Extracorporeal Membrane Oxygenation (ECMO)/Extracorporeal Carbon Dioxide Removal ($ECCO_2R$)

10

Nicole Lena Werner and Pauline K. Park

Introduction

Extracorporeal membrane oxygenation (ECMO) is a means of supporting severe pulmonary and cardiac dysfunction. It stabilizes critical derangements of oxygenation and ventilation, allowing time to diagnose, treat, and recover from the underlying cause of organ failure. This technology was first successfully employed by Hill et al. [1] in 1972, who used it to support an injured patient who developed acute respiratory distress syndrome (ARDS). This was quickly followed by successful use of ECMO for cardiogenic shock (1973) and newborn respiratory failure (1975) [2]. Since that time, the technology has matured and been validated as an effective therapy [3]. It is currently used in more than 200 centers around the world to care for over 4,500 neonatal, pediatric, and adult cases per year (Fig. 10.1) [4].

Physiologic Basis of Therapy

Extracorporeal support is employed to guarantee adequate oxygen delivery and carbon dioxide clearance to meet systemic needs. Oxygen delivery (DO_2) is a function of arterial oxygen content (CaO_2) and cardiac output (CO) (Eq. 10.1). Arterial oxygen content, measured in mL/min, is dependent upon the hemoglobin concentration (Hgb), its oxygen saturation percentage (SaO_2), and the partial pressure of the oxygen dissolved in the plasma (PaO_2) (Eq. 10.2). Mathematical review of this equation reveals that oxygen content is largely driven by hemoglobin concentration in contrast to the amount of oxygen dissolved in plasma.

$$CaO_2 = 1.34 * Hgb * SaO_2 + 0.003 * PaO_2 \quad (10.1)$$

$$DO_2 = CaO_2 * CO \quad (10.2)$$

Normal adult human oxygen consumption (VO_2) is 3–5 mL/kg/min. It is decreased by rest, paralysis, and hypothermia and increased with activity, infection, and hyperthermia. It is dependent on tissue metabolism and is independent of the oxygen supply until the supply is very low.

At rest, oxygen delivery is normally five times the oxygen consumption. As consumption changes, normal homeostasis measures attempt to keep this ratio fixed and respond by altering the cardiac output. When compensation fails and the DO_2:VO_2 ratio falls to 2:1, there is increased oxygen extraction, which is evidenced by decreased venous oxygen saturation (SvO_2).

Carbon dioxide production is a by-product of tissue metabolism and is approximately equal to the oxygen consumed per minute. The normal amount of CO_2 dissolved in plasma ($PaCO_2$) is 40 mmHg. The body adjusts the depth and rate of breathing to keep this value constant. Excretion of CO_2 is an efficient process compared to oxygenation and in many cases is achieved even in the setting of severe oxygenation dysfunction.

The Circuit

Components

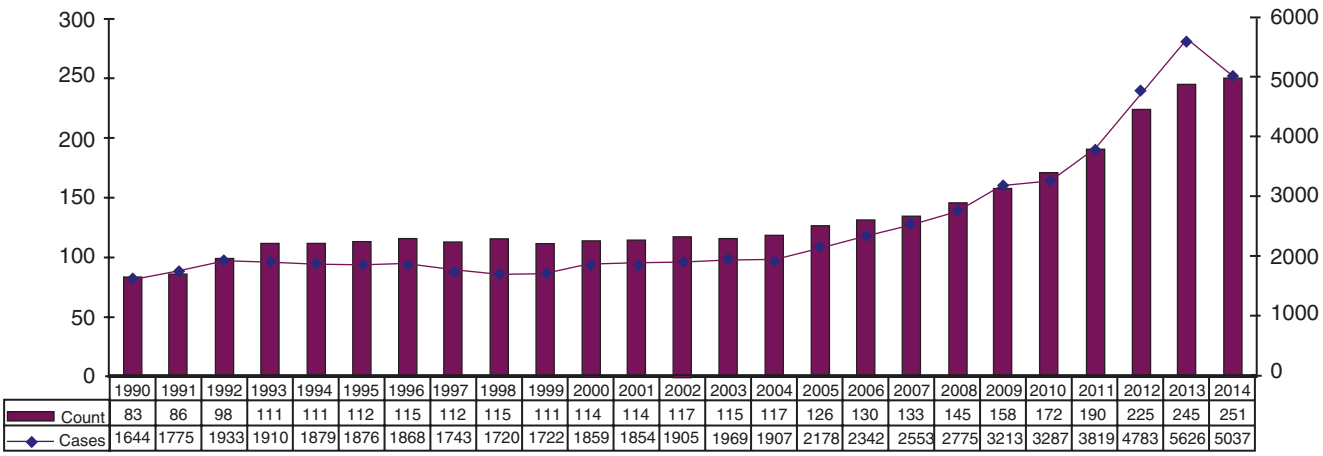
Three main components make up the extracorporeal cardiopulmonary support circuit:

