



RESEARCH ARTICLE

Effectiveness of Extracorporeal Membrane Oxygenation in Adults

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Abstract

Background: With patients for whom it is difficult or near impossible to maintain adequate oxygenation by conventional means, it may become necessary to oxygenate the blood outside the body. One method used with moderate success is the procedure of extracorporeal membrane oxygenation (ECMO). The purpose of this study was to determine the effectiveness of ECMO in adult patients suffering from conditions associated with respiratory failure that is refractory to conventional means of treatment.

Methods: A systematic review of available studies was utilized to answer the earlier research questions. Reputable research journals were combed for articles pertaining to ECMO use in adult, pediatric, and neonatal populations and their effectiveness. Included in this study were articles that met the eligibility criteria. Relevant information was summarized and applied to the research questions.

Results: Ten Studies were identified for analysis (3 neonatal, 3 pediatric, and 4 adult). Each study showed a benefit in survivability from the use of extracorporeal life support (ECLS) in conditions of respiratory failure that was deemed refractory to conventional means of treatment. The Extracorporeal Life Support Organization (ELSO) registry contained the most comprehensive data, with the neonatal population being the most robust, followed by the pediatric and adult populations respectively. Neonatal indications for ECLS administration were less difficult to reverse than are adult conditions.

Conclusion: Though not as effective as the pediatric and neonatal populations, adult ECLS was still determined to have some effectiveness. The indication or diagnosis played a significant role in the utilization and effectiveness of ECLS. Complications associated with the use of ECLS were of great concern for all patient populations. The adult population had a higher incidence of infection, cannula site bleeding, and surgical site bleeding than neonatal and pediatric populations. As the technology continues to evolve and the practice of ECLS use in adults continues to progress and increase, there is a potential to realize increasing effectiveness.

Introduction

With patients for whom it is difficult or near impossible to maintain adequate oxygenation by conventional means, it may become necessary to oxygenate the blood outside the body [1]. One method used with moderate success is the procedure of extracorporeal membrane oxygenation (ECMO) [1]. Oxygenation of blood outside the body through a membrane oxygenator was first developed for use in open-heart surgery in the 1950s [1]. The technology continued to improve, and modifications allowed long-term use of the technique in the 1960s [1]. The first use of the extracorporeal membrane oxygenator on an infant was done and described in 1971, paving the way for perfection and refinement of the technique [1].

As centers gathered experience and ECMO systems improved, applications expanded, including pediatric and adult patients with respiratory and cardiac failure [2]. The hospital survival rates with these applications have not been as favorable as were those with the early neonatal experience. However, the populations are more heterogeneous and include many diagnoses and comorbidities [2]. Nonetheless, survival rates such as 50-60% for pediatric and adult respiratory failure and 30-40% in ECMO cardiopulmonary resuscitation (CPR) support the use of ECMO beyond its proven niche [2]. Today ECMO is used in many institutions across the country.

Significance of the Research

ECMO has proven benefits when used in neonatal and pediatric populations. The use of ECMO in the adult population has traditionally been limited. Recent evidence suggests that ECMO may positively impact

survival in adult patients with refractory respiratory failure [3]. Refractory respiratory failure is a set of terms synonymous with acute respiratory distress syndrome (ARDS). ARDS is associated with high mortality and morbidity in adults. More facilities utilize ECMO to treat patients when conventional ventilation modes fail with each passing year. In addition to ARDS, ECMO has begun to establish a role in managing other disease processes such as sepsis and CPR [4].

Some reports demonstrate survival > 70% in some circumstances for patients requiring ECMO for refractory respiratory failure [3]. The LUNG SAFE study shows that about 3% of invasively ventilated patients with ARDS received ECMO, including almost 7% with severe ARDS [5]. Though the expansion of ECMO use in more facilities has been an ongoing trend, it is still primarily used as a “rescue” therapy. The earlier implementation of ECMO may be beneficial as a lung-protective strategy and may increase its effectiveness.

Purpose of the Study

The purpose of this study was to determine the effectiveness of ECMO in adult patients suffering from conditions associated with respiratory failure that is refractory to conventional means of treatment. The associated hypotheses were:

- ECMO is effective in adults with more than 50% surviving to discharge.
- ECMO is more effective than conventional means of mechanical ventilation in patients suffering refractory respiratory failure.
- ECMO in adults has similar efficacy when compared to neonatal and pediatric populations.

