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Anaesthetic Management of Patients on ECMO: Literature Review

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ABSTRACT

Extra Corporeal Membrane Oxygenation (ECMO) has remarkably progressed over the recent years; it became invaluable tool in the care of adults and children with severe cardiac and pulmonary dysfunction refractory to conventional management.

ECMO does not come without potential risks, including vascular injury and haemorrhage at the puncture site, bleeding due to heparinization, thromboembolism, lipid deposition on the oxygenator membrane due to propofol infusion, sequestration of other drugs in the circuit, and mechanical failure resulting in hypoxia. Therefore, the risks and benefits should be weighed before a decision is made.

Moreover, consideration about cannulation and priming of the ECMO circuit (not in a "standby" manner) or further initiation of ECMO before induction may be another issue. In the present

review, we will highlight important aspects of Anaesthetic Management of Patients on ECMO.

Key words: ECMO, Anaesthetic.

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INTRODUCTION

Extra Corporeal Membrane Oxygenation (ECMO) has remarkably progressed over the recent years; it became invaluable tool in the care of adults and children with severe cardiac and pulmonary dysfunction refractory to conventional management. Nowadays ECMO has become more reliable with improvement in equipment, and increased experience, which is reflected in improving results. The indications are extended to more prolonged use in intensive care unit, such as bridge to transplant, for both cardiac and lung transplant and support for lung resections in unstable patients. According to the Extracorporeal Life Support Organization (ESLO) registry, ECMO was used in over 5,000 cases in 2014, this immense increase of patients treated with ECMO and the vast expansion to its indications raises ethical questions about choosing what patients should be treated with ECMO, and when the ECMO support should be stopped.¹⁻⁵

ECMO should only by performed by clinicians with training and experience in its initiation, maintenance, and discontinuation. ECMO is a supportive therapy rather than disease modifying treatment in itself; best results are obtained if we chose the right patient, the right type of ECMO and the right type of configuration (site, management and complication anticipation).³⁻⁶

ROLE ECMO IN RESPIRATORY FAILURE

ECMO is typically used for respiratory support in the following settings: (1) acute respiratory distress syndrome (viral or bacterial pneumonia, aspiration, acute alveolar proteinosis); (2) assistance

with lung rest (e.g., for traumatic lung injury or pulmonary contusion, smoke inhalation); (3) severe acute asthma (persistent bronchospasm with CO2 > 80); (4) pulmonary haemorrhage/ diffuse alveolar haemorrhage; (5) bridge to lung transplant; (6) primary graft dysfunction after lung transplant; and (7) pneumonectomy.⁷⁻⁹

Both venovenous (VV) and VA-ECMO can be used in patients with acute respiratory failure, and ECMO can be used for both hypoxemia and hypercarbia. Since the CESAR trial supporting ECMO for ARDS patients,3 multiple studies have been done to further evaluate the outcomes of ECMO use in ARDS because questions remained as to whether or not ECMO should be used as rescue therapy or more proactively as protective mechanical support. ECMO has been successfully used for lung rest in patients with inhalation injuries and traumatic lung injuries. Outcomes in patients with severe traumatic lung injury treated with ECMO appear to be better than those in patients treated with conventional modalities. 7-9

ECMO MANAGEMENT

General Management

The attending ICU consultant is the primary intensivist. While the patient is on ECMO support, an ECMO consultant (intensivist or cardiac surgeon) should always be available as a resource. The ECMO consultant and perfusionist on-call contact information should be kept by the patient's bedside. The ECMO consultant

role is to manage the ECMO parameters and help in optimizing the patient condition while on ECMO, working closely with the primary intensivist to come up with a daily plan aiming for weaning the patient off ECMO in a reasonable time when the patient recovers. The perfusionist role is to review the patient with the medical team each morning and again before leaving for the evening. 10-12

