Chapter

Extracorporeal Membrane Oxygenation: Beyond Conventional Indications

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Abstract

Over the last several years, the use of extracorporeal membrane oxygenation (ECMO) has exponentially increased. As the technology advanced, the rate of devastating complications has decreased somewhat, and the utility of ECMO has expanded beyond its conventional uses in cardiogenic shock and acute respiratory distress syndrome (ARDS). Currently, ECMO can be deployed in the perioperative period with high-risk surgeries where cardiac or respiratory compromise is anticipated. Moreover, it can be utilized in difficult airway patients or patients undergoing airway surgeries, thoracic surgery patients, trauma victims and many other conditions previously excluded. The aim of this review is to highlight the ECMO-patient interaction, the indications for ECMO in the non-cardiac surgery population, ECMO management and potential complications.

Keywords: extracorporeal membrane oxygenation, ECMO, extracorporeal life support, ECLS, trauma, peripartum

1. Introduction

Fifty years ago, the first use of extracorporeal membrane oxygenation (ECMO) was for long-term respiratory support in an adult patient with post-traumatic acute lung injury [1]. Since that report, there has been an exponential increase in the use of ECMO for both circulatory and respiratory support. Due to the advances in technology, surgical techniques, and critical care medicine, ECMO has become part of standard care for many diseases in centers which can provide ECMO support. An analysis on ECMO data from 34 states enrolled in the Healthcare Cost and Utilization Project showed a significant increase in ECMO use from 2011 through 2014 [2], with an overall rate 1.34 per 100,000 patients per year. Similarly, the analysis of The Extracorporeal Life Support Organization (ELSO) international registry from 1989 to 2013 revealed an increase in ECMO use predominantly in adult patients [3].

This substantial increase and availability have expanded the utilization of ECMO beyond being a last-resort salvage intervention when other modalities are deemed insufficient. Currently, ECMO is deployed electively to mitigate the risk and ensure the safe and successful performance of high-risk procedures in at-risk patients. Elective initiation of ECMO has been associated with better outcomes than emergent rescue placement in the setting of cardiopulmonary arrest [4]. Further, by anticipating operative risks, a multidisciplinary team can decide on and prepare the most appropriate ECMO modality to provide support if needed. Venovenous (V-V) ECMO provides adequate gas exchange if the airway or the pulmonary function is compromised but cardiac function is adequate. However, venoarterial (V-A) ECMO will provide organ perfusion when both heart and lung function are inadequate. The perioperative use of ECMO requires an understanding of the basic physiology of ECMO, when to initiate the extracorporeal support, and how to manage and monitor for potential complications. This chapter will highlight common areas of ECMO management to provide the best care for those critically ill patients.

2. Methods

To address our research questions, we conducted a comprehensive review of the literature by using MEDLINE and EMBASE database on July 25th, 2022. The search strategy was focused on the indications for ECMO. Keywords and MeSH term relating to these categories were used to optimize the database search. We searched with keywords and MeSH term "Extracorporeal membrane oxygenation" OR "ECMO" OR "ECLS" AND "TREATMENT INDICATION". All relevant articles were screened. We included any related work that was published in English; explicitly described the approach and specific methods; and identified issues, challenges, strengths, and limitations. The search returned 265 titles from which 240 focused on different indications for ECMO and 25 centered around ECMO management and transport (Supplementary). We thoroughly reviewed and categorized the included articles according to their format and relevant clinical themes.

3. Basics and physiology of extracorporeal membrane oxygenation

3.1 Basics of extracorporeal membrane oxygenation

ECMO is an Extracorporeal Life Support (ECLS) modality, where deoxygenated blood flows into a membrane lung (oxygenator- where gas exchange occurs) and returns to the patient. The presence of the membrane lung (oxygenator) and a pump, which ensures circuit flow, are required features for ECMO. Other key components are cannulas, tubing, air-gas blender, and heat exchanger. Pressure and flow sensors are also commonly integrated into the ECMO circuit. The artificial lung is a microporous hollow fiber made from polymethylpentene (PMP) [5]. The blood surrounds the fibers and flows in the opposite direction of oxygen to obtain optimal gas exchange. The difference in partial pressure between the gas phase and the venous blood allows diffusion of oxygen (O_2) across the membrane into the blood and carbon dioxide (CO_2) from the blood into the fiber gas. The oxygenator is connected to, or integrated with, a heat exchanger that controls the blood temperature through conduction from warm water for warming or cooling with ice or other means. The most used pump is a centrifugal device that creates suction to drain blood and propels it forward to the return site. The positive pressure generated by the centrifugal head must be higher than the pressure in the returning site from the circuit to allow forward flow. There

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are multiple factors determining the blood flow through the ECMO circuit: preload (patient blood volume, vascular tone and patency, and the size and the location of the drainage cannula), afterload (size and location of the reinfusion cannula, patient blood pressure/systemic vascular resistance, the length of the tube between the pump and patient), and the resistance throughout the ECMO circuit (kinking of the tubes, connections, the degree of oxygenator clot burden). Viscosity and temperature may also affect blood flow and gas exchange.

