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EXTRACORPOREAL MEMBRANE OXYGENATION (ECMO)

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EXTRACORPOREAL MEMBRANE OXYGENATION

INTRODUCTION

In 1869 Ludwig and Schmidt, attempted to oxygenate blood outside the body by shaking together defibrinated blood with air in a balloon. The first device used for extracorporeal oxygenation was founded in 1885 by van Frey and Gruber. They used an inclined rotating cylinder with an inner surface covered with a thin film of blood to conduct oxygen, allowing for gas exchange.(Sangalli, Patroniti et al. 2014)

In 1937 Gibbon developed a machine which would be used during open heart transplant. Complications from its use included haemolysis, thrombocytopenia and organ failure secondary to direct blood contact, and because of this it became unpopular.

Clowes, in 1956 improved on this device by creating an artificial lung which allowed for clear separation of blood and gas using a membrane oxygenator. Over the years this has since been improved upon with safer cannulas, improved pump design and more efficient membrane oxygenators, yielding a decrease in complications and a growing interest in the intervention.

WHAT IS ECMO

Extra corporeal membrane oxygenation (ECMO), is an adaptation of cardiopulmonary bypass which is used to promote gaseous exchange outside the body(Martinez and Vuylsteke 2011). Deoxygenated blood is diverted from the systemic circulation into an extracorporeal gas exchange device by an external pump. Blood is delivered to the membrane oxygenator, made up of a semi-permeable membrane consisting of hydrophobic polymers separating the blood component and the gas component, making sure only gas particles diffuse between components. After removal of carbon dioxide and oxygenation blood is reinfused back to the patient via a warmer. This can either be to the venous circulation, venovenous-ECMO or to the arterial circulation, venoarterial-ECMO.

The Extracorporeal Life Support Organization (ELSO) was established in 1989 and publishes guidelines on the use of ECMO that are updated every three years with over two hundred international centres adhering to them.

TYPES OF ECMO

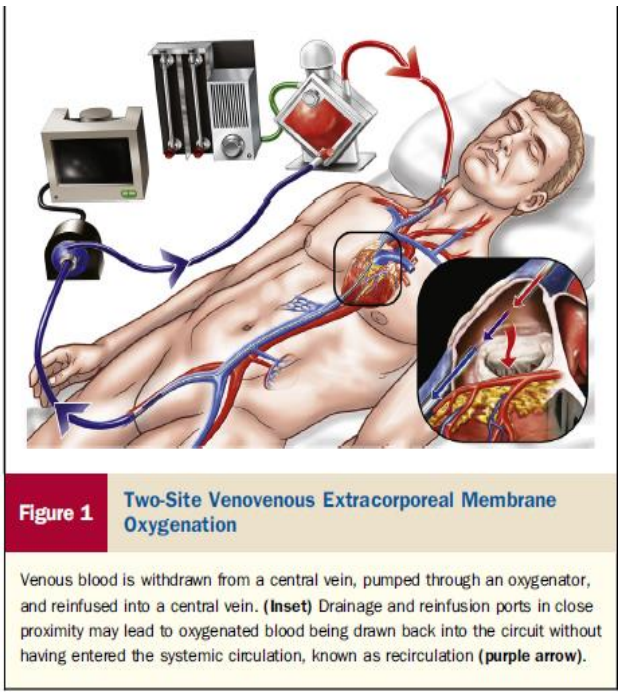

Figure 1 Two-Site Venovenous Extracorporeal Membrane Oxygenation

Venous blood is withdrawn from a central vein, pumped through an oxygenator, and reinfused into a central vein. **(Inset)** Drainage and reinfusion ports in close proximity may lead to oxygenated blood being drawn back into the circuit without having entered the systemic circulation, known as recirculation **(purple arrow)**.

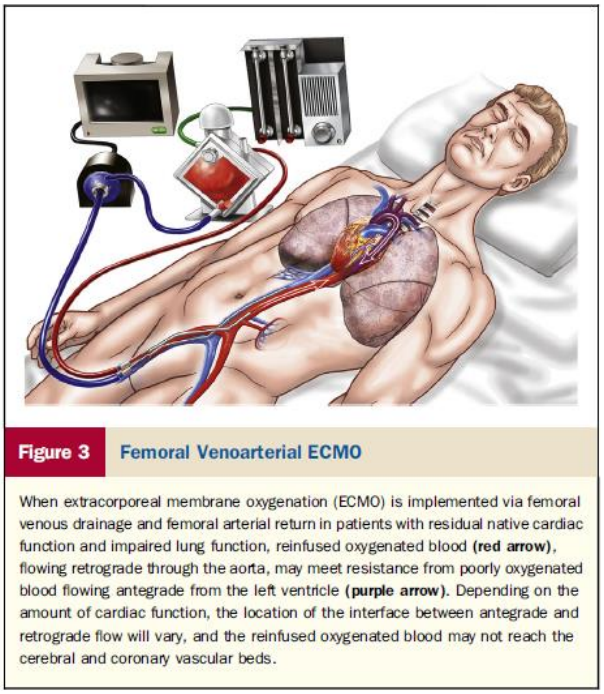

Figure 3 Femoral Venoarterial ECMO

When extracorporeal membrane oxygenation (ECMO) is implemented via femoral venous drainage and femoral arterial return in patients with residual native cardiac function and impaired lung function, reinfused oxygenated blood **(red arrow)**, flowing retrograde through the aorta, may meet resistance from poorly oxygenated blood flowing antegrade from the left ventricle **(purple arrow)**. Depending on the amount of cardiac function, the location of the interface between antegrade and retrograde flow will vary, and the reinfused oxygenated blood may not reach the cerebral and coronary vascular beds.