Anticoagulation on ECMO

Heparin is the most common anticoagulant drug used for preventing clot formation inside the cannula, circuit, and membrane lung targeting an activated clotting time (ACT) goal or activated partial thrombin time (aPTT) adjustment. Systemic anticoagulation is usually used to prevent thrombotic complications (in the machine and the patient). However, this should be carefully monitored and adjusted to prevent bleeding complications, which are unfortunately are still high. If ACT is used, a range of 180-200 seconds (sec) has been suggested for VV-ECMO. However, different ACT platforms and their relationship to the measured heparin levels and aPTT are inconsistent, especially in the lower ACT target ranges for ECMO. There are >300 laboratory methods for monitoring aPTT, with different results obtained depending on the method utilized. As a result of this wide variation, the PTT target (1.5 times the normal value) range used at one ECMO center should not be translated to other centers without confirming the type of assay used for aPTT. The evidence for low-dose heparin during an ECMO run is evolving; however, all expert opinion ensures its safety. A VV ECMO run can be maintained off heparin for days in individual cases, complicating moderate to severe bleeding providing adequate pump flow to avoid blood clotting; in this case, we advise a backup primed machine to be always available. Bleeding and thrombotic complications during ECMO are common and have a significant impact on patient outcomes. 10-12

Anaesthetic Management of Patients on ECMO

Extracorporeal membrane oxygenation (ECMO) therapy removes blood from a patient, circulates it thru a pump and an oxygenator, and returns oxygenated blood to the patient. Gas exchange is facilitated in the oxygenator by diffusion across a semi-permeable membrane, allowing oxygenation and carbon dioxide removal from the blood. ECMO is a well-established therapy for neonatal patients in respiratory failure, and its applications have continued to evolve in recent years for patients requiring pulmonary (venovenous or VV ECMO), cardiac or cardiopulmonary support (venoarterial or VA ECMO). ¹⁰⁻¹²

Nomenclature to describe the ECMO circuit begins with the letter representing the location or locations (venous (V)) of the blood drainage cannula or cannulas followed by the location or locations (venous (V) or arterial (A)) of blood return cannula or cannulas. Hybrid configurations such venovenous-arterial (VVA) ECMO provide the benefits of VV ECMO in addition to the hemodynamic support VA ECMO. Depending upon the sequence of cannulation or progressive physiologic need, this hybrid configuration maybe referred to VAV ECMO. These configurations provide a more balanced delivery of oxygenated blood to the patient and avoid the differential oxygen delivery that can develop in femoral VA cannulation. An ECMO "sport model" refers to upper body ECMO e.g. internal jugular vein drainage with return to the axillary or

subclavian artery which improves patient mobility and balances O_2 delivery. $^{13-15}$

The anesthesiologist should investigate the underlying organ failures, indication for ECMO and cannulation strategy employed, as these will differ per patient. Patients requiring ECMO often require medical hemodymanic support so inotropic and vasopressor support should be continued by the anesthesiologist. Other medications such as antimicrobials and anticoagulants should be continued as indicated. The anesthesiologist should consult with the intensive care team to determine if the goal of ECMO is to facilitate extubation, if so, the anesthesiologist should consider minimizing the use of sedative agents so as to expedite extubation after ECMO placement. Peripheral ECMO placement can usually be done under high- quality local anesthesia and minimal intravenous sedation. These critically ill patients usually have arterial monitoring in place but if arterial monitoring has not vet been established, the anesthesiologist should do so, taking into consideration the planned location ECMO cannulas and the effect on interpreting blood gasses sampled. Central venous access should also be established should vasopressor support be required, again considering ECMO insertion sites plan when selecting access sites. 13-15

Optimal ventilation strategies on ECMO are still being studied, but there is evidence that tidal volumes below 6ml/kg and plateau pressures less than 29 cmH20, with extracorporeal removal of carbon dioxide, may reduce pulmonary cytokines and morphologic signs of pulmonary damage. A multicenter study of ARDS patients receiving ECMO revealed a possible mortality benefit of higher levels of positive end expiratory pressure during the first 3 days of ECMO. ¹³⁻¹⁵