1. Large-bore cannulae and circuit tubing to provide access to the native circulation
2. An artificial membrane lung to provide gas exchange
3. An active pump, either roller pump or centrifugal pump, to facilitate perfusion

N.L. Werner, MD, MS
Department of Surgery, University of Michigan Health System, Ann Arbor, MI 48109, USA
e-mail: niwerner@med.umich.edu

P.K. Park, MD (✉)
Division of Acute Care Surgery, Department of Surgery, University of Health System, Ann Arbor, MI 48109, USA
e-mail: parkpk@umich.edu

N.D. Martin, L.J. Kaplan (eds.), *Principles of Adult Surgical Critical Care*, DOI 10.1007/978-3-319-33341-0_10



	1990	1991	1992	1993	1994	1995	1996	1997	1998	1999	2000	2001	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011	2012	2013	2014
Count	83	86	98	111	111	112	115	112	115	111	114	114	117	115	117	126	130	133	145	158	172	190	225	245	251
Cases	1644	1775	1933	1910	1879	1876	1868	1743	1720	1722	1859	1854	1905	1969	1907	2178	2342	2553	2775	3213	3287	3819	4783	5626	5037

Fig. 10.1 The number of ECMO centers and annual cases over time as voluntarily reported to the Extracorporeal Life Support Organization registry (From www.ELSO.org, accessed June 2015)

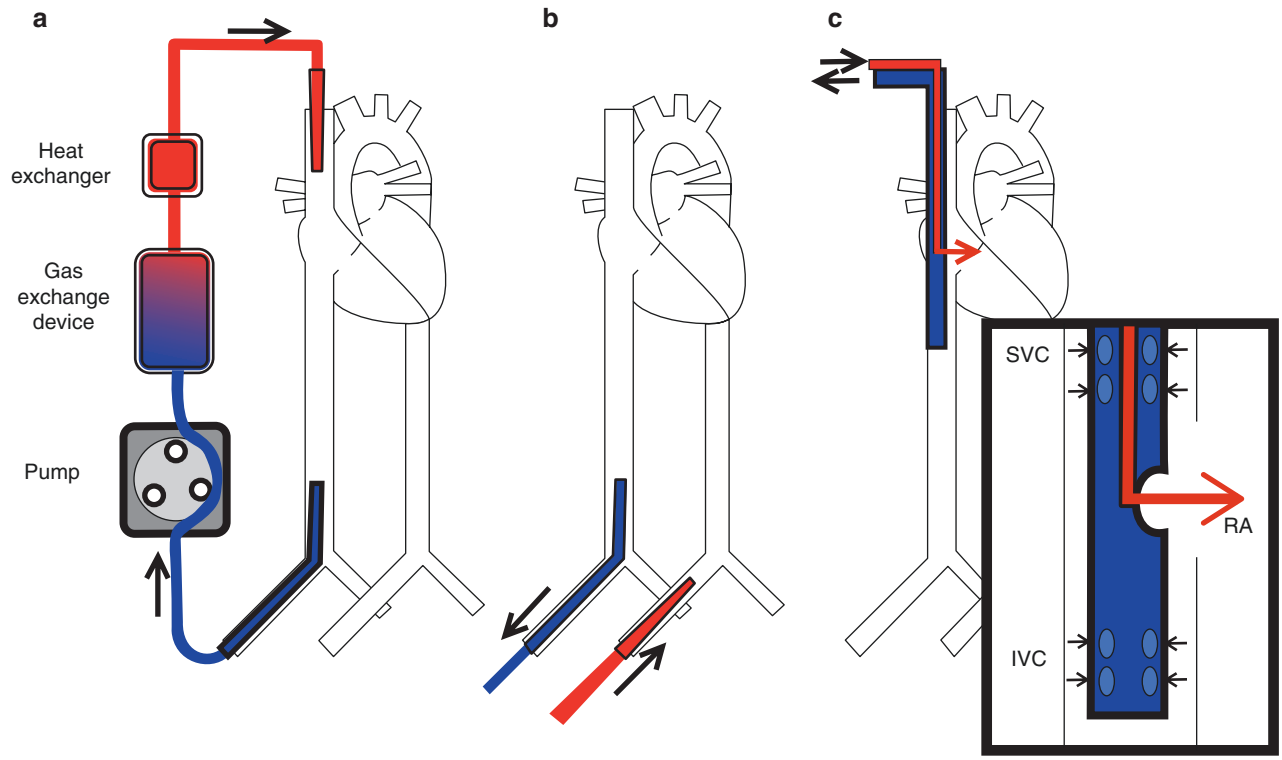


Fig. 10.2 (**a**) Venovenous ECMO support. This circuit drains deoxygenated blood from the femoral vein that is then taken through a pump, gas exchange device, and heat exchanger before returning the oxygenated blood to internal jugular vein. (**b**) Venoarterial ECMO via the femoral vessels. Blood is drained from the femoral vein and, after going through the ECMO circuit, is returned into the femoral artery in a retrograde fashion. (**c**) Venovenous support with a double lumen cannula. Insert shows drainage occurs from both the superior vena cava (*SVC*) and inferior vena cava (*IVC*), while infusion is directly into the right atrium (*RA*)

A schematic of common extracorporeal circuit configurations (venovenous, venoarterial, and single-cannula venovenous) is shown in Fig. 10.2.