ECMO cannulas are made from polyurethane and commonly have biocompatible hydrophilic coatings, although each manufacturer may use a different coating [6]. The drainage (inflow) cannulas are multi-stage with sizes that range from 8–32F. The return (outflow) cannulas are single stage with variable sizes and lengths based on the ECMO modality, the size of the accessed vessels, and the targeted ECMO flow. In V-V ECMO dual cannulation, femoro-femoral (V_f-V_f) configuration, the return cannula size used most in adults are 23–27F and should be placed so the distal port is at the level of the vena cava / right atrium junction. In femoral-jugular (V_f-V_j) configuration, the return cannula sizes are usually 17–25F short cannulas. In peripheral V-A ECMO, the return cannula sizes range from 15–21F. It is recommended that a distal perfusion cannula is additionally inserted (usually in the superficial femoral artery) to prevent lower limb ischemia. The size of the distal perfusion cannula often ranges from 6–8F. Finally, in dual-lumen (DL) V-V ECMO configuration, cannula sizes range from 13–32F.

3.2 Physiology of extracorporeal membrane oxygenation

There are two main modes for ECMO, V-V and V-A. However, hybrid modes such as V-AV can be adopted in certain clinical situations to provide extra support or to reduce risk such as differential hypoxia (North-South syndrome).

3.2.1 Venoarterial extracorporeal membrane oxygenation (V-A ECMO)

In V-A ECMO, deoxygenated venous blood is drained from the patient into the ECMO circuit, passes through the pump and oxygenator for gas exchange, and oxygenated blood is then returned to the patient's arterial circulation (**Figure 1a**). Thus, V-A ECMO provides both circulatory and respiratory support until either the heart recovers, more durable options become available, transplant occurs, or the decision is made that further care is futile and ECMO is withdrawn. The flow in V-A ECMO is adjusted to maintain adequate tissue perfusion but does not totally capture all of the native cardiac output. Providing oxygenated circulatory support reduces the requirements for vasopressors and inotropes that might increase myocardial oxygen demand, inhibit myocardial recovery or result in secondary organ damage. However, as flow back into the arterial circulation on V-A ECMO results in higher afterload than a normal physiologic state, V-A ECMO can exacerbate left ventricular (LV) failure and cause left atrial (LA) hypertension with resultant pulmonary edema or pulmonary hemorrhage. Failure of the aortic valve to open also increases risk of thrombosis from static blood in the LV [7]. As a result, offloading the LV in this circumstance is required via left ventricular venting techniques, such as low dose inotrope support or more invasive unloading efforts, through intra-aortic balloon pump, Impella device, atrial septostomy or direct placement of venting cannulas via the pulmonary vein, LA, or LV.

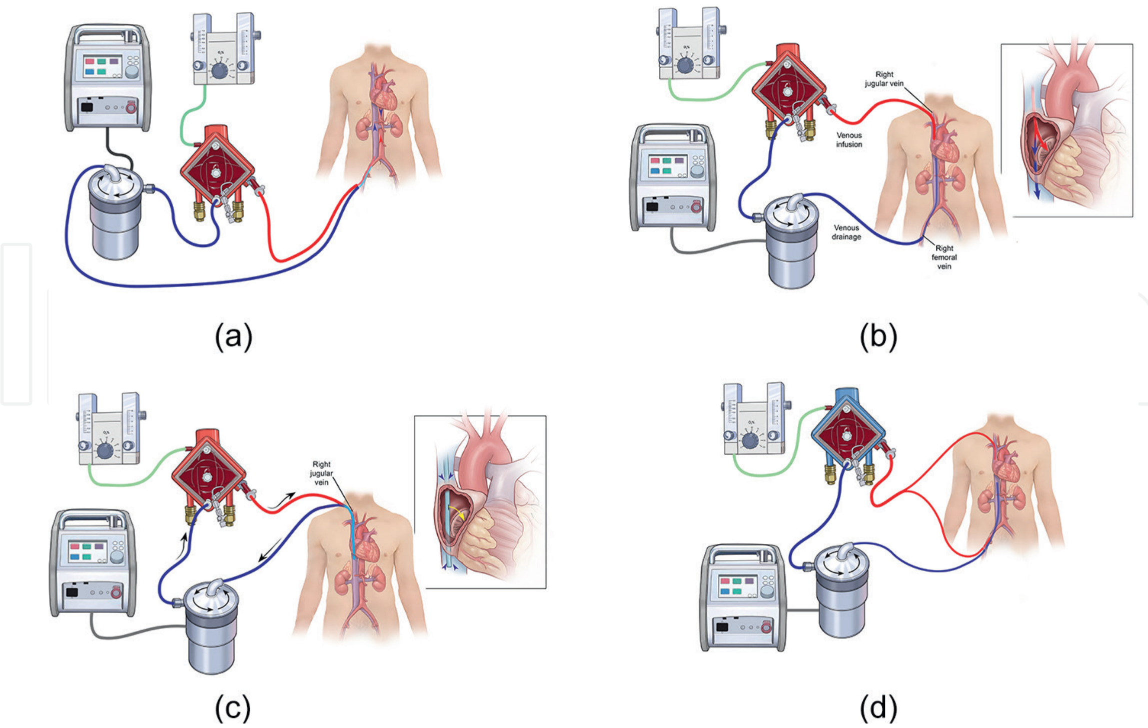

Figure 1.
Different modes and configurations of extracorporeal membrane oxygenation (ECMO). a: Venoarterial (V-A) ECMO; b: Two cannulas V-V ECMO; c: Double lumen venovenous (V-V) ECMO; and d: Veno-arteriovenous (V-AV) ECMO.