Figure 1 VV-ECMO, Figure 3 VA-ECMO (Abrams, Combes et al. 2014)

Veno-venous ECMO (VV-ECMO)

In VV-ECMO deoxygenated blood is drained from the venous circulation and oxygenated blood returned to the right atrium. In this configuration the ECMO circuit is in series with the cardiorespiratory system. This theoretically gives a period of rest to the diseased lung by reducing ventilatory support needs leading to a potential reduction in ventilator-induced lung injury. VV-ECMO is exclusively for respiratory support and has no haemodynamic support. VV-ECMO has a higher capacity for carbon dioxide removal compared to oxygen delivery, achieving arterial oxygenation of 55mmHg to 90mmHg.

Proficiency of VV-ECMO depends on pump flow comparative to cardiac output, more blood needs to go through the oxygenator to achieve higher oxygenation. It is commonly indicated for refractory reversible lung pathology which has not been responsive to conventional mechanical ventilation. This includes ARDS, pneumonia, lung contusions, failed lung transplant graft and pulmonary embolism when there is no cardiac affectation.

Venous-Arterial ECMO (VA-ECMO)

Deoxygenated blood is drained from the venous circulation and oxygenated blood is returned to the arterial circulation, meaning blood bypasses both the respiratory and cardiac system. Compared to VV-ECMO the circuit is parallel to the cardiorespiratory system. There is respiratory and cardiac support by reduction in cardiac work load and oxygen consumption while there is optimised oxygen tissue delivery. Because oxygenated blood is delivered directly to the arterial system, partial pressures of oxygen can range from 400mmHg to 500mmHg.

To note, the counter current of the blood flow from the ECMO machine to the blood from the heart can cause a discrepancy in the oxygenation between the upper extremities compared with the lower extremities. This occurs when there is significant lung disease with poor ventilation, with upper extremities receiving less oxygenated blood.

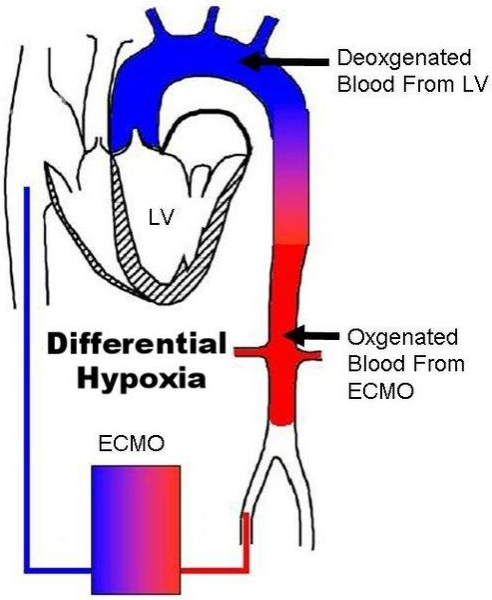

Figure 1 Oxygen discrepancy between extremities in severe lung disease(ECMO 2016)

VA-ECMO is indicated as bridge therapy in cardiac shock, weaning off cardiopulmonary bypass, myocarditis, intractable arrythmia, local anaesthesia toxicity, patients awaiting definitive therapy e.g. Cardiac transplantation.

Arterio-Venous ECMO (VA-ECMO)

Blood flow is from the femoral artery and returned to the femoral vein. This promotes gas exchange by using the patient's arterial pressure to pump blood through the circuit. This is predominantly used for carbon dioxide removal with minimal oxygenation.

CANNULATION

Site

Good vascular access is of paramount importance when instituting ECMO, this can be achieved by a skilled intensivist, but cardiothoracic or vascular surgeon cover is strongly recommended in cases of potential difficult cannulation or where VA-ECMO needs to be commenced urgently. Approach can be percutaneous, semi-open or surgical. As a rule, the cannula should not be more than 2/3 of the vessel diameter. As blood flow is directly related to the power of four of the cannula radius, the choice of vessel used will affect the maximum flow needed for ECMO.

Percutaneous cannulation is preferred as it is easy and allows for quick insertion, has less complications and allows for non-laborious nursing care. Ultrasound guidance is important for vessel visualisation and diameter estimation. A surgical approach has the benefit of direct vessel visualisation with better cannula size estimation, direct placement and better haemostasis. It is reserved for patients with severe peripheral vascular disease or patients that require a sternotomy. Because of the larger vessels with central cannulation (right atrium and ascending aorta), there is better flow because of the reduced resistance and better venous flow drainage is achieved.(Sangalli, Patroniti et al. 2014)

Cannulation sites in VV-ECMO are internal jugular-femoral, femoral-femoral, saphenous - saphenous and single sites are the internal jugular and the atrium.