Cannulae come in a variety of designs and sizes, but are typically made of polyurethane. Double lumen cannulae have been developed (Fig. 10.2c) that drain from both the superior and inferior vena cava and reinfuse into the right atrium with only a single access site. Cannulation can be performed percutaneously or via cutdown, with percutaneous access being more common. When selecting a drainage cannula for the circuit, the largest appropriate internal diameter should be chosen. This is to maximize flow, which increases by a power of four with increases to the internal radius. In general, 60–80 mL/kg/min of blood flow is needed for

supporting for hypoxemia. Central cannulation of the great vessels is performed in some cases when cervical or femoral access is not possible; it also is utilized for patients that have failed to wean from cardiopulmonary bypass [5].

The gas exchange device, also known as the membrane lung or oxygenator, is the core of the circuit. The patient's deoxygenated blood is distributed onto membrane surfaces, on the other side of which sweep gas flows past; the membrane surface allows for gas exchange between the two flows via diffusion. Oxygenation is increased by increasing blood flood through the device. Carbon dioxide clearance, however, is a function of sweep gas flow: increased sweep gas flow rates remove more CO_2 from the blood. Typically 100% oxygen is chosen as the sweep gas. Increases or decreases in sweep gas rate do not affect oxygenation except at extremely low sweep rates because of the efficiency of the membrane surfaces.

There are two types of pumps that are commonly employed in the extracorporeal circuit, the roller pump and the centrifugal pump. The roller pump is simple in concept; it creates a positive displacement on the circuit tubing, forcing blood forward. It carries a risk of circuit rupture if there is an occlusion downstream of the pump. The centrifugal pump, in contrast, utilizes an impeller design that is coupled with an electric motor to generate flow in a nonocclusive manner that cannot over-pressurize, but can have heating in the pump head that leads to thrombus formation. An important characteristic of all active circulatory drivers is that excessive negative pressure placed on the drainage catheter increases the risk of endothelial damage or air entrapment. While neither type of pump has been shown to be superior to the other [6], the smaller, lighter design footprint of centrifugal pumps has helped to facilitate patient transport on ECMO.

A heat exchanger is often used to maintain normal patient temperature, as blood in the extracorporeal circuit is exposed to ambient temperatures and there is risk of unintentional core cooling. Some companies have combined a heat exchange device with the gas exchange device into a single unit.

Configurations

Naming convention for extracorporeal support is based on the routes by which blood is drained and returned to the corporeal circulation. Venovenous (VV) support refers to venous drainage and venous reinfusion, whereas venoarterial (VA) is configured to reinfuse blood via an artery. VV ECMO support places the circuit in series with the native lung, allowing for total or partial respiratory support. In contrast, in VA ECMO support, the circuit is in parallel with the native lung and heart and allows for both pulmonary and cardiac support.

Pumpless arteriovenous (AV) [7, 8] ECMO takes advantage of native cardiac output to propel blood through the oxygenator, accepting lower flow rates than those achievable with an external pump. Sufficient support of severe hypoxia may not be feasible, but, because of the greater diffusibility of carbon dioxide, satisfactory ventilation with $ECCO_2R$ can be accomplished [9]. Access is most frequently obtained through the femoral artery and femoral vein.

Patient Selection

Patients with acute, potentially reversible, life-threatening respiratory or cardiac dysfunction refractory to conventional therapy are potential candidates for ECMO support. Respiratory support can be considered for hypoxemic respiratory failure, hypercarbic respiratory failure, or as a temporary means to bridge-to-lung transplantation. As a respiratory support modality, ECMO is most appealing for its potential to reduce or eliminate the injurious effects of positive pressure mechanical ventilation. It can minimize or, in some cases, replace mechanical ventilation while maintaining gas exchange, allowing for "lung rest." Cardiac support is used in acutely decompensated patients, including those with persistent shock despite volume administration, inotropes, and vasoconstrictors, failure to wean from cardiopulmonary bypass (postcardiotomy), acute myocardial infarction, and acute myocarditis. ECMO has also emerged as a temporary bridging strategy until cardiac recovery or implementation of definitive therapy such as ventricular assist devices or transplant.

There are no absolute contraindications to ECMO, as each patient should be considered individually with respect to the risks and benefits [7]. There are conditions known to be associated with poorer outcomes and thus are considered to be relative contraindications: mechanical ventilation at a high setting for 7 days or more, major pharmacologic immunosuppression, CNS hemorrhage that is recent or expanding, non-recoverable comorbidity such as terminal malignancy, or baseline advanced organ failure without options for potential salvage or transplantation.