3.2.2 Venovenous extracorporeal membrane oxygenation (V-V ECMO)

In V-V ECMO, the flow is in series with the native lung and heart, hence V-V ECMO does not provide circulatory support (**Figure 1b** and **c**). It is usually utilized in patients with hypoxic and hypercapnic respiratory failure such as severe acute respiratory distress syndrome patients. By providing adequate oxygenation and ventilation, V-V ECMO reduces the injurious effect of mechanical ventilation and thus may provide the most optimal environment for lung recovery. The ECMO flow is adjusted to capture native cardiac output and maintain set gas exchange goals. Recirculation, defined as a portion of the oxygenated blood returning from the ECMO circuit being drawn back into the drainage cannula without reaching the systemic circulation, is common to some extent in all V-V support. Recirculation can be minimized by keeping return and drainage cannulas separated by 5–10 cm and is also usually less with double lumen cannulas. Recirculation is also exacerbated by anything that restricts forward flow from the right ventricle, such as pulmonary embolus or right ventricular failure. One unique configuration of V-V ECMO is the V-PA one, in which a double cannula is inserted into the pulmonary artery. This configuration has the advantage of right ventricular support, less recirculation of oxygenated blood, and single site access with subsequent easier mobility for the patient.

3.2.3 Hybrid configurations

Hybrid configurations for ECMO are considered when the patient on either V-V or V-A ECMO experience certain complications that further impact the heart or the lung functions during the ECMO support (**Figure 1d**). V-A ECMO provides circulatory and respiratory support. However, it increases the left ventricular afterload, impairs ventricular drainage, and predisposes the patient to pulmonary edema. As the heart recovers, differential oxygenation happens in the upper body because of partially impaired lung function [8]. This "North-South" phenomenon necessitate consideration of hybrid configuration such as V-AV ECMO to overcome [9]. In V-V ECMO, the development of myocardial dysfunction such as right ventricular failure, might require insertion of arterial return cannula to provide the required circulatory support, for example VV-A or VV-VA ECMO configuration [10].

3.2.4 Targets of extracorporeal life support

Targets for ECMO support depends on the indications for ECMO initiation, the patient clinical conditions, and the degree of underlying organ dysfunction. In V-A ECMO, the main goal is to maintain the organ-systems perfusion and to prevent organ-system failure until the heart recovers or more durable option is established. In V-A ECMO the ECMO flow determines the oxygen delivery to the tissues. Most centers aim for mixed venous oxygen saturation > 70% [11]. In addition to ECMO flow, increasing the oxygen carrying capacity can be increased by blood transfusion to higher hemoglobin goal or reducing the oxygen consumption by sedating the patient and establish invasive mechanical ventilation. On the other hand, in V-V ECMO the main goal is to establish adequate gas exchange to the tissues and allow resting settings on mechanical ventilation. Generally, tidal volume less than 4 cc/kg of IBW, plateau pressure around 25 cm H2O, and driving pressure < 14 [12].

3.2.5 Monitoring of extracorporeal membrane oxygenation

Monitoring of the ECMO circuit performance is of the utmost importance because it reflects the interaction between the patient and the machine, and changes noted earlier can prevent compromise of the patient's clinical status. Upon ECMO initiation, the flow that meets the patient's clinical needs and goals for hemodynamics and gas exchange is established. This becomes continuously monitored and adjusted to meet set goals. Serial correlations between the rotations per minute (RPM) and the resultant ECMO flow is important to be aware of, and when it changes (the same RPM achieving lower ECMO flows), this could indicate hypovolemia, vasodilation, blood loss, a kink in the circuit or anything that prevents drainage of blood to the circuit or return to the body. Ideally ECMO flows in adults should target above 2 LPM to avoid circuit clotting.

Additionally, multiple points of pressure measurements across the ECMO circuit are often continuously monitored and important to be aware of. Venous pressure (P vein, also called P1 or other names dependent on manufacturer) is the pressure in the drainage line, and it is usually a negative pressure measurement as the centrifugal pump suctions blood from the body. Normal values should be set based on maintaining negative pressure values <100 cm H20 across the pressure drop of the cannula. These values are provided by pressure flow charts for every cannula via the manufacturer. An increase in the venous pressure (more negative) is indicative of hypovolemia, kinking of the drainage line or clot in the drainage cannula. Arterial pressure (P artery) is the positive pressure in the reinfusion cannula and should not exceed 300 cm H_2O. An increase reflects an increase in the afterload (e.g., hypertension), kinking in the reinfusion line or a clot in the return cannula. Δ P is the pressure across the membrane lung and is measured at pre and post membrane lung sites. Values may change based on surface area and flow but should be tracked serially and often initially are less than 20 cm H2O. The increase in Δ P across the membrane lung may indicate significant clot in the oxygenator. The ability to be aware of and understand the significance of other changes is also important as an ECMO provider, with many courses available internationally and knowledge assessments available via industry (Innovative ECMO Concepts; ECMO advantage and others) as well as organizations such as ELSO, CHEST, ATS, SCCM, and others.

3.3 Extracorporeal membrane oxygenation related complications

The complications related to ECMO support are relatively common and associated with increased morbidity and mortality. These complications can be categorized into general complications related to ECMO use, mode specific as well as disease related (**Table 1**). Bleeding is the most common complication; it occurs in almost 10–30% of patients [13]. It occurs more frequently in V-A ECMO patients than in V-V patients. In a cohort study of 158 patients, 37% of V-A ECMO patients required interventions to control the bleeding, while only 17% of the V-V ECMO ones [14]. The most common sites of bleeding are the invasive procedure sites such as the surgical incisions, cannulation sites, thoracostomy tubes, tamponade, or retroperitoneal bleeding. However, bleeding can occur anywhere, such as intracranial hemorrhage, pulmonary hemorrhage, or gastrointestinal bleeding [15]. The risk of bleeding on ECMO is related to the use of systemic anticoagulants, depletion of the coagulation factors, mainly Von Willebrand factor (vWF) by the extracorporeal circuit, platelet activation, and consumption [16]. The management of bleeding relay on stopping anticoagulants, correct coagulopathy, transfuse as needed, and surgical interventions as indicated.

