with vasodilators/vasoconstrictors
- Decreasing serum lactates
- Improving urine output
- PaO_2 > 100 mmHg (V-A ECMO)
- SpO_2 > 80% and PaO_2 > 40mmHg if no other evidence of impaired oxygen delivery (V-V ECMO)
- $PaCO_2$ 35-40 mmHg
- In certain subgroups of patients (eg. patients with cyanotic heart conditions), V-V ECMO or V-A ECMO via femoral routes, goals may be different and should be reflected on the daily ECMO goals

1. **Respiratory**

Ventilation should be adjusted to allow for lung rest but maintain coronary oxygenation:

- Minimise barotrauma
- Avoid/ treat lung collapse; consider bronchoscopy prior to coming off ECMO if persistent lung collapse
- V-A ECMO: peak pressures < 25, PEEP 5-15, RR 15-20/min, F_iO_2 < 30%
- V-V ECMO: may need higher ventilatory settings to achieve adequate oxygen delivery
- Daily CXR to assess lung recovery

2. Haematology

If no active bleeding, transfuse to maintain:

- Hb >10 g/dL
- platelets > 100
- PTT < 17 seconds
- fibrinogen > 1.0g/L

If active bleeding, transfuse to maintain:

- Hb > 12 g/dL
- Platelets > 120
- PTT < 15 seconds
- Fibrinogen > 1.5g/L

3. Fluids and nutrition

Total daily fluid prescription depends on renal function and fluid balance:

- Aim for total fluids at 80-100ml/kg/day depending on fluid status, avoid fluid overload
- Consider pharmacological diuresis if renal perfusion is adequate
- Consider CRRT if there is a need for fluid removal, removal of toxins/electrolytes/acid, removal of cytokines or to allow optimisation of nutrition
- Enteral feeding should be started as soon as possible as per our unit's feeding protocol
- Consider dietician referral if fluid-restricted to optimize caloric intake

4. Neurology

- Daily neurological examination should be performed looking for any new neurological deficits
- Ensure adequate sedation and analgesia to decrease metabolic demands
- Consider daily sedation/neuromuscular blockade holiday for neurological assessment once stable
- Initial cranial USS and PRN subsequently for infants with an open fontanelle
- Watch for possible seizures
- A falling haemoglobin may be indicative of a new intra-cranial haemorrhage

Anti-coagulation

After successful cannulation and establishment of ECMO perfusion flows, heparin infusion should be started once the activated clotting time (ACT) < 220 seconds and there is no active bleeding.

- Perform ACT every hour or more frequently as indicated.
- Maintain ACT 200-220s with heparin infusion rate 10-40 units/kg/h. See unit protocol on anti-coagulation in ECMO and bleeding.
- If ACT decreases rapidly, a bolus of 10-25 units/kg of heparin may be necessary
- Aim for anti-Xa levels between 0.3-0.7 IU/ml

Specific problems

1. ECMO flow problems

The ECMO centrifugal pump is sensitive to preload and afterload. Changes in either of these will alter circuit and patient blood flow, and hence oxygen delivery.

Markers of insufficient oxygen delivery include:

- Decreased circuit SvO_2

- Increased arterial blood lactate
- Decreased arterial pH and increased anion gap
- Decreased urine output
- Hypotension – late

In V-V ECMO, low ECMO flow may also cause:

- Low patient arterial oxygen saturation
- Increased arterial CO_2

a. Inadequate flow with negative venous pump inlet pressures

The most likely cause is a decrease in pump pre-load. Possible contributing factors include patient hypovolaemia, a change in patient head position, change in venous cannula position, kinking or pressure on pump inlet line or clot in pump inlet line.

Management:

- Check circuit and patient's head position
- Consider small volume bolus (5% albumin) and watch effect on CVP, flows and inlet pressures
- If there is no improvement after the above, consult surgeon regarding inlet cannula position

b. Decreasing flow with no negative venous pump pressures

The most likely cause is an increase in pump afterload. Possible contributing factors include an increase in vascular resistance, change in arterial cannula position or clots in oxygenator, arterial tubing or arterial cannula.

Management:

- Check circuit and patient's head position
- Consider afterload reduction (vasodilator) if no hypotension
- If no improvement, consult surgeon regarding outlet cannula position

2. Abnormal patient PCO_2 or PO_2 levels

Oxygenation of the blood on ECMO is determined mainly by FiO_2 of sweep gas through the oxygenator and by blood flow through the oxygenator.

CO_2 transfer out of the blood is determined mainly by total sweep gas flow and blood flow through the oxygenator.

Consideration must be made of the ventilation settings (usually set at rest parameters) as they will also influence gas transfer depending on mode of ECMO and amount of pulmonary blood flow.

a. Low PO_2

A deteriorating PO_2 may be due to a low ECMO flow rate, decreased pulmonary flow, gas tubing leaks, oxygenator failure or if the sweep gas FiO_2 is too low.

Management:

- Increase sweep FiO_2 and check for gas leak
- Optimise ECMO blood flow and Hb
- Check oxygenator for clots (pre and post oxygenator PaO_2 readings should be checked)
- 2DE to rule out right to left shunt (eg PDA)
- Increase patient's FiO_2 via the mechanical ventilator (temporary solution)

b. Abnormal PCO_2

A rising PCO_2 may be due to inadequate total sweep gas flow or large clots in the oxygenator.
A falling PCO_2 may be due to an excessive sweep flow rate or over-ventilation of the lungs.