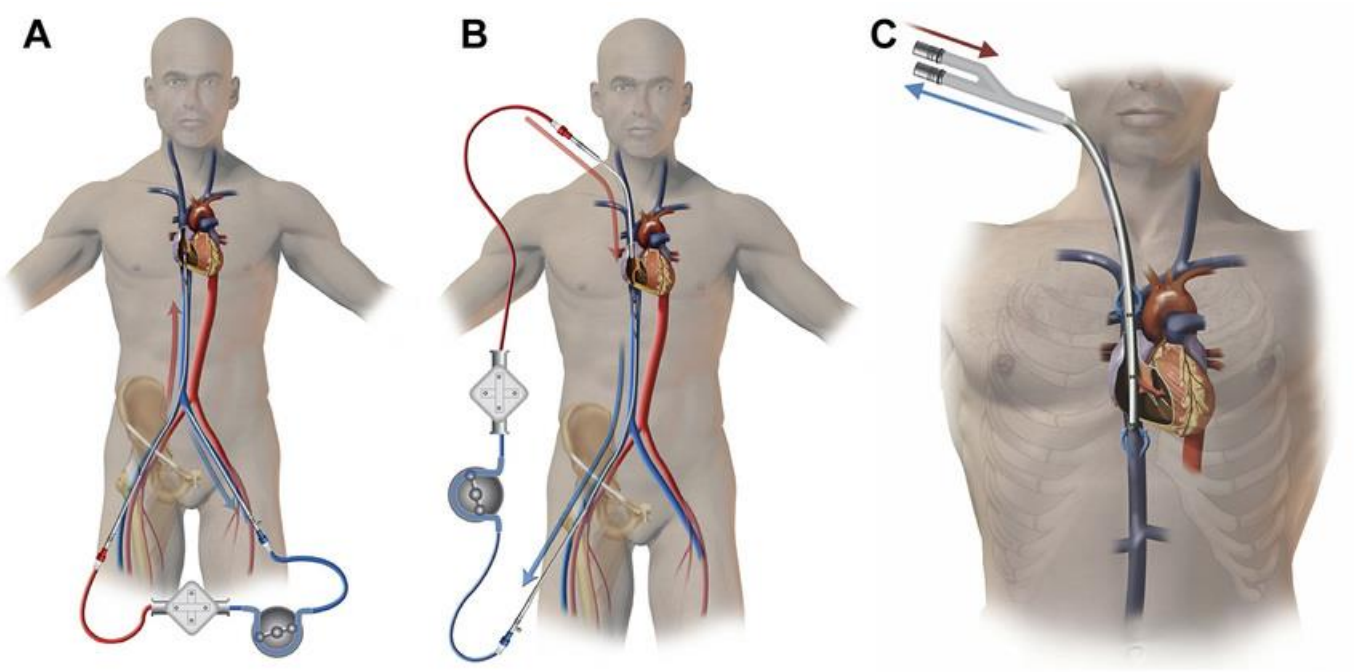

Figure 2 A) VV-ECMO with long venous cannula in the right atrium and shorter cannula in the inferior vena cava, B) cannulation of the right atrium and a long venous cannula in the inferior vena cava , C) Double lumen bicaval cannula inserted into the RIJV (Gate 2018)

For VA-ECMO venous access is from the internal jugular and femoral artery, where arterial access is from right common carotid, axillary, femoral and aorta

To reduce recirculation in femoral-femoral approach, the drainage cannula is inserted up to L1/L2 and the second cannula at T10/T11 whereas in femoral-jugular approach the drainage cannula must be in the inferior vena cava and the second cannula in the proximal right atrium. (Sangalli, Patroniti et al. 2014)

A double lumen canula is an improvement on the traditional two site cannulation, allowing for better patient comfort and ease of mobilisation. The canula is inserted in the internal jugular with placement guided by an ultrasound or fluoroscopy. Adequate position will be with the drainage tip in the inferior vena cava and the reinfusion lumen facing the right tricuspid valve

Complications

Percutaneous	Surgical
Guidewire kinking/unable to advance, pneumothorax, air emboli	Aortic injury, arrhythmias, embolic events, mediastinitis
Vascular tears, intimal dissection, perforation	Limb ischaemia and reperfusion injury
Right ventricular rupture, cardiac tamponade, myocardial infarction	Neurological complications
Haemorrhage, haematoma, thrombosis	Haemorrhage, haematomas, thrombosis
Limb ischaemia, compartment syndrome	Nerve injuries
Pseudoaneurysm, arteriovenous fistulae	Arterial/venous laceration and perforation
Infection	Infection