Thromboembolic complications could happen but now with biocompatible devices it is less of an issue. Thrombosis could happen in the patient or the circuit. Micro thrombosis of the oxygenator is common. It is estimated 10–16% of the oxygenator develop thrombi with subsequent decrease in the ECMO efficiency [17]. Air embolism can happen if there is a break in the negative side of the circuit or with excessive drainage and subsequent air cavitation. There thrombotic event can lead to devastating neurological or systemic complications. Hence the routine use of systemic anticoagulation is adopted by most ECMO centers. A challenging scenario is heparin induced thrombocytopenia (HIT). Despite being a rare complication, it carries significant morbidity and mortality. So early recognition and utilization of direct thrombin inhibitors are advised [18].

Another common complication for patients on ECMO is secondary infection. In a retrospective cohort analysis of 145 patients on ECMO, 44.8% developed sepsis [19]. The risks for infection in patients with ECMO are related to the severity of illness, the immunocompromised status related to the underlying medical condition, the presence of invasive devices. Diagnosis of infection requires a high index of suspicion. The presence of hypo or hyperthermia, hemodynamic instability, increased oxygen requirement with desaturation, respiratory secretions, frank pyuria or worsening of renal or liver function, alteration in sensorium, coagulopathy, and new skin lesions [20]. White blood cell count might not a reliable marker for infection [21]. Other markers of inflammation like C-reactive protein (CRP) or erythrocyte sedimentation rate (ESR) could be helpful but remain non-specific. In a study of 220 V-A ECMO patients on ECMO, the most common sources of infection were ventilator-associated pneumonia (VAP) (55%), blood-stream infection (18%), cannula infections (10%), and mediastinitis (11%) [22]. Infection control should focus on prevention by

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Device-related	Common Complications and risk factors	
	Cannula	
		Bleeding
		Vascular Dissection
		Malposition
		Accidental decannulation
	Circuit	
		Rupture
		Air embolism
	Pump failure	
	Oxygenator	
		Thrombosis
		Malfunction
	Heater	
		Sepsis
		Malfunction
		Electrolytes imbalance
Patient-related		
	Bleeding	
		Cannula site
		Mucosal bleeding / ENT
		Gastrointestinal bleeding
		Hemothorax
		Pericardial tamponade
		Respiratory hemorrhage
		Cerebral hemorrhage
	Coagulation abnormalities	
		Consumptive coagulopathy
		Thrombocytopenia
		Altered vWF
		Platelet dysfunction
		Decrease anti-thrombin III
		Increase D-dimer
		Increase prothrombin fragment
		Increase prothrombin-antithrombin complex
	Thromboembolism	
		Deep venous thrombosis
		Pulmonary embolism
		Ischemic stroke
		Limb ischemia

		Mesenteric ischemia
		Myocardial infarction
	Secondary infections	
		Ventilator associated pneumonia
		Blood stream infection
		Cannula related infection
		Mediastinitis
	Neurological complications	
		Ischemic stroke
		Intra-cranial hemorrhage
		Hypoxic encephalopathy
		Spinal cord injury
Mode-specific		
	V-A ECMO	
		Differential oxygenation
		Limb ischemia
	V-V ECMO	
		Recirculation
		Venous thromboembolism

ENT = ear, nose, and throat; V-A ECMO = venoarterial extracorporeal membrane oxygenation; and V-V ECMO = venovenous extracorporeal membrane oxygenation.

Table 1.
Common complications during extracorporeal membrane oxygenation (ECMO) support.

adherence to the universal hand hygiene and sterile techniques during the insertion. There is no evidence to support the use of prophylactic antibiotics in ECMO patients. For treating a suspected infection, the choice of antibiotics should be made based on the index of suspicion and the local antibiogram recommendations for each institution.

Neurological complications rates vary based on the patient characteristics, underlying medical conditions, and the mode of ECMO support. In a retrospective analysis of single-center experience, 13.3% of ECMO patients experienced neurological complications [23]. Most commonly ischemic stroke (7.0%), intracerebral hemorrhage (3.4%), hypoxic ischemic encephalopathy (3.6%), and spinal cord injury (1.2%). Neurological complications were more common in V-A ECMO (18%) rather than V-V ECMO (4.6%). ECMO especially V-A increases the risk of stroke through thromboembolism, differential oxygenation, and the associate coagulopathy. It is imperative to monitor the patient neurological examination and conduct frequent neurological assessment to recognize early neurological complications and to provide the appropriate interventions.

Vascular complications are more common in the V-A ECMO patients as well. Vascular complications are major cause of mortality. In a study, the vascular complications led to increase the mortality from 18 to 49% [24]. Acute limb ischemia affects 10–70% of the V-A ECMO patients [25, 26]. Other forms of vascular complications are dissection, pseudoaneurysm, and retroperitoneal hematomas. The risk of vascular complications is higher in women, small patients, difficult cannulation, and patients without distal perfusion cannulas. Early identification is by physical examination that shows signs of malperfusion, near infrared spectrometer (NIRS), and Doppler ultrasound. These conditions require emergent vascular surgery assessment and intervention.

