The Miniaturization of ECMO for Emergency Procedures and Ambulatory Patients

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Background and introduction to ECMO:

Extracorporeal Membrane Oxygenation (ECMO) is a life-support process that uses an external circuit to take over the functions of the heart and lungs [1]. The system utilizes a pump to guide the blood through an artificial lung that oxygenates the blood and removes the carbon dioxide. After the blood is sent through the artificial lung, it is rewarmed and injected back into the circulatory system of the body where the oxygen is then utilized in energy production.

The Extracorporeal Life Support Organization (ELSO) is an organization that maintains the world's largest ECMO registry [2]. IN 2022, the ELSO recorded the 200,000th ECMO patient as well as the 100,000th ECMO patient to be discharged alive. From 2009 to 2022, the ELSO recorded 154,568 patients that were administered ECMO [2]. In 2009, the median annual ECMO runs in each center per year was 4. By 2022, the same statistic had increased to 15 [2]. As time and innovation progresses, ECMO is becoming more and more mainstream in the world of respiratory treatment and transplant bridging.

There are two types of pumps often used in ECMO machines–roller pumps and centrifugal pumps [3]. Originally, roller pumps were used in all ECMO machines but centrifugal pumps are now standardized in most centers. Centrifugal pumps are better for this function because they are able to provide a consistent and steady flow rate whereas the roller pumps provide periodic flow.

The configuration of ECMO used depends on the desired function of the procedure. There are two types of configurations that differ based on where the blood is returned to the body. In veno-venous configuration (VV), the oxygenated blood is returned via a cannula to the venous system which is responsible for delivering deoxygenated blood back to the heart [3]. In veno-arterial configuration (VA), the oxygenated blood is returned to the arterial system using a return cannula. The arterial system is responsible for distributing oxygenated blood from the heart to the rest of the body. VV and VA configurations both have their advantages and are used in different circumstances. VV configuration improves oxygenation by increasing the saturation of oxygen in the blood traveling through the shunted areas in the lungs but still utilizes the heart as a distribution center [3]. VA configuration both oxygenates and distributes the blood throughout the body. VV is useful when the lungs need support but the heart is still functioning properly, and VA is useful when both the heart and lungs are not functioning currently and the entire system needs to be bypassed. Because of the nature of VA ECMO, there is a high risk of ischemia in the lower extremities since the heart is not adequately pumping blood throughout the body [3]. There is also a risk of the left ventricle of the heart continuing to pump out deoxygenated blood to the brain and upper extremities while the ECMO delivers oxygenated blood to the lower extremities. This can cause hypoxia in the brain and upper body.

ECMO is most commonly used as a bridge to transplant in patients with a failing heart, failing lungs, or both [4]. VV ECMO is used as a bridge to lung transplant as the heart is still functioning properly, and VA ECMO is used as a bridge to heart transplant and occasionally heart-lung transplants. This is a vital procedure that can make it possible for a patient to live long enough to receive donor lungs or a donor heart even if their own organs have already failed to an irreparable point. ECMO is also considered more desirable than a ventilator because it allows the patient to be ambulatory and perform physical therapy which increases the survival and recovery rates of organ transplants.

The current standard of care utilizing ECMO and the limitation associated with it:

ECMO is used to treat both respiratory and heart failure but it is not often the first line of defense against these afflictions. There are a multitude of treatments for both respiratory and heart failure that include medications, surgical procedures, and mechanical intervention. While these treatments are important first steps, they are often not able to fully resolve the underlying pathology or stop disease progression. There are also situations in which a patient is not eligible for a certain treatment due to various risk factors or health conditions. These situations are where a more extreme option, such as ECMO, might be an option to consider.

Intervention for heart and lung failure often begins with pharmacological treatments and therapies including angiotensin-converting enzyme (ACE) inhibitors and beta-blockers for heart failure and neuromuscular blockers (NMB) and systemic corticosteroids for respiratory failure [5][6]. These drugs have the primary purpose of enhancing the function of their respective target and treating the symptoms of organ failure, but are very unpredictable since each body responds differently to certain medications. As of right now, there are no specific drugs available to treat or prevent Acute Respiratory Distress Syndrome (ARDS), only to treat the symptoms and promote lung function [6]. Allergies and tolerance contribute heavily to the varying impact of certain medications in different patients [5]. Another type of treatment for heart and lung failure involves mechanical support devices such as implantable cardioverter defibrillators (ICDs) and cardiac resynchronization therapy (CRT) for heart failure and a ventilation machine for respiratory failure [5][6]. These machines are great for treatment but are very limited in their functions and can cause other conditions to arise. Cardiac devices are often limited to specific arrhythmias or conduction delays so they can not treat other conditions as they occur [5]. Ventilation can cause barotrauma and ventilator-associated pneumonia (VAP) to occur in patients that are on it for an extended period of time [6]. It is commonly agreed that the best treatment for end-stage heart or respiratory failure is a full organ transplant from a compatible deceased organ donor; however, there is a very limited supply of donor organs available so this is not always an option. This is where bridge transplant therapies, including ECMO, are helpful to extend the life of the patient until such an organ becomes available.