ECMO CIRCUIT

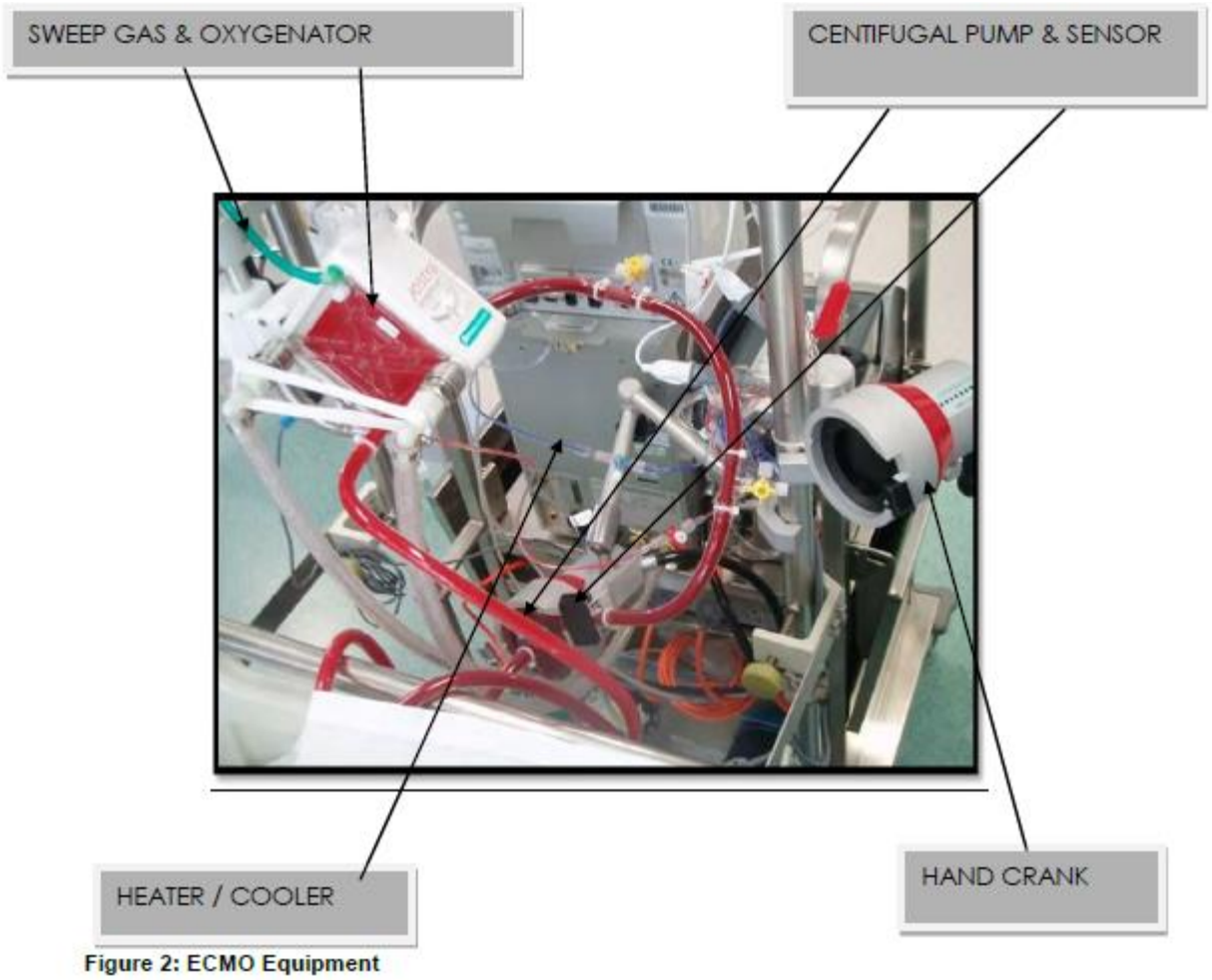

Figure 3 ECMO equipment(Nekic and SWSLHD 2016)

The ECMO circuit is made up of a pump which is used to achieve adequate circuit flow. Most circuits now use the centrifugal pump, which uses centrifugal force to generate flow. For adequate preload this pump needs to be allocated below the level of the right atrium. The membrane oxygenator is located distal to the pump. It is made up of a semi-permeable membrane (polymethylpentene/polypropylene/silicone caoutchouc), a heat exchanger to allowing cooling and warming of blood and a gas flow, sweep gas, which delivers oxygen to the blood. There is no contact between the blood and gas interface.

Oxygenation is not affected by sweep flow but is determined by:
- The pressure gradient across the membrane
- The time the blood is in contact with the membrane
- Laminar flow: peripheral blood is better oxygenated compared to central blood, so disruption of laminar flow improves oxygenation
- Increase in surface area, native lung has an increased surface area (100-150m^2) and thinner membrane (1-2µm) compared to the ECMO membrane with 1-4m^2 and 10-30µm

Carbon dioxide removal is not affected by blood flow but is determined by
-Gas diffusion gradient (CO_2 being more soluble than O_2)
-Surface area
-Sweep flow gas(Chauhan and Subin 2011)

Circuit blood flow is related to the size, diameter, length, design, pressure drop and positioning of the cannula. Wire reinforcement reduces any haemodynamic changes that can occur during position change and mobilisation.
Resistance of the cannula can be affected by circulatory temperature as well as intraabdominal and intrathoracic pressures, this can cause compression and lead to haemodynamic complications.
Venous cannulas have a multi perforated, longer and wider inflow cannula compare to the outflow cannulas.
Arterial outflow cannulas have a smaller diameter, a shorter length and minimal perforations at the tip.

Figure 4 Different types of ECMO cannulas(IndiaMart 2018)

HEAMOSTASIS

Blood contact with the circuit induces an inflammatory response which promotes a hypercoagulable state that require anticoagulation to minimise thromboembolic events. Technical measure such as biocompatible coated tubing, shorter circuits, modern hollow fibre oxygenators and having a pump speed of 2-2.5L/min can reduce the risk of thrombosis(Murphy, Hockings et al. 2015). Anticoagulation is almost always necessary, and one needs to strike a balance between adequate anticoagulation and risk of bleeding or thrombosis.

Thrombosis is related to the level of anticoagulation and is more common at decannulation with a 20% incidence of deep venous thrombosis in patients. Bleeding occurs in 30% of patients with 5-19% of those being associated with life threatening intracranial haemorrhage. Factors associated with increased risk of bleeding include, major surgery before ECMO, cardiopulmonary bypass and patients with coagulation abnormalities.

Unfractionated Heparin (UFH) is the main anticoagulant used, a dose of 50-100U/kg is used to prime the circuit and a maintenance infusion dose of 7.5U-20U/kg/min, with the goal to achieve an Activated Clotting Time (ACT) of 180s-220s(Sangalli, Patroniti et al. 2014).