V-A ECMO specific complications are differential oxygenation, left-ventricular distension, and cardiac and systemic thromboembolism. The retrograde arterial flow, particularly in peripheral V-A ECMO, increases the left ventricular afterload and impairs its drainage. As a result, cause left ventricular distension, stagnation of the blood, and backflow into the lungs. The left ventricular distension cause increase of the wall stress and could hinder left ventricular recovery [27]. The stasis of the blood can cause intra and extra-cardiac thrombi. In a retrospective analysis, the authors showed that 4% of patients on femoral V-A ECMO developed intra and extra-cardiac thrombosis despite adequate anticoagulation [28]. Another potential complication with V-A ECMO is the North-South syndrome or the Harlequin syndrome. It is characterized by lower oxygen saturation in the upper right extremity, cerebral, and coronary blood supply in comparison to the lower part of the body. It is best monitored by examining the blood from the right upper extremity or cerebral NIRS [29].

3.4 Prevention of complications

The staffing model adopted by different institutions has the most impact on the ECMO patients' outcome and plays a major role in prevention of complications. ECMO specialist has the knowledge to understand the patient-circuit interaction, conduct frequent surveillance to prevent complications, and equipped to manage circuit emergencies. There is institutional variation in the staffing model due to the available resources and staffing capabilities. In an international survey of 177 ECMO centers, most institutions adopt 24/7 ECMO nurse specialist at 1:1 ratio with backup from perfusionists [30]. The ECMO specialist works collaboratively with the bedside nurse to ensure safe care for the critically ill patients with multiple organ dysfunction.

Usually, patients supported by ECMO do not require sedation during the ECMO run. There are multiple benefits associated with being awake while on ECMO support. For instance, ability to communicate, engaged in decision making, participate in active physical activity, and elimination of side effects of sedatives with delirium being the most prominent one [31]. We understand it might not be feasible for some patient populations, however having a timeline to achieve these goals is important. Patients might need to be sedated immediately after ECMO initiation, to ensure hemodynamic stability and proper gas exchange. Afterwards, gradual weaning of sedation is advised [32].

4. Emerging indications for extracorporeal membrane oxygenation

There are many operative indications for ECMO that can be categorized based on the required support and modality (**Table 2**).

4.1 Anticipated difficult airway

ECMO can be used in patients with anatomically difficult airways, especially at or below the level of glottis, such as in patients with near complete tracheal

Organ—system	Indications
Airway	
	Anticipated difficult airway
	Complex airway surgery
Thoracic	
	General thoracic surgery
	Peri-lung transplantation
	Trauma—lung contusion
	Massive pulmonary embolism
	Surgical embolectomy for massive pulmonary embolism
	Acute respiratory distress syndrome—bacterial pneumonia
	Acute respiratory distress syndrome—viral pneumonia
	Acute respiratory distress syndrome—Aspiration
	Acute asthma exacerbation
	Chronic obstructive pulmonary disease (COPD) exacerbation
	Interstitial lung disease as bridge to lung transplant
	Inhalation lung injury
	Acute eosinophilic pneumonia
	Diffuse alveolar hemorrhage or pulmonary hemorrhage
	Large bronchopleural fistula
Heart	
	Post-cardiotomy shock
	Ventricular tachycardia ablation
	High-risk percutaneous coronary intervention (PCI).
	Transcatheter aortic valve implantation (TAVI)
	Pulmonary hypertension
	Cardiogenic shock—acute on chronic heart failure
	Cardiogenic shock—myocardial infarction
	Cardiogenic shock—myocarditis
	Cardiogenic shock—structural heart disease
	Cardiogenic shock—congenital heart disease
	Refractory ventricular tachycardia
	Heart transplantation—primary graft dysfunction or rejection
	Isolated right ventricular failure
High-risk pregnancy	
	Severe acute respiratory distress syndrome
	Peripartum cardiogenic shock
	Massive pulmonary embolism
	Amniotic fluid embolism

Organ—system	Indications
	Cardiac arrest
Liver transplantation	
Cardiac arrest	
Hypothermia	
Cardio-toxins / medications overdose	

Table 2.
Some of the indications for extracorporeal membrane oxygenation (ECMO) in the operative setting.

obstruction [33]. Induction of general anesthesia leads to the loss of the respiratory muscle tone and collapse of the airway [34]. In some situations, bag mask ventilation and positive end expiratory pressure (PEEP) are ineffective to maintain oxygenation and ventilation. In a systematic review of literature from 1976 to 2017, 45 patients were placed on ECLS for critical airway diseases [35] pre-induction, with 18 patients placed on V-V ECMO, two patients on V-A ECMO, and 24 patients on cardiopulmonary bypass; one patient did not have a support mode not specified. The airway pathologies ranged from tracheal tumors, tracheal stenosis, and head and neck cancers. All patients survived to hospital discharge without significant complications.