Supporting Literature

Hypoxemic Respiratory Failure

ECMO was adopted into standard neonatal and pediatric practice because of the success of early trials [8, 10]. In contrast, the initial two randomized trials of ECMO support in adult respiratory failure conducted in the 1970s and 1980s failed to show advantage over conventional therapy [11, 12]. These negative results restricted the use of ECMO to a few centers, which continued to find benefit in ECMO support when conventional measures had failed [13–17]. Brogan et al. [18] published a summary report from the Extracorporeal Life Support Organization (ELSO) registry, which included 1,473 adult

patients who received ECMO for respiratory failure between 1986 and 2006. This series had a median patient age of 34 years, median PaO_2/FIO_2 ratio of 57, and overall survival of 50 %. It was not until 2009, when a third randomized controlled clinical trial, the Conventional Ventilation or ECMO for Severe Adult Respiratory Failure (CESAR) trial [19], was published. This study found a survival advantage for patients referred to a specialized center using a treatment protocol that included ECMO compared to those treated at alternate tertiary care centers (63 % survival without severe disability at 6 months versus 47 %). The study has been criticized, as only 75 % of patients randomized to the ECMO group actually received ECMO and because of lack of a control group receiving standardized mechanical ventilation and ICU care [20]. Nonetheless, it remains the single modern randomized trial available.

In 2009, the H1N1 influenza pandemic renewed the interest of ECMO for respiratory failure. Investigators from Australia-New Zealand described their experience treating suspected or confirmed influenza A patients and reported patient survival of 75 % [21]. Noah et al. [22] reported the UK experience in 80 patients who were referred to the national H1N1 ECMO service. The median age was 36.5 years, the median PaO_2/FIO_2 ratio was 54.9, and the overall survival was 72.5 %. They matched their patients with patients enrolled in a concurrent Swine Flu Triage study who were not referred for ECMO and found the relative risk of death was 0.45–0.51 in the ECMO-referred patients compared with the non-ECMO-referred patients. A severe H1N1 cohort from Utah, however, reported equivalent survival (83 %) without the use of ECMO, calling into question the necessity for invasive therapy [23].

Looking forward, additional controlled trials have been initiated. The Extracorporeal Membrane Oxygenation for Severe Acute Respiratory Distress Syndrome (EOLIA) trial is an international, multicenter effort begun in 2011 that is comparing survival between rapid initiation of ECMO (within 3–6 h of optimal medical management) to standard low tidal volume ventilation for moderate to severe ARDS patients. A second study, Strategies for Optimal Lung Ventilation in ECMO for ARDS (SOLVE) study, is a pilot trial evaluating mechanical ventilation strategies while on VV ECMO for ARDS. It is anticipated that this study will provide insight into the ventilator-induced lung injury that may occur despite ECMO support.

Hypercarbic Respiratory Failure

Research on extracorporeal carbon dioxide removal ($ECCO_2R$) has primarily focused on hypercarbia occurring in the setting ARDS and lung-protective ventilation. Starting in the 1980s, Gattinoni showed that venovenous $ECCO_2R$ with minimal ventilator settings resulted in lower mortality in an observational study of ARDS patients [24]. Subsequent work was initially reassuring [25] but a randomized control trial in 1994 revealed no survival advantage to this technique [12]. The incidence of device-related complications was high in this study, with clotting seen in 20 %, resulting in discontinuation of therapy. Improvement in circuits and oxygenator design prompted continued $ECCO_2R$ study. Bein et al. used a pumpless system in a series of 90 ARDS patients and achieved rapid normalization of carbon dioxide levels, but most patients required vasopressors to support blood minimum flow through the device and 10 % developed lower limb ischemia [26]. A follow-up randomized trial (Xtravent Study) using $ECCO_2R$ combined with very low tidal volume mechanical ventilation (3 cc/kg) showed improvements in the overall complication rate (8 %) but failed to demonstrate advantage for $ECCO_2R$ in ventilator free days [27]. The SUPERNOVA (Strategy of UltraProtective lung ventilation with Extracorporeal CO2 removal for New Onset moderate to severe ARDS) study will further investigate the value of $ECCO_2R$ in ARDS mortality, morbidity, and ability to reduce ventilator-induced lung injury and is planned to start in 2015.

$ECCO_2R$ use for adult airway disease has not been studied as extensively as ARDS, although the potential population that could benefit from this application is large. Small studies have shown that $ECCO_2R$ may have a role in asthma exacerbations [28] and may avoid or replace ventilation in acute exacerbations of COPD [29, 30]. In a stimulating pilot study, $ECCO_2R$ facilitated both early extubation and ambulation in COPD exacerbations requiring mechanical ventilation [31].

Bridge-to-Lung Transplant

The use of ECMO as a temporary destination therapy for patients with chronic lung disease awaiting transplantation is controversial. The concept is founded by evidence that mechanically ventilated patients prior to transplant have worse survival after lung transplant [32]. Retrospective observation studies using ECMO as a bridge to transplant have been mixed [33–36]. The largest of these was based from the UNOS database and found pretransplant ECMO use resulted in higher rates of retransplantation and was a predictor of mortality posttransplant [35]. Nonetheless, the implication is that many of these patients would have otherwise died without the opportunity to receive an allograft.