UFH is preferred because of its fast onset and the easy reversibility with protamine sulphate(Mulder, Fawzy et al. 2018).
However, UFH is unpredictable and it is associated with Heparin Induced Thrombocytopaenia (HIT). Lower molecular weight heparin is easier to administer and has low risk for HIT, it can be used but accumulates in renal failure and is not easy to monitor.

Some centres use Direct Thrombin Inhibitors (DTI), which have a shorter half life and do not induce platelet antibodies. However, DTI's lack an antidote and clearance is by the hepatic and renal system, which will increase their half life is patients with failure of such systems.

Other alternatives not readily used are anti platelet inhibitors, citrate nafamostat mesylate and Factor XII. Studies have not shown these agents to be superior and more research needs to be done.

Activated partial thromboplastin (aPTT) which monitors the old intrinsic pathway is gold standard when using UFH(Taylor and Maldonado 2016). Confounders like lab variability, factor XII deficiency and antiphospholipid antibodies can make this test unreliable.

Activated clotting time (ACT) which is low cost, readily available and a good point of care test. Other tests, Antithrombin (AT) assays and viscoelastic tests are available. An estimate of 42% of centres use aPTT/ACT with 11% using AT assays and 9% using viscoelastic tests or combination of tests. No consensus has been reached a which test is the best however it is recommended to use a combination to yield better accuracy.

Suggested monitoring interval for daily bloods are fibrinogen, maximum amplitude in thromboelastography /maximal clot firmness in rotational thromboelastometry (ROTEM), lysis index, AT assays and D-dimers. Haemoglobin and platelets to be done two times a day with aPPT /ACT, R time in TEG/Clotting time in ROTEM done three times a day.(Lango, Szkulmowski et al. 2017, Mulder, Fawzy et al. 2018)

Table 2. Monitoring coagulation

	Advantages	Disadvantages
Standard coagulation tests		
aPTT (sec)	Well known Monitoring UFH Easy to interpret	Inter-laboratory variance (could be excluded by using ratio) Time consuming
ACT (sec)	Bedside method Easy to use Immediate results	Relatively insensitive to low doses of UFH Different devices with different reference ranges
Anti Xa assay (IU/ml)	Sensitive to UFH	Time consuming Needs calibration Free haemoglobin & bilirubin could be underestimated
VETs (ROTEM/TEG)	Inhibit coagulation at starting point Might reduce platelet consumption	Poor specificity and sensitivity regarding therapy adjustment
Fibrinogen mg/l	Consumption marker	Increased in inflammatory situations Time consuming
D-dimer (mg/l)	Prognostic value for oxygenator failure	Time consuming Expensive
AT (%)	Heparin resistance (partial) Pro-coagulatory marker	Heparin resistance not completely relying on AT
Haemoglobin (g/dl)	Easy and fast	Not very relevant for coagulation
Platelet count 10^9/l	Easy and fast	No proven threshold Platelet count does not reflect platelet function

ACT = activated clotting time; aPTT = activated partial thromboplastin time; AT = antithrombin; ROTEM = rotational thromboelastometry; UFH = unfractionated heparin; TEG = thromboelastography; VET = viscoelastic test.

Figure 5 Standard coagulation tests in ECMO(Mulder, Fawzy et al. 2018)

INDICATIONS

ECMO is a temporary medical intervention employed to support patients with severe, reversible, respiratory and cardiac failure, when conventional methods have been unsuccessful. Extracorporeal Life Support Organization (ELSO) dictates that ECMO should be considered when the risk of mortality is 50% or greater and is indicated when the risk of mortality is >80%.

Respiratory
- Pao2/Fio2 <80 on Fio2 >90%*a*
- Hypercapnia with a Paco2 >80 mmHg
- Inability to achieve a plateau pressure of 30 cm·H2O or less
- Severe air leak syndromes (compromising appropriate ventilation, in many cases, requiring time for lung healing)

Cardiac
- Need for cardiac and respiratory support (otherwise ventricular assist device)
- Inadequate tissue perfusion despite adequate intravascular volume (Undefined)
- Hypotension with low cardiac output
- Persistent shock despite therapy (volume administration, vasoconstrictors, inotropes, and intravascular support including an intra-aortic balloon counter pulsation)
-Myocardial infarction
-Myocarditis
-Peripartum cardiomyopathy
-Decompensated chronic heart failure
-Septic shock

Cardiopulmonary resuscitation (CPR)
- Consider extracorporeal membrane oxygenation to aid CPR efforts who have had an “easily reversible event with excellent CPR”

CONTRAINDICATIONS

Respiratory
- ≥7 days of mechanical ventilation with fractional inspired oxygen of 90% and peak plateau pressures higher than 30 cm·H2O
- Absolute neutrophil count <400mL

Neurological
- Recent or expanding central nervous system haemorrhage
- Unable to receive anticoagulation secondary to intracranial process

Cardiac
- **Absolute**
    - Heart that cannot be salvaged, AND the patient is not a candidate for transplant or ventricular assist device
    - Prolonged cardiopulmonary resuscitation without adequate tissue perfusion
    - Chronic organ dysfunction including emphysema, cirrhosis, renal failure (No end points are listed)
- **Relative**
    - Patient cannot receive anticoagulation
    - Advanced age (no limits listed)
    - Obesity (more associated with technical difficulty and a possible inability to achieve flow necessary to maintain perfusion of the tissues)

CPR
- Unsuccessful CPR, considered no return of spontaneous circulation, for 5 to 30 min. (Though it may be indicated if perfusion is adequate with appropriate metabolic support.)
(Esper, Levy et al. 2014)