4.2 Complex airway surgeries

ECMO facilitates complex tracheobronchial resection surgeries by providing adequate ventilation, hemodynamic support, (in the case of V-A ECMO) and allowing proper surgical exposure. In a single center, retrospective analysis of 10 patients who underwent complex tracheobronchial reconstructions on peripheral V-A ECMO, complete resection was accomplished in 8 patients with no perioperative mortality [36]. Another retrospective analysis highlighted 19 patients supported via V-V ECMO during malignant mass removal requiring rigid bronchoscopy and insertion of tracheal stents. V-V ECMO was weaned successfully in 18 patients, with one patient dying from massive bleeding [37]. Finally, there are multiple case reports that describe utilizing ECLS as an adjunctive intervention in the endoscopic removal of tracheal papillomas and repair of tracheobronchial fistulas [38, 39]. Use of ECMO to prevent any instrumentation of the airways without need for intubation is also described.

4.3 General thoracic surgeries

ECMO is a reasonable alternative for selective lung ventilation when it is difficult or not possible. Selective lung ventilation is usually required in tracheobronchial surgeries or single-lung surgery. In a retrospective questionnaire of 34 centers in France from 2009 to 2012, 36 patients required ECMO support during surgery (16 V-A and 20 V-V ECMO) [40]. Patients were divided into three groups (complete respiratory support, partial support, and patients with ARDS on ECMO preoperatively). The survival at 30-days were 7%, 40%, and 67% respectively. The authors concluded that ECMO is a valid alternative for in-field ventilation, with the outcome depending on preoperative respiratory status of the patient. In addition, there have been many reports regarding the use of ECMO in lung volume reduction surgeries [41]. These reports must be interpreted in the context of the outcome for such surgeries.

4.4 Lung transplantation

ECMO is used at various stages in patients who require lung transplantation (bridge to transplant, intra-operatively, and post-transplantation in the case of primary graft dysfunction). The primary aim for ECMO as a bridge to transplant is to provide adequate gas exchange while maintaining the patient's functional status, with dual-lumen cannula V-V ECMO ideal for that goal. The presence of pulmonary hypertension can require assessment for other configurations such as V-PA or V-A ECMO to offload from the dysfunctional right ventricle. In a single-center study of 72 patients receiving ECMO as a bridge to lung transplantation, 42 patients received lung transplant from which 92.5% survived to hospital discharge and 84% survived at 2-years post-transplantation [42].

Intra-operatively, V-A ECMO is preferred over conventional cardiopulmonary bypass (CPB). V-A ECMO use is associated with a lower incidence of acute renal failure requiring dialysis post-transplantation, lower risk of bleeding, less requirement for blood transfusion, less incidence of primary graft dysfunction, shorter intensive care unit (ICU) and hospital length of stay [43, 44]. Post-lung transplantation, ECMO is used for primary graft dysfunction. The choice of which modality depends on the presence of associated pulmonary hypertension. In absence of pulmonary hypertension, V-V ECMO can provide the required support and the configuration is subject to the anticipated patient needs. However, if the patient has pulmonary hypertension, those patients are better served with V-A ECMO, V-PA, or hybrid configuration. In a single-center study of 58 patients required ECMO support for primary graft dysfunction, the survival rate was 58% at 30-days. There was no difference between V-V and V-A ECMO outcomes [45].

4.5 Severe trauma victims

There are multiple indications for ECMO in chest trauma patients. V-A ECMO can be used in patients with cardiopulmonary failure such as myocardial contusion, myocarditis, cardiac ischemia, and massive pulmonary embolism. On the other hand, V-V ECMO is used in lung contusions, or severe ARDS [46]. In a systematic review of 58 articles analyzing a total of 548 trauma patients who required ECMO support [47] the overall in-hospital mortality was 30.3%. Most of those patients (71.3%) received V-V ECMO and 24.5% were supported through V-A ECMO. Only 60% of the patients received systemic anticoagulation, 22.9% had hemorrhagic complications, and 19% experienced thrombotic events.

4.6 Liver transplantation

ECMO has been used in the setting of orthotopic liver transplantation. Patients with liver failure are at risk for ARDS either before or after liver transplantation. The successful use of V-V ECMO in the pre-transplant setting has been described in the literature but it is unclear if it is a contraindication for liver transplantation [48], considering that the presence of mechanical ventilation and moderate ARDS is associated with poor outcomes in this patient population [49]. One of the major challenges with these patients is anticoagulation management since they are coagulopathic due to the underlying liver dysfunction and ECMO-related coagulopathy is an added layer of risk and complexity. More commonly, ECMO has been used after liver transplantation in the form of V-V ECMO to overcome hepato-pulmonary syndrome or pulmonary infection; additionally, liver transplantation induces pulmonary remodeling, causing ventilation/perfusion mismatch that may require V-V ECMO support. Some patients post transplantation may also be supported with V-A ECMO, such as when they develop hemodynamic compromise in the setting of pulmonary embolism or right ventricular failure [50, 51]. Also, because liver transplantation patients are predisposed to right ventricular failure which could cause hepatic congestion and impair the freshly transplanted liver, V-A ECMO can facilitate decompression of the right ventricle, supporting the transplanted organ. In a recent case series of eight liver transplantation patients requiring ECMO support, 38% survived to hospital discharge [52]. However, utilization of ECMO in liver transplantation patients remains a challenge given the hematological, hemodynamic, and the immunological profile of this patient population.

