EMERGING TECHNOLOGY REVIEW

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Extracorporeal Membrane Oxygenation for Treating Severe Cardiac and Respiratory Disease in Adults: Part 1—Overview of Extracorporeal Membrane Oxygenation

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EXTRACORPOREAL MEMBRANE OXYGENATION (ECMO) is mechanical support of the lungs and/or heart for a period of days to weeks by a modified heart-lung machine. There are 2 basic types of ECMO: venovenous (VV), which provides support for the lungs only, and venoarterial (VA), which provides support for both the heart and the lungs. VV ECMO is primarily used for treating severe but potentially reversible respiratory failure, and VA ECMO is primarily used for treating severe cardiac or cardiorespiratory failure. Because VA ECMO may be used as a bridge to a longer form of mechanical support or to a heart transplant, the underlying cause of the cardiac failure need not necessarily be reversible.

The Extracorporeal Life Support Organization (ELSO, www.elso.med.umich.edu/), based in Ann Arbor, MI, provides an important source of information on the indications for, outcomes from, and complications of ECMO. ELSO is an international consortium of health care professionals from over 100 medical centers that maintains a database, develops guidelines, and produces an annual report. Data from the 2008 annual report[1] are widely quoted in this article and summarized in Table 1. ELSO also publishes a textbook called *Extracorporeal Cardiopulmonary Support in Critical Care*,[2] but it is widely known as "the red book"; this is an excellent resource.

ECMO is a well-established therapy in pediatric patients, particularly for treating neonatal respiratory failure; a survival advantage in pediatric patients for ECMO over conventional treatment has been convincingly shown in 4 randomized trials.[3] ECMO is less commonly performed in adults than in pediatric patients and is associated with a lower overall survival (Table 1).[1] However, it is timely to review the role of ECMO in adults for 3 reasons. First, over the last decade, there have been major technological improvements in circuit components that allow ECMO to be performed relatively safely and easily for several weeks. Second, the results of several recent case series[4-7] and 1 randomized trial[8] have shown high survival rates with ECMO in appropriately selected patients. Finally, there is currently a global pandemic caused by a novel influenza type A virus (H1N1). Although the majority of patients infected by H1N1 suffer no major ill effects, a small proportion develop severe respiratory failure.[9] Although firm data are not yet available, in the authors' own experience, the proportion of ventilated intensive care unit (ICU) patients infected with H1N1 influenza who go on to require ECMO is high (up to 5%-10%).

This article is divided into 2 parts. In the first part, the role of ECMO for treating severe respiratory and cardiac failure in adults is reviewed, including the rationale, indications, contraindications, and outcome from ECMO. In the second part, the physiology, technical considerations, and complications of ECMO are discussed.

RATIONALE FOR ECMO

Respiratory Support

The majority of patients who receive ECMO for respiratory failure have acute respiratory distress syndrome (ARDS), which is most commonly caused by severe pneumonia. ARDS is defined according to the American-European Consensus criteria as (1) the ratio of the partial pressure of arterial oxygen (PaO_2) to the fraction of inspired oxygen (F_IO_2) ≤200 mmHg (≤26.7 kPa), (2) the presence of bilateral pulmonary infiltrates on the chest radiograph, and (3) the absence of raised left atrial pressure.[10] Causes of ARDS are listed in Table 2.[11]

Treatment of ARDS in the 1960s through the 1980s consisted of positive-pressure ventilation (PPV) with high tidal volumes (≥10 mL/kg), high peak inflation pressures (≥40 cmH_2O), and no or low levels of positive expiratory pressure (PEEP). It is now known that this ventilatory strategy exacerbates lung injury, in part because of alveolar overdistention and shearing injury from repetitive opening and closing of the alveoli.[12,13] By contrast, limiting the tidal volume to ≤6 mL/kg

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Table 1. Cumulative Outcome From Extracorporeal Life Support (1985-January 2008) Reported by the ELSO[1]

	Total Patients	Survived ECLS (%)	Survived to Discharge or Transfer (%)
Neonatal (<1 year)			
Respiratory	21,916	85	76
Cardiac	3,266	58	38
ECPR	354	63	38
Pediatric (1-16 years)			
Respiratory	3,693	64	56
Cardiac	4,036	61	45
ECPR	691	51	39
Adult (>16 years)			
Respiratory	1,416	59	51
Cardiac	825	46	33
ECPR	269	36	26