Table 1 Indications and Highest Level of Evidence for ECMO in Cardiopulmonary Disease

Respiratory		
	ARDS	Randomized controlled trials
	Hypercapnic respiratory failure	Prospective feasibility studies
	Bridge to lung transplantation	Cohort studies
	Primary graft dysfunction after lung transplantation	Cohort studies
Cardiac		
	Myocardial infarction–associated cardiogenic shock	Cohort studies
	Fulminant myocarditis	Cohort studies
	Sepsis-associated cardiomyopathy	Case series
	Pulmonary hypertension	Case series
	Extracorporeal cardiopulmonary resuscitation	Cohort studies with propensity analyses
	Post-cardiotomy cardiogenic shock	Cohort studies
	Primary graft failure after heart transplantation	Cohort studies
	Bridge to VAD implantation or heart transplantation	Cohort studies
	Prevention of acute right ventricular failure after LVAD implantation	Cohort studies

ARDS = acute respiratory distress syndrome; ECMO = extracorporeal membrane oxygenation; LVAD = left ventricular assist device; VAD = ventricular assist device

Figure 6 Indication and highest level of evidence for ECMO in cardiopulmonary disease(Abrams, Combes et al. 2014)

WEANING

Weaning off ECMO should be considered 24-48hrs after initiation of ECMO. The goal is to wean when primary indication has resolved. This is often a challenging decision to be made by the physician.

VA-ECMO

NT-pro-BNP is initially elevated in the first week but has no predictive value in recovery, so markers for organ perfusion lactate and SvO2 are used instead to assess recovery.
Daily transthoracic echocardiogram (TTE) is used to assess cardiac function recovery.

Echocardiogram predictors for difficult weaning:
- right ventricular failure vs left ventricular failure
- systolic vs diastolic failure
- regional wall abnormalities
- severe post ischaemic mitral regurgitation
- dynamic outflow tract obstruction
- pericardial tamponade
- pulmonary hypertension
- hypovolaemia

To wean patients the pump flow is gradually decreased, this will increase the preload, reduce afterload, subsequently increased stroke volume and cardiac output.

Goals for successful weaning are;
-MAP>70 on low inotropes,
-SPO2 >95%,
-SVO2 >70%
-EF >23-30%
-Improved radiological changes.
(Sangalli, Patroniti et al. 2014)

If above is not met, patients are considered for Ventricular Assisted Devices until transplant or family is counselled for patients that are not candidates.

VV-ECMO

ELSO guidelines use the assessment of:

- Improving static compliance,
- Decreasing airway pressure,
- Native lung supporting 50%-80% of gas exchange
- FiO2 <0.6-0.5.

In patients with hypoxia blood flow is reduced where as in patients with hypercarbia sweep flow is reduced gradually. Patients can either be weaned to full ventilation, pressure support or in immunocompromised patients extubated on ECMO, should a need to restart arise, access is still available. When ventilation is adequate, flow is switched off and a clamp applied for 20min to allow oxygen consumption. Tidal volume, respiratory rate, minute volume, haemodynamic stability, mixed oxygen saturation and arterial gases are monitored. After a successful trial of 1-6hrs, ECMO can be stopped and patient decannulated. (Sangalli, Patroniti et al. 2014)

ECMO AND ARDS

Acute respiratory distress syndrome (ARDS) is defined by the Berlin classification as:

1. Acute, meaning onset over 1 week or less
2. Bilateral opacities consistent with pulmonary oedema must be present and may be detected on CT or chest radiograph
3. PF ratio <300mmHg with a minimum of 5 cmH20 PEEP (or CPAP)
4. Must not be fully explained by cardiac failure or fluid overload

With a more accurate definition, a better understanding of the pathophysiological process involved and newer management strategies the management of ARDS has improved but the mortality still stood at 50% in 2016 with associated reduced quality of life.(Rozencwajg, Pilcher et al. 2016)
ECMO which has had widespread use in the neonatal and paediatric population has had minimal use in the adult population. With that said more and more studies over the years are showing benefit of its use in patients with respiratory failure, including ARDS.

In the 1970's a trial of ninety randomised patients comparing conventional management and VA-ECMO showed an improvement in gas exchange but a high mortality and no benefit when considering hospital stay or long-term survival.(Turner and Cheifetz 2013)

Follow up research over the following ten years showed better neonatal outcomes whilst the adult population had no advance in survival and clinical outcomes compared to conventional management. From 1986 to 2006 only 67 adult cases were reported per year compared to 1207 in the paediatric population.(Rozencwajg, Pilcher et al. 2016)

In 2009 the conventional ventilator/ECMO for severe adult respiratory failure was published. CESAR trial was looking at six months survival without severe disability (assessed by inability to dress or bath) in patients with respiratory failure compared to conventional ventilation. They also looked at the cost effectiveness of this treatment modality. 180 subjects 11 hospitals where seen one ECMO centre was used. The study showed that patient survival was higher when patients were transferred to the ECMO centre compared to patients treated with conventional therapy.(Peek, Mugford et al. 2009)

The release of CESAR came about the same time as with the international H1N1 pandemic which caused severe acute lung injury in the young population and ECMO was used to treat these patients.