Literature Review

ECMO is a form of cardiopulmonary life-support separated into two types, veno-venous (VV) or veno-arterial (VA). With VV ECMO, blood is drained from a central vein, passed through an oxygenator, and pumped back into the patient’s venous system [3]. ECMO does not fix the underlying lung issues of the patient or any other disease processes. It is simply a means of allowing the lungs to rest and recover. When adequate gas exchange can be realized with no substantial compromise of cardiac function, VV ECMO is often the preferred approach over VA ECMO due to its generally lower risk of complications [3]. Patients with respiratory failure refractory to conventional mechanical ventilation have the potential of being supported by way of VV ECMO as a mechanism to enhance gas exchange while avoiding toxic ventilator settings and allowing for the minimization of ventilator-induced lung injury (VILI).

Regarding VA ECMO, blood is removed from a central vein in a manner analogous to VV ECMO. However, it is

returned to the arterial system, generally via the carotid artery in neonates and children and the femoral artery in adults [3]. VA ECMO is essentially cardiopulmonary bypass for a period of days to weeks and is highly effective at both oxygenation and ventilation [3]. VA ECMO oxygenates the blood and supports the patient’s cardiac function by returning blood to the aortic arch by the ECMO machine [1]. In cardiac and pulmonary compromise cases, VA ECMO is the preferred method.

In the mid-1980s, the application of ECMO in newborns with severe respiratory failure gained a footing when fewer than a dozen ECMO centers became established [2]. Inclusion and exclusion criteria were established, and ECMO became an essential option in caring for newborns with severe respiratory failure unresponsive to conventional measures [2]. ECMO has been commonly used in neonatal ICUs to treat respiratory failure due to primary pulmonary hypertension of the newborn, meconium aspiration syndrome, persistent fetal circulation, congenital diaphragmatic hernia, and other reversible lung diseases. This yielded survival rates of > 80% for all neonates cost-effectively, except those with congenital diaphragmatic hernia [6]. Around the early 1990s, the use of ECMO in newborns began to decline due to the introduction of high-frequency oscillatory ventilation (HFOV), surfactant replacement therapy, and inhaled nitric oxide. As a result of these advancements, the treatment algorithm for respiratory failure in newborns was recalibrated, with ECMO used more in a rescue manner [2].

Pediatric ECMO therapy is used routinely in pneumonia, ARDS, and pulmonary hemorrhage patients. The best data supporting its use in the pediatric population come from a multicenter, retrospective cohort of 331 patients from 32 hospitals from the Pediatric Critical Care Study Group [6]. The study showed that ECMO reduced mortality due to disease from 47% to 26% [6]. More recently, a survival rate of 60 to 73% in 128 children, depending on the cause of the respiratory failure [6]. Pediatric ECMO cases started levelling off in 1994, likely due to improvements in open-lung strategies for treating severe hypoxemic respiratory failure [6].

Methods

The purpose of this study was to determine the effectiveness of ECMO in adult patients suffering from conditions associated with respiratory failure that was refractory to conventional means of treatment. A systematic review of available studies was utilized to answer the earlier research questions. Reputable research journals were combed for articles pertaining to ECMO use in adult, pediatric, and neonatal populations and their effectiveness. Included in this study were articles that met the eligibility criteria. Relevant information was summarized and applied to the research questions [7].

The eligibility criteria for the systematic review were:

1. The Articles were published in reputable journals.
2. The articles measured the effectiveness of ECMO in adult, pediatric or neonatal populations.
3. The articles measured the effectiveness of ECMO versus conventional means of treatment.
4. The patients in the studies suffered from a disease process that caused refractory respiratory failure excluding COVID-19.
5. The articles had defined criteria for when ECMO use was initiated.
6. The articles performed that appropriate statistical analysis.
7. The articles could not be sponsored by industry-sponsored or industry conducted.
8. The articles were required to be in the English language.

