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ORIGINAL ARTICLE

# ECMO: The next ten years

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**KEYWORDS**

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**Abstract** Extracorporeal support (ECMO) is indicated in severe heart or lung failure with 80% risk of mortality. In experienced centers, overall survival to discharge ranges from 40% in cardiac arrest (ECPR) to 70% for respiratory failure in adults, 80% in children and newborns with prolonged ECMO support, severe lung injury can recover to normal function, re-defining irreversible lung injury. In the future ECMO will be automatically controlled with care out of ICU or at home.


ECLS (ECMO) has been standard care for newborn infants and children with heart and lung disease since 1990, and for adults with cardiac and respiratory failure since 2009 [1]. There are currently over 70,000 cases in the ELSO Registry. 28,271 of these cases are newborn infants with respiratory failure [2]. 14,851 of these cases are patients managed with ECMO for severe respiratory failure in the pediatric (6929) and adult (7922) age groups [2]. The balance is cardiac support in children and adults. The survival (hospital discharge) for adults with severe respiratory failure in the last 5 years is 60%. The indications for ECLS are 80% risk of mortality, measured by appropriate parameters for each diagnosis and age group. Since the first cases in the early 70s until 2005, ECMO circuits were assembled on-site from a variety of devices. Despite the variation in devices, the technology was relatively standardized. Patients were deeply sedated, anticoagulated with heparin titration, and regular efforts were made at lung recruitment (often resulting in barotrauma and pneumothorax). Bleeding was the major complication. ECMO was often terminated on day 14, 21, 30 because the lung failure appeared permanent and irreversible. Transplantation was not an option. This era is referred to as ECMO 1.

Major changes in the technology occurred in 2008 with entire ECMO systems being developed by the Maquet, Sorin, and Novalung companies in Europe [3–5]. The Maquet devices were available in the United States in 2009. The new devices resulted in much safer, simpler, prolonged management of extracorporeal support and have led to a much wider use of ECMO in respiratory failure. Prior to 2009 there were fewer than 100 cases per year, and survival varied widely because of the small numbers in each diagnostic group. With the new devices there have been hundreds of cases each year and survival stabilized at about 60%. Improved devices have also resulted in a change in patient management emphasizing minimal sedation, spontaneous breathing, and active physical therapy. Bleeding is still the most common complication but is manageable. Lung recovery occurs regularly after as much as 1 or 2 months of minimal or even no lung function [6,7]. Consequently, "irreversible" lung failure is being re-defined. Bridging to lung transplantation is now a routine with ambulatory ECMO [8]. We refer to this era as ECMO 2. Patient management in ECMO 1 and ECMO 2 is demonstrated in Fig. 1.

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| ECMO I, 1980-2008 | ECMO II, 2009-2017 | ECMO III, 2018- 20?? |
|---|---|---|
| Sedation, paralysis | Awake, spontaneous breathing | Awake, ambulatory |
| Intubated | Tracheostomy, extubate | Extubated |
| Rest vent settings | CPAP | Off vent |
| Specialist 24-7 | ICU Nurse,<br>ECMO team support | Conventional care, weeks<br>Home, months |
| Lung recruitment | Watch and wait | Spontaneous breathing |
| Bleeding:major | Bleeding : minor | No anticoagulation |

**Figure 1** Patient care during ECMO, 3 eras.

ECMO for cardiac support requires the venoarterial (VA) mode of access. VA includes right atrial and systemic artery cannulation, often done urgently during ECPR. Unique problems are perfusion to the distal leg when femoral artery access is used: left atrial venting if there is no cardiac function, and differential circulation if lung failure coincides with cardiac failure treated by femoral perfusion. VA perfusion is short (3–6 days) because the heart often recovers quickly, or not at all (about 10–20%). When there is no heart recovery in a day or two the patient should be converted to a VAD and considered for transplant. The overall survival from cardiac support is 30–50%. Many cases sustain irreversible brain injury prior to ECMO.