ECMO is a very useful procedure in the treatment of heart and lung failure, but it is not without its faults. Complications such as ischemia in the lower extremities, cerebral hypoxia, and bleeding are often seen in the usage of ECMO [3][7]. With ECMO there are also risks of hemolysis, coagulation disorders, and infection in prolonged use. Another area in which ECMO machines fall short is their hindrance of the patient's mobility. Due to the sheer size of ECMO machines, it is hard for a patient undergoing ECMO therapy to be ambulatory while connected to the machine. A critically ill patient confined to bed rest can result in significant muscle weakness which is commonly referred to as ICU acquired weakness (ICU-AW) [8]. ICU-AW is thought to be caused by a combination of lack of muscle use and increased inflammatory processes although the full extent of the cause is not fully understood. A full recovery from ICU-AW can take 1-2 years and there are some patients that experience permanent loss of muscle strength and function [8]. ECMO is an extremely useful tool and a life-saving intervention, but the mobility limitations, the risks associated with it, and the resources required to utilize it highlight the need for technological innovation in order to increase the patient outcomes and the quality of life while waiting for transplant.

Innovation for the design of ECMO:

Studies have shown that active mobilization while still in the ICU had no effect on patient mortality but did improve muscle strength, bodily ability, and activate participation in patients that received it [8]. This shows that mobility is extremely important for patients residing in the ICU. Although there is always a safety risk when it comes to ambulatory therapy in chronically ill patients , studies focused around mobilization in the ICU have shown that there is only a 2.6% chance of potentially unsafe events from mobility intervention and only a 0.6% chance of consequence from said events [9]. Both of these findings show that mobilization of patients in the ICU is not only safe but recommended for optimal recovery after transplant surgery. The problem with patient mobilization before heart or lung transplant is oftentimes the patient is connected to an ECMO machine. ECMO machines are large machines that make patient mobilization difficult because of their size. If there was an ECMO machine designed and manufactured on a smaller scale, ambulatory patients would have a much easier time moving around and would therefore be able to more easily reap the benefits of mobilization while still residing in the ICU.

Even though there have been many innovations in extracorporeal technology, the components of ECMO circuits have remained largely unchanged since the widespread development of them in the 1980s [10]. The technology that has developed since then could be very beneficial when applied to the ECMO circuit design currently in place. An ECMO machine incorporating a hollow fiber oxygenator and a remote mounted centrifugal pump was tested in vivo in a sheep model [10]. When this test was performed, there was no evidence of the oxygenator failing, no plasma leak observed, and no visual evidence of blood clotting. This study is very promising for the future of miniaturizing ECMO devices to allow for patient mobilization while in the ICU. Since the device was tested successfully in an ovine test subject, a claim could be made that the device would also be successful in a human patient.

The ECMO circuit used in the sheep study had a 70% reduction in priming volume when compared to a standard ECMO circuit meaning that 70% less solution is needed to prime the ECMO circuit before it is connected to the patient [10]. Additionally, since the size of the device is smaller than a standard ECMO machine, the surface area that the blood would come into contact with would be lesser and therefore the risk of blood clotting would be reduced [10]. This claim is supported by the design for a miniature long-term extracorporeal gas exchange device that was approved in Europe in 2009 [11]. The design of this device significantly decreased the anticoagulation that the system required by incorporating a smaller surface area, a plasma-resistant membrane, and a heparin coating.

A study using the device was performed from April 2006 to December 2008 where it was implemented into 60 patients with severe lung failure [11]. Out of the 60 patients, 58 of them met the requirements to be diagnosed with ARDS. The devices were connected using the veno-venous configuration in all 60 cases. In each patient, the device was utilized after standard ventilation treatment or prone positioning was used and failed to effectively treat the condition. 37 of the 60 patients that the device was administered to were able to be weaned from the device [11]. 10 of the weaned patients died later in the ICU. The survival rate after 30 days was 52% and 45% of the patients survived until they were discharged from the hospital. Even though the results were not optimal, they provide strong proof of concept and demonstrate the viability of the miniaturized ECMO system as a bridge to transplant solution.

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