Fluoroscopic and echocardiographic imaging is utilized to ensure **ECMO** cannula placement. Transthoracic transesophageal imaging can provide useful information during insertion, monitoring, repositioning and weaning of ECMO. Assessment should focus on chamber size and structure, biventricular function, evaluation of the interatrial septum for septal defect or patent foramen ovale, shape and motion of interventricular septum, valvular abnormalities (severe regurgitation or stenosis), vascular abnormalities (vessel size, thrombus, aortic dissection), presence of pericardial fluid, and position of guide wires for percutaneous insertion, and the ECMO cannulas for position, flow and thrombus if suspected. Once on ECMO support, the pressure gradient from right atrium to right ventricle is altered as flow is withdrawn from or recirculated to the right atrium or venous system, thus assessment of tricuspid regurgitation and estimation of right ventricular systolic pressure are inaccurate.15-18

Anesthetic Management of Patients with Existing ECMO

Undergoing Procedures Patients on ECMO support may require procedures such bronchoscopy, laparotomy, and endoscopy. Due to mild systemic anticoagulation, bleeding is the main complication that the anesthesiologist must consider during these procedures. Blood products should be available and transfusion of coagulation factors and platelets should be done with caution to prevent thrombosis in the ECMO circuitry. Half the usual dose aminocaproic acid or tranexamic acid has been employed in patients who need surgery while on ECMO to inhibit fibrinolysis and to prevent additional bleeding secondary to anticoagulation while on ECMO.¹⁵⁻¹⁸

ISSUES, CHALLENGES, AND COMPLICATIONS

Cannulation for ECMO is one of the major sources of morbidity. Although a full surgical review of cannulation is out of the scope of this article, the main goal of ECMO cannulation is to provide the least traumatic and most durable and simplified method of delivering blood to and from the pulmonary circuit. In peripheral VA-ECMO, the femoral artery is the most common cannulation site. Oxygenated blood is delivered to the aorta via the femoral artery in retrograde fashion and competes with native antegrade circulation generated by the heart. Potential problems include separate perfusion of the upper and lower parts of the body, left ventricular distention, reduced coronary flow, and pulmonary edema due to the increased afterload produced by ECMO. One specific complication is lower limb ischemia due to partial occlusion of the femoral arterial lumen by the cannula. This can be overcome by using a reperfusion circuit inserted into the femoral artery distal to the cannula or by cannulating the tibial artery to perfuse the lower limb. 15-18

Bleeding is the most frequent and serious complication associated with ECMO support and can stem from heparin overdose, thrombocytopenia, platelet dysfunction, coagulopathy, acquired von Willebrand syndrome, and hyperfibrinolysis. Bleeding may occur at the site of cannula insertion, lung, gastrointestinal tract, mouth, nose, thoracic or abdominal cavity, and brain. These ECMO-related bleeding complications can be managed successfully with surgical and endoscopic approaches. ¹⁵⁻¹⁸

Complications on ECMO could be related to the underlining pathology needed ECMO, or of the ECMO condition itself (surgical insertion, circuit tubing, anticoagulation etc.) and as a rule of thumb, the ECMO inserted for pulmonary support has less complication than the ECMO inserted for cardiogenic support. The worst outcomes are reported when ECMO is used after ECPR. VV ECMO has fewer complications than VA ECMO, the children have less complications than adults except for neurologic complications. The most frequent complication during ECMO is hemorrhage, ranging between 10-30%. 19,20

Bleeding may occur at the surgical site, at the cannula site, or into the site of a previous invasive procedure, intrathoracic, abdominal, or retroperitoneal hemorrhage may also occur. Bleeding is increased because of systemic heparinization, platelet dysfunction, and clotting factor hemodilution. Bleeding is managed by decreasing or stopping heparin and infusion of platelets and clotting factors.²¹ Infusion of activated factor VII has been reported with mixed results and should only be considered for life threatening hemorrhage after all other options have failed.²²