In a metanalysis by Zangrillo eight studies were looked at with a total of 1357 patients with suspected or confirmed H1N1 infection. 19.6% of these patients were treated with ECMO with a median duration of 10 days, having have been on conventional ventilation for two days. ECMO was found to be more feasible and effective with a 78% weaned off ECMO and 71% discharged from ICU even though most cases needed more than a week support and they found that patients with more comorbidities and/or multiple organ failure had a high chance of death in hospital.(Zangrillo, Biondi-Zoccai et al. 2013)

With the improvement in devices and a reduction in complications ECMO has yielded better long outcomes. Respiratory recovery assessed by lung function, parenchymal changes on imaging and respiratory symptoms in the CESAR and H1N1 trials showed no difference in both study and control group. It is to be noted that 75% of the patients in the HIN1 ECMO group showed dyspnoea on strenuous exercise at one year. Quality of life was also assessed with ECMO survivors showing moderate critical illness, psychological disorders (depression, anxiety and post traumatic disorder), to note this was not isolated to only ECMO patients but has been seen in other post ICU patients.(Schmidt, Zogheib et al. 2013, Kalzén, von Bahr et al. 2015, Rozencwajg, Pilcher et al. 2016)

The ECMO to rescue lung injury in severe respiratory distress syndrome study compared ECMO and conventional management (lung protection, neuromuscular blockage use and prone position) showed no significant decrease in 60-day mortality between the two after it was stopped for futility. However, questions on whether emergency ECMO improve outcomes in hypoxic patients and whether patients had better outcomes because of the reduction in lung trauma exist and are unanswered. The argument looks at the 15 patients that crossed over to the ECMO group and survived and the reduction in tidal volume and respiratory rate in the ECMO group.(Combes, Hajage et al. 2018)
This can be supported by Xtravent study results, that patients who were ventilated with tidal volumes of 2-3ml/kg had shorter ventilation period, so the potential benefit to early ventilation with ECMO is important in respiratory failure.(Richards and Joubert 2013)

ECMO AND THE ANAESTHETIST

With advancing medicine and improving survival rates it is estimated 48% of patients on ECMO will require some surgical procedure. This ranges from tracheostomies, vascular procedures, laparotomies, thoracotomies, video assisted thoracoscopies surgery and cannulation(Fierro,

Daneshmand et al. 2018). A good understanding of ECMO and trouble shooting will be a skill required by the anaesthetist attending to the patient.

At the preoperative visit it is important to assess for any complications that may arise from ECMO. This will be looking for any arrythmias, coagulopathy, bleeding, venous thrombosis etc. Recording of current settings (blood flow/sweep gas flow) along with the trends of premembrane oxygen saturation will give an idea of oxygen delivery. Assessment of the circuit should be carried out, confirming adequate position of the cannula by echo or X-ray, assessing the membrane oxygenator for clots or fibrin deposits that may accumulate and subsequently lead to hypoxia and hypercarbia.

Blood products must be readily available as patients have an increased risk of bleeding, Hb must be optimised to improve oxygen delivery.
Patients on prolonged ECMO have associated platelet dysfunction(Millar, Fanning et al. 2016) and acquired von Willebrand disease. Preop coagulation studies must be done (TEG, aPTT, ACT) and any coagulopathy must be corrected. Anticoagulation can be stopped four to six hours preoperatively unless there is a history of previous thromboembolic event. To remember, low flows increase risk of blood stasis when heparin has been stopped.

ELSO guidelines recommend an INR of 1.5-2.0, Platelet >100000cells/mm3/ Fibrinogen 100-150mg/dl. Aminocaproic acid can be used as an antifibrinolytic and desmopressin can be used in acquire haemophilia in ECMO(Lequier, Annich et al. 2014).

Transporting a patient on ECMO is critical(Broman and Frenckner 2016), it is advised to have someone who is skilled present. Standard ICU monitors and ventilator are used, bag valve mask ventilation is not recommended as there is a risk of atelectasis, volu/barotrauma and decruitment. Before leaving ICU, emergency drugs are prepared, alarm limits must be set, oxygen cylinder and all batteries are assessed to be at optimum level.

TIVA is the preferred form of anaesthesia, it is more practical, there is no need to transition to the theatre ventilator. Lipophilic drugs (propofol/fentanyl/midazolam) must be titrated carefully as they can be absorbed in to the system(Shekar, Roberts et al. 2012). Inhalation anaesthesia may have poor delivery because of the reduced tidal volumes, poor gas exchange, increase dead space and poor elimination via the membrane especially the polymethylepentene membrane fibre.

The altered pharmacology in critically ill patients with liver and renal dysfunction needs to be considered. ECMO increases volume of distribution with reduced drug clearance and there is absorption of lipophilic drugs into the circuit with a 60% reduction in their bioavailability. 14.4 % of patients on ECMO over 48 hours have cultured gram-negative bacilli and will require antimicrobial treatment(Taylor and Maldonado 2016). Antibiotics are said to be prone to sequestration, levels in these patients should be monitored and medication adjusted accordingly. Most of these studies were done in neonates and have not been proven in adult population.

Standard monitoring includes arterial line for pulse pressure variation and frequent arterial sampling. Reliable cardiac output monitoring is done using echocardiography, this can assess myocardial dysfunction, cannula site and thrombus assessment(Taylor and Maldonado 2016). Thermostatic cardiac output monitor is not routinely used as it is affected by the ECMO heat exchanger. CVP and SVV monitoring are a poor volume marker(Fierro, Daneshmand et al. 2018). Depth of anaesthesia must be monitored continuously because of the altered pharmacokinetics and some patients may have blunted surgical response.

Patient positioning intraoperative can interfere with ECMO, head down reduces lung compliance whereas reverse Trendelenburg reduces preload and can cause low blood flow.