Recently there has been a focus on managing ECMO patients awake and spontaneously breathing. This management strategy avoids the complications and drawbacks associated with sedation, intubation, and long-term ventilation, thereby decreasing infectious risk, increasing mobility and strength from being able to participate in physiotherapy, and ability to consume enteral feeds. This strategy has been applied to bridge to transplant patients and appears to have better outcomes.

Fuehner reported a single center experience and found awake ECMO recipients had a higher likelihood of survival at 6 months and shorter posttransplant ventilator course when compared to historical ventilator controls [37]. Furthermore, limited data suggests the survival of these patients may be equivalent to non-supported transplant patients [38].

Cardiac Failure

VA ECMO is one of many therapies available that provide mechanical support for acute cardiac failure. There have not been any controlled trials, however, comparing VA ECMO to other temporizing therapies (intra-aortic balloon pump [IABP] or temporary ventricular assist devices) but several observational studies have shown possible benefit. For patients with acute myocardial infarction, when VA ECMO was combined with coronary revascularization, there appeared to be a survival benefit at 30 days and 1 year compared to those temporized with IABP alone [39, 40]. Favorable survival has also been observed when the cause of failure is fulminant myocarditis [41, 42], sepsis-induced cardiomyopathy [43, 44], and pulmonary-embolism-induced cardiac failure [45]. VA ECMO also provides support for postcardiotomy cardiogenic shock until myocardial recovery or definitive therapy, but mortality in this cohort remains high (67–75%) [5, 46]. ECMO as a bridge to cardiac transplant has been described but has worse survival than those bridged with ventricular assist devices [47]. Larger, randomized trials are needed for this application of ECMO to support its routine application.

VA ECMO has also been used to restore circulation in patients with ongoing cardiac arrest, a strategy known as extracorporeal cardiopulmonary resuscitation (ECPR). The basis for this application is to improve cardiopulmonary support during the resuscitation period prior to emergent myocardial revascularization. Although it has yet to be studied in a randomized fashion, observational studies appear promising [48–50]. One study reported an almost doubled survival of in-hospital cardiac arrest patients resuscitated with ECPR compared to standard CPR (33% vs. 17%) [48]. Some evidence also suggest there may be reduced neurological injury with ECPR patients [50], which is a devastating and common complication in cardiac arrest survivors.

Management of ECMO

Patient Management

The primary goal of ECMO is to permit time for treatment of the underlying lung and cardiac injury; reversible causes should be sought and promptly treated. Supportive ICU therapy should continue concurrently for all patients. Neuromuscular blockade and sedation may be weaned as tolerated. In some cases, commonly the bridge-to-lung transplant setting, ECMO is performed in awake and spontaneously breathing patients. Ventilator settings are managed at low settings to allow for lung rest. Some have advocated for extubation of these awake patients [37]. Hemodynamics often improve after beginning ECMO support, allowing the discontinuation of vasopressors. Fluid shifts and blood product consumption may persist for variable periods, thought to be secondary to blood exposure to the nonbiologic extracorporeal circuit [51, 52]. Continuous renal replacement therapy to assist with volume management can be used concurrently with ECMO, with the dialyzer incorporated directly into the ECMO circuit.

Pharmacokinetics are affected by the ECMO therapy. The circuit increases the overall volume of distribution and many medications are known to adhere to circuit components [53]. The kinetics may additionally be modified by acute kidney injury or continuous renal replacement therapy. Sedation and antibiotic therapies seem to be appreciably affected and often require increased dosing [54]. When available, drug-level monitoring should be performed to ensure adequate dosing and avoidance of toxicity or subtherapeutic concentrations.

Surgical procedures from venipuncture to liver transplantation can be done with success while on extracorporeal support; however, the hemorrhage risk may be substantial. The absolute necessity of every procedure should be questioned to minimize the risk to the patient. Even small procedures, including tube thoracostomy, should be performed with liberal use of electrocautery. When an operation is necessary, anticoagulation may be held and even cautiously reversed, taking into consideration the risk of thromboembolic events and acute, life-threatening circuit failure.

Circuit Management

The extracorporeal circuit can be adjusted to meet gas exchange needs. Oxygenation is primarily proportional to the blood flow rate and the surface area of the membrane lung; it is managed by titrating pump speed. Oximetric measurements from the drainage limb of the circuit may be used as a surrogate for mixed venous saturation and thus provide a measure of the adequacy of oxygenation. In VV ECMO, this measure may be falsely elevated by recirculation (oxygenated blood from the reinfusion cannula crossing directly into the drainage limb rather than entering the right heart). In VA ECMO, oxygenated blood returns retrograde through the aorta so flow dynamics must be monitored closely to ensure adequate cerebral perfusion. The native cardiac circulation may exceed circuit flow, causing only the lower half of the body to be perfused, which is referred to as the Harlequin or North-South syndrome. The retrograde flow may also result

in significant venous admixture and lowered arterial oxygen saturations. In these cases, a high hematocrit target has been advocated to maintain oxygen delivery in the face of relative hypoxemia. Ventilation is managed by titrating the sweep gas flow through the membrane lung. CO_2 clearance can be accomplished at lower blood flow rates, permitting the use of lower flow arteriovenous ECMO or extracorporeal CO_2 removal for patients with hypercarbia.