Pulmonary hemorrhage is seen commonly in patients on ECMO. Management includes bleeding control as above, using steroids, and frequent bronchoscopy to clear the airway over time.²³

Intracerebral hemorrhage or infarction occurs in approximately 10-15% of ARDS patients on ECMO. Forty-three percent of the deaths in the ECM series were associated with intracranial hemorrhage.²⁴

Hemolysis does not occur during ECMO unless there is a problem in the circuit or the patient. Plasma free hemoglobin should be checked frequently; values over 10 mg% requires further investigation in identifying and repairing the cause.²³

Systemic thromboembolism due to thrombus formation within the extracorporeal circuit, although it can be devastating, it is an infrequent complication. Its impact is greater with VA ECMO than

VV ECMO because infusion is into the systemic circulation. Heparin infusion to achieve activated coagulation time (ACT) target, and vigilant observation of the circuit for signs of clot formation successfully prevents thromboembolism in most patients. Intracardiac thrombus formation was also reported in literature.²⁵

Heparin-induced thrombocytopenia (HIT) can occur in patients receiving ECMO. When HIT is proven, heparin infusion should be replaced by a non-heparin anticoagulant. We favor using Bivalirudin in spite of Heparin even without HIT when anticipating long term ECMO use. Some authors prefer to use Argatroban because its half life is short and a similar ACT target range is effective.²⁶

Neurological complications are highly variable ranging between 4-37%^{24,27} according to the ELSO registry²⁸ the incidence of major neurologic morbidity in cardiac patients as reported to ELSO is highest in neonates, with 7% suffering seizures, 3.5% infarction, and 11% intracranial hemorrhage. Children have slightly lower incidence of seizures and hemorrhage and a slightly higher incidence of infarction. Adults have the lowest incidence of major neurologic morbidity with 2% suffering seizures, 4% infarction, and 2% hemorrhage. In all age groups those patients who suffer major neurologic complications have a lower hospital survival.²⁷

MEDICAL COMPLICATIONS

Hypertension is a dangerous complication because of the risk of hemorrhage and stroke. Arrhythmias may occur as a result of hypoxia and electrolyte imbalance or an underlining cardiac pathology. Oliguria is a commonly observed renal complication during the early part of ECMO; acute tubular necrosis is observed in some patients and may require hemofiltration and dialysis. GI tract complications include hemorrhage²⁹, which may occur as a result of stress, ischemia, or bleeding tendencies. Direct hyperbilirubinemia and biliary calculi may occur secondary to prolonged fasting and total parenteral nutrition (TPN), hemolysis, and diuretics.²³

Septic complications may also result because the ECMO circuit represents a large intravascular foreign body, and frequent manipulation increases the risk of infection. Metabolic complications include electrolyte imbalances, and hypo or hyperglycemia. ECMO may alter serum concentration of drugs due to increased volume of distribution, and decreased Kidney or liver function. Caution is warranted when narrow therapeutic drugs are administered, and dose alterations may be necessary.³⁰

Mechanical complications: clots in the circuit are the most common mechanical complication (19%). Major clots can cause oxygenator failure, consumption coagulopathy, and pulmonary or systemic emboli. More recently, heparin-coated ECMO systems have been used to decrease the frequency of this complication.²³

VA ECMO-SPECIFIC COMPLICATIONS

Cannulation related complications: a variety of complications can occur during cannulation, including vessel perforation with hemorrhage, arterial dissection, distal ischemia, and incorrect location (e.g., venous cannula within the artery) or development of pseudoaneurysm at the site of insertion. These complications are rare <5%. A skilled and experienced surgeon is important to avoid or address such complications.²³

Cardiac thrombosis: occurs secondary to retrograde blood flow in the ascending aorta whenever peripheral cannulation through the femoral artery and vein are used for VA ECMO. Stasis of the blood can occur if left ventricular output is not maintained, which may result in cardiac thrombosis.²³