To reduce ventilator induced lung injury recommended ventilator settings are of TV 4ml/kg, PEEP 10-15cm/H2O, Plat Pressure of <25cm/H2O. These must be maintained intraoperative, if need to increase ventilation arises, exclude causes like surgical manipulation and bleeding, adjusting blood flow and sweep gas should correct hypoxia. If this is not effective ventilation may be increased by to the bare minimum required to achieve oxygenation.

Trouble-shooting (Mulder, Fawzy et al. 2018)

Hypoxia	Assess perfusion markers, lactate, SVO2 and organ function. Exclude flow reduction, Oxygenator failure, Recirculation Worsening lung pathology.	-Increase flow, look out for chattering -Assess membrane for fibrin/clots with a flashlight -Assess position of cannula? migration -Pre and post oxygenator ABG -If suspected hypovolaemia can try a fluid challenge -Haematocrit <21-30% red pack cell transfusion -Reduce oxygen demand by sedation and paralysis -Nitric oxide/prostacyclin
Hypercarbia/ Acidosis	Exclude membrane failure	-Increase sweep flow -Increase blood flow -Increase MV (consider lung protection) -Pre and post ABG -Reduce CO2 production, cooling, paralysis, sedation
Line Chatter Low blood flow	Collapse of drainage cannula secondary to hypovolaemia Increase negative pressure collapsing the atria/vena cava Blood loss, kinked tubing, malposition, PE	-if normal delivery of oxygen, reduce pump -if DO2 is reduced crystalloid or blood bolus Assess canula
Venous Air Embolism	Increased risk at line placement Hypovolaemia Increase sub atmospheric pressure at venous cannulation	-Trendelenburg -Decrease pump flow at insertion
Pulmonary Embolism	Commonly line associated	Inotropic support Reduce right ventricle afterload Transition to VA-ECMO
Myocardial dysfunction	Right- respiratory failure, cardiomyopathy, PHT Left sided	Improve oxygenation Pulmonary vasodilators Inotropic support Intra-aortic balloon pump Transition to VA-ECMO

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ETHICS

In 2015 there was a reported number of 7900 cases that were treated with mechanical circulatory support by ELSO (Makdisi and Makdisi 2017). As advances are being made in this field there is an expected rise in number of patients that will receive ECMO over the years. This opens the conversation of what is ethically correct when treating these patients.

The decision to start ECMO is commonly made in a state of urgency with a non-verbal patient, leaving the decision to the family members. With introduction of a new medical intervention, with the potential to reverse disease process, families often opt in out of emotional persuasion and the patients right to govern their own care is evoked.

Ethical issues pertaining to ECMO look at which patients are candidates. South Africa has the biggest HIV profile epidemic in the world with a reported 7.1m infected people in 2016, with the largest antiretroviral programme in the world which has shown success based on the increase in life expectancy (Avert 2018). Previously it was thought that HIV infected patients with Pneumocystis Jirovecci Pneumonia were not candidates, but studies have shown that patients when controlled on treatment with CD4 of above 500cells/ul were comparable to the generation population and there have been successfully treated cases referenced to in multiple articles.(Cawcutt, De Moraes et al. 2014, De Rosa, Fanelli et al. 2014, Park, Lim et al. 2016, Capatos 2017)

The average hospital cost published by the South African Journal of Critical Care for 2010/2011 was estimated at R31 883 306 with a mortality rate of 41.5% (Richards and Joubert 2013). With an already destitute health care system one may ask, is the use ECMO practicing the best of distributive justice?
As this intervention is merely a bridge, what do we do with patients that are on ECMO but have shown no recovery and are not candidates for definitive treatment? Do we stop ECMO or continue? If we stop who makes the decision, the family or the treating physician? It has been suggested that at the initiation of ECMO the goals and expected outcomes are clearly defined and discussed with the family and the managing team early. Of note is that there is great psychological distress experienced by the health team, especially nursing staff as they interact the most with the patient(Courtwright, Robinson et al. 2016).

ECMO must be extended to all populations including patients that for religious reason refuse blood products. Two cases of successful treatment have been reported with circuit miniaturisation, erythropoietin stimulation, retrograde circuit priming and good haemostasis.(Preston, Olshove Jr et al. 2012, Lawson and Ralph 2015)

In organ donation, ECMO is used to maintain circulation to allow for tissue harvesting.
It is believed that initiation will improve graft function by early restoration of haemostatic function to donor organs, it allows for assessment of suitability of organs for transplant and reduces the warm ischaemia time. The decision of when the best time is to cannulate still under argument (Dalle Ave, Shaw et al. 2016). Some believe that premortem cannulation will inflict pain, damage body integrity, is too invasive and the patient demises attached to many machines, which is undignified. Another school of thought is of the belief that premortem cannulation allows for immediate resumption of circulation after the no touch period, insertion of cannulation is easier with an active circulation, reducing multiple attempts, and that there may be better graft outcomes.

CONCLUSION

ECMO is a lifesaving medical intervention to large group of patients with reversible disease. With the growing population and more centres offering these services anaesthesiologist understanding of the physiology and management of such patients is off paramount importance. Well equipped centres with trained staff members and ambulance services can offer better outcomes to the general population. The impoverished health system and shortage in nursing staff in South Africa limit its widespread availability. The ethical conundrum needs expert review along with extensive family counselling to provide the best care for patients. More research needs to be done to improve on what is known and potentially widen the net intervention and prognosis.

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