Systemic anticoagulation is required to prevent circuit clotting. The ideal goal and the best method of anticoagulation monitoring are not known. Regular monitoring of platelet levels is recommended; platelet consumption at the oxygenator interface may necessitate regular platelet transfusion to prevent thrombocytopenia in the anticoagulated patient. Hemolysis can also occur and free hemoglobin should be checked daily. Values greater than 10 mg/dL require further investigation to identify the cause of hemolysis. Circuit-related hemolysis is caused by cavitation that occurs when blood is exposed to significant negative pressure or repeated cycles of transient low flow, known as "line chatter" [55].

Weaning is the strategic decrease in extracorporeal support to assess if a patient can be sustained without it. In VV ECMO, a slow, systematic decrease in circuit flow, sweep rate, or a combination of the two is initiated while monitoring for adequate oxygenation and ventilation. Lung recruitment may be necessary if substantial collapse has occurred. The patient should be monitored for signs of pulmonary fibrosis that may have developed while on ECMO support. This presents as pulmonary hypertension and right-sided heart failure and is fatal. In weaning VA ECMO, the flows are decreased while simultaneously assessing tissue-level perfusion. Echocardiography is used to assess native cardiac function. Inotropes, vasotropes, and vasodilators are typically necessary and their use does not equate to an unsuccessful wean. Trialing is the process of temporarily discontinuing ECMO after the patient has been weaned to less than 30 % of native heart or lung function. Cannulae are removed 24 h after a successful trial off of support.

A concern for futility of treatment should be raised if a patient has been placed on ECMO but the therapy appears to be ineffective or if there is no evidence of recovery. The duration of time after which this determination should be made is unknown and thresholds are rapidly evolving. Historically, respiratory survival was felt to be poor after 2 weeks [56] and cardiac survival after 5 days [57]. More recently, patients have been sustained on prolonged ECMO support [58] and data from the ELSO registry suggest that even after 14 days of support, while survival rates are lower than in shorter runs, they have improved to 48 % over the period from 2007 to 2013 [74]. The potential for late pulmonary recovery is also not known, and the decision to discontinue support for futility should be periodically reevaluated by a multidisciplinary team.

Multidisciplinary Team

A dedicated institutional infrastructure is mandatory for safe ECMO practice. A multidisciplinary team approach to caring for ECMO patients is necessary for the best outcomes [59]. This team includes physicians, nurses, respiratory therapists, pharmacists, dieticians, and care coordinators. Many centers have elected to have a dedicated ECMO team member stationed at the bedside to supervise the circuit who works along side with the bedside nurse providing direct patient care. As ECMO circuits continue to become simpler and easier to manage, the bedside care model will likely continue to evolve, and careful attention must be paid to workload and safety considerations, including alarm fatigue.

The increased use of ECMO in adult patients has led to a proliferation of centers and has brought renewed focus on considerations of training, credentialing, optimal practice, and regionalization of service. A recent position paper on the organization of ECMO programs for adult acute respiratory failure encouraged practice in centers with sufficient experience volume and expertise to ensure safe use [60]. Interpretation of individual center outcomes must be carefully considered; with the absence of clear consensus indications for ECMO, survival reporting is prone to bias from patient selection. Nevertheless, age-specific volume outcome relationships have been demonstrated in registry studies of neonatal and adult, but not pediatric populations [61].

Outcomes

Survival

ECMO has a reported survival of 55 % when used for respiratory support and 40 % for cardiac support [62]. Mortality is associated with many factors including advanced patient age, pre-ECMO arterial pH, increased duration of pre-ECMO ventilation, decreasing patient weight, underlying cause of respiratory failure, the presence of complications, gender, and the initial PaO_2/FiO_2 ratio [13, 18]. To help practitioners stratify the risk of ECMO for individuals with respiratory failure, the Respiratory ECMO Survival Prediction (RESP) score has been developed [63]. This score uses 12 pre-ECMO variables to determine a probability of survival after ECMO (Table 10.1). Unfortunately, no similar score for cardiac failure patients has been developed. A key caveat in using prognostic scores for patient selection is that as they are derived from selected cohorts consisting only of patients who received ECMO, the corresponding outcomes of similar patients who did not receive ECMO cannot be considered.