Coronary or cerebral hypoxia: during VA ECMO, fully saturated blood infused peripherally into the femoral artery from the ECMO circuit will preferentially perfuse the lower extremities and the abdominal viscera. Blood ejected from the heart will selectively perfuse the heart, brain, and upper extremities. As a result, cardiac and cerebral hypoxia could exist and be unrecognized if oxygenation is monitored using only blood from the lower extremity. To avoid this complication, arterial oxyhemoglobin saturation should be monitored in both the upper extremity and the lower extremity. Poor arterial oxyhemoglobin saturations measured from the upper extremity is corrected by infusing some oxygenated blood into the right atrium.²³

INVASIVE BLOOD PRESSURE MONITORING

Mean arterial pressure (MAP) should be monitored during ECMO with an invasive blood pressure catheter. End-organs typically require a MAP greater than 65 mmHg in order to maintain an adequate perfusion pressure. Hypotension may be corrected by increasing ECMO flows and/or administering volume. If the hypotension is secondary to a decreased systemic vascular resistance, then vasopressor agents may be needed to increase MAP.¹⁹

There should be a degree of pulsatility even while on higher levels of ECMO support. Lack of pulsatility may point toward stagnation, which can cause overdistension of the left ventricle (LV) and lead to thrombosis. LV decompression is imperative to prevent ventricular ischemia and allow ventricular recovery. In these cases, ECMO flow can be reduced, or a vasodilator may be administered to attempt afterload reduction or inotropic agents may be added. ¹⁹

INTERPRETATION OF ARTERIAL BLOOD GASES FROM DIFFERENT ANATOMICAL SITES

The location of the arterial inflow cannula determines the best site for arterial blood sampling and/or monitoring of SpO2. With axillary cannulation, radial artery catheters should be avoided on the ipsilateral side, as the values obtained are not reflective of the net gas exchange. With femoral cannulation, the right radial artery should be monitored. If heart function is poor, then arterialized blood flow to the coronary and cerebral circulations will occur through retrograde flow in the aorta. As heart function begins to recover, the mixing point within the aorta travels distally, and perfusion will be provided by the native cardiac output. If the patient is on venovenous (VV) ECMO, the infusion blood will mix with the systemic venous return blood. The typical ratio of infusion to deoxygenated blood is approximately 3:1. As a result, blood analysis will demonstrate approximately a PO2 40, PCO2 41, and saturation of 80%.²⁰⁻²²

MIXED VENOUS BLOOD SATURATION AND OTHER HEMODYNAMIC MONITORS

An arterial oxygen saturation (SaO2) greater than 80% may be sufficient to monitor appropriate systemic oxygen delivery during ECMO. SaO2 alone, though, may not always be a suitable

monitor, as various variables including hemoglobin, degree of recirculation, membrane oxygenator function, extracorporeal blood flow to cardiac output ratio, and venous oxygen saturation contribute to systemic oxygen delivery (DO2) and oxygen consumption (VO2). Pulmonary artery catheters (PACs) can be difficult to place once ECMO has been initiated and may not be a valuable monitor.²⁰⁻²²

CEREBRAL OXIMETRY

A high percentage of ECMO patients unfortunately suffer a neurological complication. These complications can run the gamut from seizure, intracranial haemorrhage, ischemic stroke to encephalopathy. Neurological complications increase the rate of mortality. Methods to monitor for neurological complications include electroencephalogram, transcranial Doppler, and cerebral oximetry.

Haemodynamic management can be particularly challenging. Initially, most patients require intravascular volume expansion. However, the institution of ECMO can lead to a rapid reduction in the doses of inotropic and vasoconstrictor drugs, as gas exchange improves, and intrathoracic pressures are decreased.