Abbreviation: ECLS, extracorporeal life support; ELSO, Extracorporeal Life Support Organization; ECPR, extracorporeal cardiopulmonary resuscitation.

to keep the plateau airway pressure ≤30 cmH_2O limits alveolar damage and improves mortality in patients with ARDS.[14] This approach, known as lung protective ventilation, is typically combined with other ventilatory strategies, such as a decelerating inspiratory flow pattern (pressure control ventilation), high levels of PEEP (10-20 cmH_2O), a long inspiratory time, and recruitment maneuvers, in an effort to limit lung injury and improve oxygenation.[15] An alternative ventilatory strategy that may be considered is high-frequency oscillation ventilation,[16] although a survival benefit for this therapy in adults has not been convincingly shown.[17,18]

Nonventilatory strategies that are used for treating ARDS include prone positioning,[19] fluid restriction,[20] and inhaled nitric oxide. Inhaled nitric oxide improves gas exchange but has not been shown to increase survival in adults with ARDS, and its routine use is not recommended.[21]

The majority of patients with ARDS who die do so from sepsis or multiple organ dysfunction and not from respiratory failure.[11,14] However, there are a proportion of patients with severe ARDS who, despite optimal conventional treatment, undergo progressive respiratory (or cardiorespiratory) failure and die, even though their underlying lung disease is potentially reversible. By 1 estimate, this amounts to 350 patients per year in the United Kingdom,[22] which equates to 1,750 patients per year in the United States. In this circumstance, ECMO provides a period of respiratory and, if necessary, cardiac support to maintain life while allowing lung rest to minimize ventilator-induced lung injury.

Cardiac Support

ECMO is also an appropriate therapy in selected patients with life-threatening heart failure. Cardiac ECMO is typically used as an emergency rescue therapy, most commonly for failure to wean from cardiopulmonary bypass (CPB) and after a myocardial infarction or cardiac arrest. Options for mechanical cardiac support in this circumstance are either VA ECMO or a ventricular assist device (VAD). The choice depends on patient requirements (single or biventricular failure with or without respiratory failure) and institutional experience. Similar results have been obtained for both forms of support.[23,24] However, potential advantages of ECMO over a VAD are as follows: (1) both ventricles and the lungs are supported by a single circuit; (2) avoidance of a sternotomy, which may result in less bleeding (if peripheral cannulation is used); (3) patients can be decannulated without the need for further surgery (if peripheral cannulation is used); and (4) ECMO is cheaper and can be more rapidly instituted. VA ECMO is a particularly useful form of support when the patient's neurologic state is unknown after a cardiac arrest. If, after several days, cardiac function remains poor but neurologic recovery is good, the patient may be transferred to a longer-term VAD while he/she awaits a heart transplant. This strategy provides rational use of an expensive resource.

HISTORY AND EVIDENCE FOR ECMO

Technical Developments

ECMO, as a bedside technique performed in the ICU, was developed as an extension of CPB used in the operating room during cardiac surgery. The most important technical innovation that has facilitated ECMO has been the development of durable, efficient oxygenators that are associated with minimal blood trauma.

The first oxygenators to be used clinically were film oxygenators, in which multiple vertical discs rotate through a pool of venous blood, and bubble oxygenators, in which oxygen is bubbled through a column of deoxygenated blood.[25,26] A major problem with these devices is the presence of a direct blood-gas interface, which contributes to intravascular hemolysis, platelet destruction, systemic inflammation, and microemboli formation. An important step was the introduction of membrane oxygenators, in which a membrane separates the blood and gas phases, thus allowing CPB to be maintained for longer than a few hours without inducing massive blood trauma. Membrane oxygenators were developed in the 1950s[27,28] but were not introduced into clinical practice until the 1980s. From the 1980s through the early 2000s, most ECMO centers used either silicone membrane or polypropylene hollow fiber oxygenators.[29] Although these oxygenators are vastly superior to bubble and disc oxygenators, both have significant limitations with

Table 2. Clinical Disorders Associated With the Development of ARDS[11]

Direct Lung Injury	Indirect Lung Injury
Common causes	Common causes
Pneumonia	Sepsis
Aspiration of gastric contents	Severe trauma with shock and multiple blood product transfusions
Less common causes	Less common causes
Pulmonary contusion	Cardiopulmonary bypass
Fat emboli	Drug overdose
Near drowning	Pancreatitis
Inhalation injury	Transfusion-related acute lung injury
Reperfusion injury after lung transplantation or pulmonary embolectomy	