Table 10.1 RESP score for risk stratification of respiratory failure patients

Parameter		Score
Age, yr		
18–49		0
50–59		−2
≥60		−3
Immunocompromised status*		−2
Mechanical ventilation prior to initiation of ECMO		
<48 h		3
48 h to 7 day		1
>7 day		0
Acute respiratory diagnosis group (select only one)		
Viral pneumonia		3
Bacterial pneumonia		3
Asthma		11
Trauma and burn		3
Aspiration pneumonitis		5
Other acute respiratory diagnoses		1
Nonrespiratory and chronic respiratory diagnoses		0
Central nervous system dysfunction†		−7
Acute associated (nonpulmonary) infection‡		−3
Neuromuscular blockade agents before ECMO		1
Nitric oxide use before ECMO		−1
Bicarbonate infusion before ECMO		−2
Cardiac arrest before ECMO		−2
$PaCO_2$, mm Hg		
<75		0
≥75		−1
Peak inspiratory pressure, cm H_2O		
<42		0
≥42		−1
Total score		−22 to 15
Hospital survival by risk class		
Total RESP score	*Risk class*	*Survival*
≥ 6	I	92 %
3–5	II	76 %
−1 to 2	III	57 %
−5 to −2	IV	33 %
≤−6	V	18 %

Reprinted with permission of the American Thoracic Society. Copyright © 2016 American Thoracic Society. Schmidt et al. [63]
ECMO extracorporeal membrane oxygenation; *RESP* Respiratory ECMO survival prediction; An online calculator is available at www.respscore.com.
* hematological malignancies, solid tumor, solid organ transplantation, human immunodeficiency virus, and cirrhosis.
† diagnosis combined neurotrauma, stroke, encephalopathy, cerebral embolism, and seizure and epileptic syndrome.
‡ another bacterial, viral, parasitic, or fungal infection that did not involve the lung.

Complications

Complications are a common occurrence in patients supported with ECMO and are associated with increased mortality [18]. Hemorrhage is the most frequently cited complication, occurring in approximately 30–40 % of patients [3, 64]. Cannula sites, surgical sites, and the airway are the most common hemorrhage locations. Hemorrhage on ECMO is managed supportively by transfusing blood products and platelets, decreasing or temporarily discontinuing anticoagulation, and, on occasion, administering antifibrinolytics. The risk of circuit dysfunction, thrombus formation, and embolus must be weighed against the risk of bleeding [65]. Infection is another commonly reported complication. Infection risk has been correlated to the duration of ECMO support [66], but routine surveillance with cultures, however, has not shown to add value, improve outcomes, and is therefore not recommended [67]. Limb-threatening ischemia has been observed in approximately 17 % of cases when the femoral artery is cannulated for VA support. Perfusion of the distal extremity with retrograde posterior tibial catheters or antegrade percutaneous femoral catheters [68] may permit limb salvage while leaving the cannula in situ; however, amputation rates are estimated at 5 %.

Equipment-related failures also contribute to patient complications. While much work has been done to mature extracorporeal technology, circuit failures (rupture, clotting) are estimated to occur in 2–20 % of patients [18]. Oxygenator run time rates vary widely and are a significant contributor to equipment-related complications.

Long-Term Outcomes

Data on long-term outcomes for patients supported with ECMO is limited. Reports on this topic have focused on the pediatric population and on adult ARDS patients. In pediatrics, survivors are reported to have normal lung function and normal growth at an older age, but neurodevelopment problems are often noted [69]. In the adult studies, many had ongoing pulmonary symptoms but these symptoms were less than those of similar but conventionally treated patients [70, 71]. The symptoms, as well as degree of lung fibrosis, appeared to correlate with the duration of ECMO support. Additionally, approximately three quarters of survivors were able to return to their former occupations. Further research in this area remains a priority.

Future Applications

Individual centers continue to apply ECMO technology in unique and innovative ways. Investigations in the areas of ARDS, COPD, resuscitation, and inter-facility transport continue. In transplantation, one such approach is extracorporeal support-assisted organ donation after cardiac death. ECMO has been initiated after pronouncement of death to restore

perfusion of abdominal organs in hopes of improving organ quality [72] and potentially increasing the number of organs available for transplantation. Additionally, researchers have used ECMO in ex situ perfusion of individual organs. The most progress has been made with pretransplant pulmonary perfusion; human lungs donated for transplant have been supported with a modified ECMO circuit for up to 6 h and then successfully transplanted [73]. Further research will be necessary before this technology becomes routinely incorporated into practice.

Conclusion

ECMO remains a promising lifesaving therapy for critically ill adults in acute pulmonary and cardiac failure who have failed conventional management. Since it was first described in the 1970s, its use has grown rapidly and more liberal application has been considered. The components of the circuit have greatly matured, making the therapy more reliable and practical to implement. Complications are still common, and thus further advances, particularly in circuit thromboresistance to reduce the need for anticoagulation, will be critical in minimizing the inherent risks of ECMO therapy. Increased use has also spurred further considerations of optimal practice, credentialing, and regionalization of practice. Additional randomized trials are needed to clarify the appropriate indications and best practices for this lifesaving therapy.

Additional Resources

The Extracorporeal Life Support Organization (ELSO) is an international consortium of healthcare professionals and scientists devoted to the development of life support therapies. ELSO has developed a Web site that contains a member list with contacts, management guidelines [7], references, and training and education materials on ECMO: http://www.elso.org.