4.7 Massive pulmonary embolism

Massive pulmonary embolism is associated with poor survival because of its association with obstructive shock, end-organ dysfunction, and cardiac arrest. High-risk pulmonary embolism is defined as persistent hypotension (systolic blood pressure less than 90 mmHg, drop in systolic blood pressure more than 40 mmHg, and the need for vasopressors for more than 15 min) despite resuscitation [53, 54]. Systemic thrombolysis and anticoagulation remain the first line therapy for high-risk pulmonary embolism. However, this can be associated with increased risk of bleeding including intracranial hemorrhage especially in the elderly patients with multiple co-morbidities [55]. When systemic thrombolysis is contraindicated, V-A ECMO can provide perfusion to the end-organs. Also, the use of systemic anticoagulation can mitigate the need for systemic thrombolysis by allowing time for endogenous thrombolytics to act [56]. V-A ECMO can also be used in scenarios when thrombolytics fail, for hemodynamic support before intervention, refractory cardiogenic shock, or cardiac arrest [57]. In a study of 59 patients with massive pulmonary embolism, 29 patients were treated by surgical embolectomy and 27 patients were placed on V-A ECMO with systemic anticoagulation with or without subsequent surgical embolectomy. One year survival was significantly higher in the ECMO group (96%) versus the control group (73%) [58].

4.8 Extracorporeal cardiopulmonary resuscitation (ECPR)

ECPR is defined as the initiation of ECMO when CPR is ongoing (i.e., the patient does not achieve return of spontaneous circulation prior to going on ECMO). There are multiple patient populations that could benefit from ECPR, such as patients who arrest from cardiomyopathy, right ventricular dysfunction, and massive pulmonary embolism. Induction of anesthesia and intubation place those patients at higher risk of cardiac arrest. The best predictors for favorable neurological outcome in these patients, like patients who sustain a cardiac arrest, include witnessed cardiac arrest, immediate initiation of chest compressions, shockable rhythm, cardiac arrest due to a reversible etiology, and low flow time of less than 60 min [59, 60]. The longer the time to ECMO, the less the benefit of ECPR [61]. In a retrospective comparison of ECPR for in-hospital cardiac arrest to conventional CPR, ECPR led to favorable neurological outcome at 3 months [62]. Use of ECPR in out of hospital arrest is also becoming of increasing use and descriptions of both on-site ECPR implementation and that using a specific algorithm to apply emergently once the patient arrives to the hospital have shown some success [63, 64].

4.9 ECMO during pregnancy

The increased use of ECMO in pregnant patients is attributed to increasing rates of cardiogenic shock in the peripartum period [65]. The presence of cardiogenic shock is associated with 18.81% of maternal mortality and usually leads to adverse events such as cardiac arrest and intrauterine fetal death. Similarly, the presence of severe ARDS in this patient population is associated with increased maternal mortality and fetal asphyxia [66]. V-A ECMO successfully provides the necessary circulatory support until the heart recovers. Also, it has been used as rescue intervention in pregnant patients with a massive pulmonary embolism, amniotic fluid embolism and maternal pulmonary hypertension [67]. V-V ECMO in patients with severe ARDS provides the necessary gas exchange when the patient's native lungs are inadequate due to increased intra-abdominal pressures in pregnancy [68]; further, it allows using ultra-protective lung settings, reducing ventilator induced lung injury.

In an analysis of the ELSO data between 1997 and 2017, the overall survival for pregnant patients who are supported on ECMO was 70%. There was no difference in the outcome between both V-V and V-A ECMO [69]. Pregnant patients who required ECPR had the same survival rate that is comparable to non-pregnant ones (54.8% versus 58%) [70].

4.10 High-risk cardiac procedures

Refractory ventricular tachycardia (VT) is associated with hemodynamic instability in the form of progressive cardiogenic shock, and even cardiac arrest [71]. Urgent VT ablation is required if the patient fails to respond to antiarrhythmics, intubation, heavy sedation, and neuromuscular blockade. Performing VT ablation on a hemodynamically unstable patient is challenging; additionally, VT ablation can exacerbate the underlying instability and worsen outcomes [72]. V-A ECMO can provide the required circulatory support before and during a VT ablation procedure. In terms of outcomes, one study, which was a systematic review of all patients that were placed on V-A ECMO for periprocedural VT ablation, showed short-term mortality of 15% and all-cause mortality at longest follow-up at 25% [73]. The most common causes of death were refractory VT, cardiac arrest, and acute heart failure. The duration of V-A ECMO support ranged from 140 min to 6 days. This study, among others, highlighted the role of V-A ECMO in refractory VT patients, and described that further data is needed on appropriate patient selection, outcomes, and procedural optimization. For patients with refractory arrhythmia, implementation of ECMO may improve myocardial oxygenation and normal rhythm may result.

Another use for V-A ECMO is in high-risk percutaneous coronary intervention (PCI). High-risk PCI carries an increased incidence of morbidity and mortality during and after the procedure. There are multiple risk factors for high-risk PCI, which include patient characteristics such as age, diabetes mellitus, chronic kidney disease, prior myocardial infarction, peripheral vascular disease, signs of heart failure and left ventricular function [74]. Other risk factors include the presence of multi-vessel disease, left main disease, and a saphenous vein graft lesion. PCI can induce transient myocardial ischemia that is not well-tolerated in the high-risk patients. V-A ECMO has the advantage of providing adequate biventricular support that can reach more than 5 LPM. In addition, it can be quickly deployed at bedside in the event of significant hemodynamic compromise or cardiac arrest. In certain circumstances, it can be initiated prior to high-risk PCI; in a case series of a single center experience, five patients were placed on ECMO in preparation for high-risk PCI. All patients tolerated their procedure and four of them were weaned off ECMO in less than 24 hours [75].