Results

The Extracorporeal Life Support Organization (ELSO) registry collects data on the use of extracorporeal life support (ECLS) use and outcomes [8]. From reviewing other studies and journals articles, ELSO appeared to be the gold standard for information pertaining to ECLS. The ELSO report analyzed patients from its inception (1989) through the calendar year of 2015 [8]. Members of the ELSO used standardized collection forms to report data [8]. Data collected included demographic information, pre-ECLS illness severity and support, diagnosis and procedures, ECLS indication, equipment used for ECLS support, details of ECLS course, ECLS complications, and survival to hospital discharge or another facility from the ECLS center [8].

The registry classified a neonate as \leq 30-days-old, pediatric from 31 days to \leq 18 years of age, and an adult $>$ 18-years-old [8]. At the time of the report, the registry contained 78,397 patients from 310 ELSO member centers [8]. The ELSO registry report was separated into three sections for each patient category, with the three sections being respiratory, cardiac, and ECLS to support cardiopulmonary resuscitation (ECPR) [8]. The number of neonatal patients suffering from a respiratory disease process was 29,153, and of that number, 24,488 (84%) survived ECLS, with 21,545 (74%) being discharged [8].

Pertaining to the pediatric population, the number of respiratory patients was 7,552, with 5,036 (67%) surviving ECLS and 4,371 (58%) being discharged [8]. The adult population had a more significant number of respiratory-related patients at 10,601 [8]. From that amount of patients, 6,997 (66%) survived ECLS, and 6,121 (58%) were discharged [8]. The results displayed that the neonatal population had a higher survival rate and discharge rate than adult and pediatric patients.

The adult and pediatric populations had similar levels of survival and discharge rate, which were markedly lower than the neonatal population.

A Cochrane review of ECLS for severe respiratory failure in newborn infants was completed using all randomized trials comparing neonatal ECMO to conventional ventilatory support (Mugford, Elbourne, & Field, 2010). The Cochrane Neonatal Group Specialized Register, the Cochrane Controlled Trials Register, and MEDLINE were searched from 1974 to 2007, and 4 trials (three USA and one UK) recruited clinically similar groups of neonates [9]. The results showed that out of a total of 116 neonatal patients, 65 (56%) died before being discharged to home when given conventional ventilator support equating to a survival rate of 44% [9]. Neonates that received ECLS amounted to 128 patients, with only 29 (23%) dying before being discharged to home, yielding a survival rate of roughly 77% [9].

A study from the Journal of Critical Care Medicine examined the relationship between hospital ECMO annual volume and in-hospital mortality and assessed if a minimum hospital volume could be recommended [10]. The study was retrospective and used information from patients admitted to children's hospitals in the Pediatric Health Information System database from 2004-2011 supported with ECLS [10]. The age range was 0 to 18 years of age [10]. Observing the neonatal population (0 to 30 days of life) showed a total of 4,414 neonates receiving treatment in this time frame with 2,498 surviving, yielding a survival rate of roughly 57% [10].

An article by Raman and Dalton found that roughly 56% of pediatric ECMO patients with respiratory failure survive [4]. A retrospective study of 331 patients from 32 hospitals showed that ECMO reduced pediatric mortality by 47 to 26% [6]. Furthermore, Swaniker, et al. reported a survival range of 60 to 73% for pediatric patients suffering from refractory respiratory failure [11], with these results dependent upon the cause of the respiratory failure [6].

A Journal of Pediatric Surgery study was conducted on ECLS outcomes for 128 pediatric patients with respiratory failure. The timeframe was from 1985 to 1998, with the median age being 1.4 years (2 weeks to 17 years of age) [11]. Results showed that 71% (91) of the patients survived [11].

A five-year study on 85 adults receiving ECLS after CPR showed that 47% of the patients successfully weaned from ECLS, with 34% surviving until hospital discharge [12]. A study comparing survival with and without extracorporeal life support treatment for severe poisoning due to drug intoxication in adults showed that 12/14 (86%) of ECLS patients survived [13]. In comparison, 23/48 (48%) non-ECLS patients survived with the study sample size at 62 adult patients

(39 women, 23 men; mean age 48 ± 17 years) [13]. A study from the *Annals of Surgery* Journal retrospectively reviewed ECLS use in adult patients suffering from acute severe respiratory failure in 100 patients [14]. Results showed an overall hospital survival of 54% [14].