During ECMO, the goal is often to reduce the excess fluid that has accumulated in the extracellular space as a result of sepsis, inflammation, or cardiac failure. Fluid restriction and diuretics may be effective, although many patients will require extracorporeal haemofiltration. This can often be performed on blood from the ECMO circuit.

Anticoagulation is critical, to avoid the formation of clots in the ECMO circuit, while balancing the patient's risk of bleeding. Heparin is commonly used to keep the whole-blood activated clotting time (ACT) at a designated level (usually 1.5 times normal for the ACT measurement system). Thrombocytopenia is a common problem and regular platelets transfusions may be necessary to keep the platelets account over an arbitrary limit to decrease the risk of spontaneous bleeding (>150 000 μl^{-1}). If heparin-induced thrombotic thrombocytopenia is diagnosed, the use of alternative anticoagulant is required. It is possible to run ECMO without heparin, but this increases substantially the thrombotic risk. $^{23-26}$

CHALLENGES IN ECMO

In veno-venous (VV) ECMO, a double lumen venous cannula is used to remove blood from the right atrium (RA), which is then oxygenated and returned back to the RA through the distal lumen of the double lumen cannula. VV ECMO does not support the circulation and hence no effects on hemodynamics are seen, as blood withdrawn from the RA is returned back into the RA. Since CO 2 is readily diffusible, relatively low VV flow is sufficient to remove CO 2. In VV ECMO, the mixed venous oxygen saturation is high. The oxygenation is blood flow dependent and more blood must pass through the oxygenator to achieve a good degree of oxygenation. Clinically, maintaining a hematocrit of >5% above normal on VV bypass helps to improve oxygenation. This type of ECMO is suitable when adequate cardiac output reserve is present to compensate for hypoxia with the systemic O 2 delivery being just adequate enough to meet the systemic oxygen requirement.

Abrupt changes and extremes in positioning associated with surgical procedures may profoundly impact VV ECMO patients.

Positions that lower the head may decrease a patient's alreadyimpaired lung compliance; however, reductions in alveolar ventilation can be offset by increasing sweep gas flows. Conversely, reverse Trendelenburg positioning can cause a reduction in preload and lead to decreased ECMO flow.

Abdominal explorations and bowel resections are among the most common surgical procedures performed on ECMO patients, with 69 abdominal procedures performed in a series of 563 VA and VV ECMO patients. Abdominal compartment syndrome, which is associated with high mortality, may be caused by resuscitative fluid shifts and/or pathophysiology related to the patient's underlying critical illness. The condition is most common in pediatrics and neonates who are highly sensitive to the increased in circulating volume introduced by the ECMO circuit.91,92In addition to causing abdominal organ dysfunction and reducing pulmonary compliance, ECMO flows are often reduced in abdominal compartment syndrome due to the decrease in venous return, necessitating decompressive laparotomy.²³⁻²⁶

Laparoscopic surgery, which utilizes carbon dioxide to insufflate the abdomen, causes systemic absorption of the gas, which challenges the decarboxylation abilities of the membrane lung, resulting in refractory respiratory acidosis VV ECMO patients. Although laparoscopy is generally discouraged, preemptively increasing sweep gas flow is advisable to prevent an acute decrease in pH upon insufflation and to manage the increased dioxide load. Abdominal insufflation may also reduce venous return, decrease ECMO flow, and result in hypoxemia, requiring vigilant monitoring during the process. Although a fluid challenge may improve venous return, a low threshold to conversion to open procedure should be held. In patients who require high degrees of sweep or high VT or Pplat to manage hypercarbic respiratory failure, safe management during laparoscopic procedures will be challenging, if not impossible.²⁷

CONCLUSION

Despite various challenges, ECMO is a vital lifesaving modality in patients with respiratory and cardiorespiratory failure. New frontiers are demonstrating the benefit of ECMO in right heart failure and as a bridge and rescue modality in lung and heart transplant, and it has recently been used for patients in cardiogenic shock due to severe sepsis.

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