4.11 Extracorporeal membrane oxygenation during coronavirus 2019 pandemic

The role of extracorporeal membrane oxygenation (ECMO) in Coronavirus 2019 (COVID-19) associated severe acute respiratory distress syndrome (ARDS) has been a subject of debate because of the early negative results [76, 77]. Despite that ECMO has been recommended as supportive intervention by multiple societies [78, 79]. However, subsequent studies from the extracorporeal life support organization (ELSO) showed that the use of V-V ECMO in COVID-19 is associated with an in-hospital mortality of 36.9–51.9% at 90 days [80, 81]. Similarly, in a French retrospective single healthcare system analysis, the estimated probability of death at 60 days post-ECMO initiation was 31% [82]. Most recently, in a comparative analysis of COVID Critical Care Consortium, the use of V-V ECMO in comparison to mechanical ventilation only was associated with a significantly reduced mortality especially in patients less than 65 years old and with a $PaO_2/FiO_2 < 80$ mm Hg or with driving pressures >15 cmH2O during the first 10 days of mechanical ventilation [83].

5. Transportation of patients on extracorporeal membrane oxygenation (ECMO)

While the transportation of patients on ECMO is usually minimized, it commonly must occur—for instance, when the patient is placed on ECMO in the Operating Room, the Emergency Department, or a different center, and requires transportation back to the ICU, or specific imaging or catheterization is required for the patient. Thus, establishing a systematic approach and becoming comfortable with the transport of patients on ECMO is an important component in any ECMO center. Some studies report the rate of complications associated with ECMO transport close to 30% [76], with most of the complications being patient related. Having a dedicated multi-disciplinary team with assigned roles and responsibilities is the first step in the process [77] to achieving safer transports. The team usually includes the ECMO specialist, with their primary focus being on the equipment function and connection, the critical care nurses who manage infusions and monitor patient vitals, the respiratory therapist who is responsible for the mechanical ventilation, and the physician who focuses on the continuous monitoring of the patient/their vitals. The roles of different team members may appear isolated but is mutual and overlapping. Transport teams which do not require as many team members, especially if the patient is already cannulated, can also be successful if experienced. Physician physical presence can also be provided remotely but medical oversight to the team should be provided. Clear, closed loop communication is an important aspect throughout. The best method to train the transport team is by conducting simulation scenarios to address the most common complications that could arise [78]. ECMO centers are highly encouraged to develop ECMO transport checklists aimed at minimizing the near misses and reduce human-factor error. The literature and ELSO guidelines have many examples that could be adopted by different institutions [77, 79]. Both hospitals based and private ECMO transport teams exist.

6. Weaning of extracorporeal membrane oxygenation

Readiness for discontinuation of ECMO is determined by the degree of heart and lung recovery. In V-V ECMO, the resolution of the lung pathology as evident by improvement of lung compliance, resolution of the lung pathology on chest imaging, and adequate gas exchange without ECMO support [80]. The adequacy of gas-exchange is usually assessed by turning of the sweep gas for at least 24-hours. If adequate oxygenation (PaO_2/FiO_2 ratio > 150), and ventilation is maintained with acceptable patient respiratory effort, V-V ECMO can be removed. In the V-A ECMO, cardiac recovery is assessed by stable hemodynamics and vasoactive medication doses on decreasing the V-A ECMO flow [81]. Echocardiography is crucial part of assessing the heart right and left ventricular function before decannulation of the V-A ECMO, which can be done in the operating room or bedside based on the institution experience.

7. Discussion

Our review highlighted some of the indications for ECMO in acute care setting. These indications represent the expansion and familiarity by the ECMO advanced technology. Barbaro et al. demonstrated that the annual extracorporeal membrane oxygenation (ECMO) patient volume has a potential impact on case-mix–adjusted hospital mortality rate for patients supported by ECMO [3]. However, a recent paper challenged this observation and did not show an associated between the hospital volume and the ECMO outcome [82]. ECMO is resource intensive technology and that might limit its use [83]. To overcome these limitations, it is important to establish an organization of ECMO centers internally and externally (in the same region or country) to optimize the cost-effectiveness. Internal organization, based on the importance of establishing protocols, investing in the technology and education. Also, having multi-disciplinary team that actively participate in decision making, reviewing the patient outcomes based on preidentified quality indicators. External organization is based on coordination of care among the ECMO centers in the same region to refer patients based on specific center expertise and resource availability [84].

Despite the expansion of ECMO use, there are variation in the selection of patients who will benefit the most of this technology. Most of the selection criteria are based on the anticipated duration of support and the likelihood of weaning of ECMO support. Hence the decision is based mostly on the local institution experience, especially in the light of absence of rigorous clinical evidence. Utilization of mortality prediction score such as Survival after Veno-Arterial ECMO (SAVE) score and Respiratory ECMO Survival Prediction (RESP) score, could be helpful in decision making and informing the caregivers regarding the potential clinical outcomes [85, 86].

8. Conclusion

In conclusion, the expansion of ECMO use and technology has created new opportunities for its utilization beyond the conventional indications for ECMO. The robust evidence for each indication is still lacking. However, the early deployment of ECMO in high-risk cases for cardiac and respiratory failure is important before the patient experiences a massive complication such as cardiac arrest. Similarly, this advanced supportive technology is associated with known complications and requires extensive expertise to manage patients on ECMO. Hence the need for expanding the clinical and scientific knowledge to delineate the best patient's population with might benefit from ECMO, in context of the best structure and staffing of the ECMO programs. The decision to place a patient on ECMO must be discussed with a multidisciplinary team weighing the risks and the benefits.

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