Management of high PCO_2 includes:

- Adjust total sweep gas flow to achieve ideal PCO_2 range
- Check for gas leak
- Optimise ECMO blood flow
- Check oxygenator for clots (pre and post oxygenator PaO_2 readings should be checked).
- Increase patient's FiO_2 via the mechanical ventilator (temporary solution)

3. Prolonged acidosis

- If inadequate oxygen delivery is suspected reassess flows, fluid status and vasodilator therapy
- If infection is suspected initiate full septic screen and consider broad spectrum IV antibiotics

4. Bleeding

Consider if:

- thoracotomy or bloody pleural fluid drainage > 4 mL/kg/hour for 4 hours
- gastrointestinal, oral or nasal bleeding associated with decrease in haematocrit/ Hb despite intervention
- Cather or cannula site bleeding with decrease in haematocrit/Hb despite intervention
- New or worsening cranial bleed

In a step-wise manner, consider:

- Decrease heparin infusion by 50%
- Accept a lower ACT of 150-180 seconds
- Keep Hb > 12g/dL, Platelets ≥ $120x10^9$/L, PT < 15 sec, Fibrinogen > 1.5g/L
- Maintain anti-Xa levels at 0.3 - 0.5 IU/ml
- Antiplatelet therapy – IV Tranexamic acid (Loading dose: intravenous 10mg/kg over 1 hour, followed by 1mg/kg/hr intravenous infusion)
- Re-evaluate every 12 hours and return to routine anticoagulation when bleeding subsides

5. Haemolysis

Usually due to poor flow dynamics in the ECMO circuit caused by:

- Clot in circuit- check for high D-dimer level, low fibrinogen
- High revolutions per minutes (RPM) needed to achieve calculated flow
- Cannula too small for calculated flow
- Excessive negative pressures

Suspect if:

- Increased plasma free haemoglobin (>0.1g/dL)
- Pink colouration of the urine and change in urine output (falling urine output)
- Continuing drop in the haematocrit levels without obvious signs of bleeding

Haemolysis can result in:

- Haemoglobin-induced acute kidney injury
- Anaemia resulting in reduced oxygen-carrying capacity of the blood
- Hyperkalaemia

Plasma free haemoglobin

- Plasma free haemoglobin is tested on a daily basis for patients on ECMO. Blood samples must first be taken and sent to the laboratory for centrifugation. The centrifuged (plasma) sample is then tested for free haemoglobin using the point-of-care measurement
- The workflow for plasma free haemoglobin testing is found in our unit's ECMO protocol

Management:

- Identify and correct causes
- High plasma free haemoglobin levels (>0.1g/dL) alone, consider changing the pump head.

- High plasma free haemoglobin levels (>0.1g/dL) with consumptive coagulopathy (low fibrinogen, high D-dimers), consider changing the pump and circuit.

6. Accidental decannulation or circuit failure

!!This is a medical emergency!!

- Clamp lines immediately and notify the ICU physician and cardiothoracic surgeon
- Take the patient off ECMO
- Begin resuscitative measures (hand ventilation, CPR, drugs, volume) as required until ECMO flows can be re-established

Venous cannula dislodged:

- Apply direct pressure to the neck or site
- If air entrained, displace it with appropriate volume
- If patient requires volume, can infuse via the arterial side of the manifold

Arterial cannula dislodged:

- Patient will need volume resuscitation
- This can be infused via the venous manifold

7. Sepsis

- Sepsis may be masked by lack of fever (as temperature will be controlled by the ECMO circuit's heat exchanger)
- Consider occult sepsis in patient with elevated CRP, white cell counts, vasomotor instability, glucose level fluctuations (hypo/hyperglycaemia) or increasing CO2 production (increasing need for higher sweep flows)

Investigations while on ECMO

	8am	12pm	8pm	12am
ABG (patient)	√	√	√	√
ABG (pre and post membrane)	√		√	
FBC	√		√	
PT/PTT	√		√	
Fibrinogen	√			
U/E/Cr	√			
Plasma free Hb	√			

- ACT every 3 hourly, more frequently if out of range or heparin turned off
- Bilirubin as indicated
- Blood culture if sepsis suspected

Echocardiogram:

- at the time of cannulation, prior to decannulation and daily/PRN to assess for readiness for weaning

X-rays:

- Chest X-ray: Post cannulation, to access lung recovery (clearing), Post chest exploration for cardiac tamponade

Weaning off ECMO

The decision to wean is made when the patient's cardiopulmonary function has recovered to an extent that is deemed adequate to be weaned off ECMO. The ECMO support is gradually reduced until the patient is eventually separated from the ECMO circuit.

- Optimal atrial filling pressure should be achieved before weaning of ECMO flow

- Inotropic infusions (dopamine, dobutamine or adrenaline) may be required after coming off ECMO. The infusions should be prepared and connected to patient PRIOR to decannulation
- In preparation for the patient to be "trialed-off" ECMO, all medications and infusions into the ECMO circuit must be transferred to the patient's own intravenous access
- During weaning, the ECMO pump flow is reduced slowly to allow patient to equilibrate to lower support. In V-A ECMO, cardiac contractility is assessed by 2D echocardiography.
- When the pump flow is less than 2000 rpm, the bridge is gradually opened until desired flow is achieved eg. 150 ml/min.
- Check ACT in circuit every 10 minutes and maintain at 200-220 seconds
- Do not "trial-off" ECMO for more than 2 hours. A decision should be made to decannulate or resume ECMO.

If the wean is successful, the patient should demonstrate:

- A normal arterial pressure trace.
- Stable LA/RA pressures, usually below 12 mmHg.
- Clinical signs of adequate haemodynamics and perfusion on ECMO flows < 50%.

The decision to decannulate is made after a successful "trial-off" period during weaning or if the cardiopulmonary failure is deemed irreversible. The general rule is that the patient must be able to maintain PaO_2 on a FiO_2 of 50% or less with moderate to low vent settings. In a cardiac patient, the amount of pressor support and ventricular function are also considered.

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