Physicians at the Taiwan National University Hospital conducted an observational study with a 3-year time frame, with patients ages 18-75 on CPR with assisted ECLS versus conventional CPR in adults with in-hospital cardiac arrest [15]. The study consisted of 975 patients with in-hospital cardiac arrest events who underwent CPR for longer than 10 minutes, 113 were enrolled in the conventional CPR group, and 59 were enrolled in the extracorporeal CPR group [15]. Results showed 17 patients in the extracorporeal group (28.8%) and 14 patients (12.3%) in the conventional group survived to discharge [15].

Discussion

As stated earlier, ECMO has proven benefits when used in neonatal and pediatric populations. The use of ECMO in the adult population had traditionally been limited. Recent evidence suggests that ECMO may positively impact survival in adult patients with refractory respiratory failure [3]. Conventional means of mechanical ventilation will not aid in treating disease processes that have caused moderate to severe respiratory failure. The ELSO registry contains the most robust findings for ECLS for neonatal, pediatric, and adult patients. The registry showed that 58% of adults were discharged [8]. This percentage carried more weight than the other adult ECLS data due to the sheer number of adult patients who survived hospital discharge (6,121) [8]. Calculation of the various study survival averages of adult ECLS patients that survived until discharge yielded an average of roughly 52%, supporting the hypothesis that ECMO is effective in adults. Patients administered ECLS usually are mechanically ventilated, though there are instances of patients ambulating on ECLS while not being mechanically ventilated [4]. The mechanical ventilator settings used while a patient is administered ECMO are very minimal and vary widely [4].

The goal is for the lungs to rest and heal while the patients are receiving ECLS. Furthermore, conventional mechanical ventilation is currently the gold standard when treating patients exhibiting refractory respiratory failure. ECMO is a last-ditch effort utilized when a patient fail to respond to conventional mechanical ventilation. As stated in the results, a study on the comparison of survival with and without extracorporeal life support treatment for severe poisoning due to drug intoxication in adults showed 86% of ECLS patients survived compared to 48% for non-ECLS patients [13]. The study of CPR assisted with ECLS by physicians at the Taiwan National University Hospital showed 28.8% of patients from the ECLS group survived compared to 12.3% of patients from the conventional group [15].

These results, as mentioned earlier, support ECMO being more effective than conventional mechanical ventilation in patients with refractory respiratory failure. Calculating averages from the results section for each patient population found adult ECLS for refractory respiratory failure is effective roughly 52% of the time. Pediatric patients had an effectiveness of 65%, while the neonatal population had an effectiveness of 69%, disproving the hypothesis that ECMO is just as effective when compared to neonatal and pediatric populations.

Conclusion

This study was conducted to answer the general question of effectiveness when using ECLS in the adult population for refractory respiratory failure. Though not as effective as the pediatric and neonatal populations, adult ECLS administration was effective. The indication or diagnosis played a significant role in the utilization and effectiveness of ECLS. For instance, the most common indications for ECLS in the neonatal population were meconium aspiration syndrome (MAS), persistent pulmonary hypertension of the newborn (PPHN), and congenital diaphragmatic hernia (CDH) [8]. Adult diagnoses of pneumonia (aspiration, bacterial, and viral) and ARDS were some of the most common indications for ECLS administration [8]. Neonatal indications for ECLS administration were less difficult to reverse than are adult conditions [8]. Primarily for adults, comorbidity factors, age, and the degree of non-pulmonary organs dysfunction played a role in ECLS outcomes and translated to decreased effectiveness compared to neonatal and pediatric populations [3].

Complications associated with the use of ELSC are of great concern for all patient populations. The adult population had a higher incidence of infection, cannula site bleeding, and surgical site bleeding than neonatal and pediatric populations [3]. ECLS is effective in adults with refractory respiratory failure despite the increasing complexity and comorbid conditions and the lack of consistent data, ECLS initiation structure, familiarity, treatment costs, and clear management guidelines [3]. As the technology continues to evolve and the practice of ECLS use in adults continues to progress and increase, there is a potential to realize increasing effectiveness if the barriers as mentioned earlier are mitigated.

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