ECMO for respiratory failure in adults and older children is usually managed by venovenous (VV) access [9]. In VV access, blood is drained from the right atrium or SVC and IVC, and reinfused into the right atrium. This access puts the artificial lung in series with the normal lungs rather than in parallel (as in CPB or VA ECMO). The well-oxygenated infusion blood mixes with the native venous return (which did not pass through the ECMO circuit) so the resultant arterial $PO_2$ and saturation represents a mixture of the oxygenated extracorporeal blood and the unoxygenated venous blood which passes through the nonfunctional native lungs. This desaturated arterial blood combined with the normal cardiac output provides more than adequate systemic oxygen delivery to support metabolism, and the airway is managed at rest settings. With VV access the patient is reliant on his or her own hemodynamics, so cardiac output, pulmonary and systemic vascular resistance are unchanged during extracorporeal gas exchange.

## Selective $CO_2$ removal

Membrane lungs are much more efficient at transferring $CO_2$ than adding oxygen. This is because the inlet minus outlet difference for oxygen is limited to around 5 $ccO_2$/dL, but inlet/outlet difference for $CO_2$ can be as high as 15–20 cc/dL. For this reason a large amount of $CO_2$ can be removed at much lower blood flow than what is required for oxygenation. Selective $CO_2$ removal in adults can be achieved with relatively low extracorporeal flows (500–1000 cc/min). Gattinoni reported a series of ARDS patients managed with extracorporeal $CO_2$ removal (ECCOR) in 1986 [10]. The technique of selective $CO_2$ removal has been investigated many times since that original publication. Selective $CO_2$ removal is ideal for the management of status asthmaticus and for COPD in exacerbation. It is currently being studied again for ARDS, with the intention of minimizing airway pressure and allowing oxygenation by insufflation into the airway. Although devices are being marketed specifically for $CO_2$ removal, any infant or pediatric system is fine for $CO_2$ clearance in adults.

## Bridge to lung transplantation

In the past the requirement for ECMO was considered a contraindication to transplantation because the patients were in severe primary respiratory failure and became wasted and frail with the heavy sedation and paralysis. With the advent of ECMO 2 bridge to transplantation has become routine practice [8]. In fact, a patient listed for transplantation who is admitted for an exacerbation (formerly removed from the transplant list) can now be managed with ECMO using double lumen venovenous access, minimizing or eliminating sedation, and encouraging ambulation, nutrition and physical therapy, thus improving the status of the patient for subsequent transplantation [11].

## ECMO in the next 10 years

### *Vascular access*

VA access using the femoral vessels is the method of choice for adults for cardiac support. VV access is preferred for respiratory failure. Currently, most venovenous access is achieved with the use of a double lumen catheter, draining blood from the vena cavae and right atrium and returning it to the right atrium, aiming the return infusion toward the tricuspid valve and right ventricle [12]. This approach will continue in the future with variations of the method of placement, imaging during placement, and new double lumen catheters. However there will always be a need for two-catheter venovenous access, draining from the femoral vessels and reinfusing into the right atrium. This technique can be accomplished very quickly at the bedside in an unstable patient, does not require radiographic imaging, and is the most reliable way to quickly establish venovenous access. When access is established in emergency situations in this fashion the cannulation is changed after a day or two to double lumen catheter via the jugular vein. This allows removal of the femoral venous catheter and facilitates ambulation.

### *The ECMO circuit*

The next generation of ECLS pumps will emphasize automation and servo regulation, such that the desired extracorporeal flow is set and the pump will automatically achieve that flow despite a variety of conditions of the patient (coughing, activity, blood volume). In similar fashion, the arterial blood saturation will be used to servo regulate the flow with calculations comparing systemic oxygenation to extracorporeal flow and mixed venous saturation built into the program so that the desired arterial saturation will be reached automatically or, if it cannot be reached, a proposed solution will be displayed. Current membrane lungs are primarily square resulting in stagnation and thrombus formation in the corners. The next generation of devices will be round in all dimensions to minimize stagnation and thrombosis. The blood flow required