References

1. Hill JD, et al. Acute respiratory insufficiency. Treatment with prolonged extracorporeal oxygenation. J Thorac Cardiovasc Surg. 1972;64(4):551–62.
2. Bartlett RH, et al. Extracorporeal membrane oxygenation (ECMO) cardiopulmonary support in infancy. Trans Am Soc Artif Intern Organs. 1976;22:80–93.
3. Peek GJ, et al. Efficacy and economic assessment of conventional ventilatory support versus extracorporeal membrane oxygenation for severe adult respiratory failure (CESAR): a multicentre randomised controlled trial. Lancet. 2009;374(9698):1351–63.
4. Paden ML, Rycus PT, Thiagarajan RR. Update and outcomes in extracorporeal life support. Semin Perinatol. 2014;38(2):65–70.
5. Rastan AJ, et al. Early and late outcomes of 517 consecutive adult patients treated with extracorporeal membrane oxygenation for refractory postcardiotomy cardiogenic shock. J Thorac Cardiovasc Surg. 2010;139(2):302–11, 311 e1.
6. Saczkowski R, et al. Centrifugal pump and roller pump in adult cardiac surgery: a meta-analysis of randomized controlled trials. Artif Organs. 2012;36(8):668–76.
7. ELSO. Extracorporeal Life Support Organization Patient Specific Guidelines. A supplement to the ELSO General Guidelines (November 2013) [cited 2015; Version 1.3]. Available from: http://www.elso.med.umich.edu/Guidelines.html.
8. Bartlett RH, et al. Extracorporeal circulation (ECMO) in neonatal respiratory failure. J Thorac Cardiovasc Surg. 1977;74(6):826–33.
9. Zimmermann M, et al. Pumpless extracorporeal interventional lung assist in patients with acute respiratory distress syndrome: a prospective pilot study. Crit Care. 2009;13(1):R10.
10. UK collaborative randomised trial of neonatal extracorporeal membrane oxygenation. UK Collaborative ECMO Trail Group. Lancet. 1996; 348(9020):75–82.
11. Zapol WM, et al. Extracorporeal membrane oxygenation in severe acute respiratory failure. A randomized prospective study. JAMA. 1979;242(20):2193–6.
12. Morris AH, et al. Randomized clinical trial of pressure-controlled inverse ratio ventilation and extracorporeal CO2 removal for adult respiratory distress syndrome. Am J Respir Crit Care Med. 1994;149(2 Pt 1):295–305.
13. Hemmila MR, et al. Extracorporeal life support for severe acute respiratory distress syndrome in adults. Ann Surg. 2004;240(4):595–605; discussion 605–7.
14. Mols G, et al. Extracorporeal membrane oxygenation: a ten-year experience. Am J Surg. 2000;180(2):144–54.
15. Lewandowski K, et al. High survival rate in 122 ARDS patients managed according to a clinical algorithm including extracorporeal membrane oxygenation. Intensive Care Med. 1997;23(8):819–35.
16. Beiderlinden M, et al. Treatment of severe acute respiratory distress syndrome: role of extracorporeal gas exchange. Intensive Care Med. 2006;32(10):1627–31.
17. Peek GJ, et al. Extracorporeal membrane oxygenation for adult respiratory failure. Chest. 1997;112(3):759–64.
18. Brogan TV, Thiagarajan RR, Rycus PT, Bartlett RH, Bratton SL. Extracorporeal membrane oxygenation in adults with severe respiratory failure: a multi-center database. Intensive Care Med. 2009;35(12):2105–14. doi: 10.1007/s00134-009-1661-7. Epub 2009 Sep 22. PMID: 19768656
19. Peek GJ, et al. CESAR: conventional ventilatory support vs extracorporeal membrane oxygenation for severe adult respiratory failure. BMC Health Serv Res. 2006;6:163.
20. Morris AH, Hirshberg E, Miller RR, Statler KD, Hite RD. Efficacy of ECMO in H1N1 influenza: sufficient evidence? Chest. 2010;138:778–81.
21. Davies A, et al. Extracorporeal membrane oxygenation for 2009 influenza A(H1N1) acute respiratory distress syndrome. JAMA. 2009;302(17):1888–95.
22. Noah MA, et al. Referral to an extracorporeal membrane oxygenation center and mortality among patients with severe 2009 influenza A(H1N1). JAMA. 2011;306(15):1659–68.
23. Miller RR, Markewitz BA, Rolfs RT, Brown SM, Dascomb KK, Grissom CK, Friedrichs MD, Mayer J, Hirschberg EL, Conklin J, Paine R, Dean NC. Clinical findings and demographic factors associated wtih ICU admission in Utah due to novel 2009 influenza A(H1N1) infection. Chest. 2010;137(4):752–8.
24. Gattinoni L, et al. Low-frequency positive-pressure ventilation with extracorporeal CO2 removal in severe acute respiratory failure. JAMA. 1986;256(7):881–6.

25. Brunet F, et al. Extracorporeal carbon dioxide removal technique improves oxygenation without causing overinflation. Am J Respir Crit Care Med. 1994;149(6):1557–62.
26. Bein T, et al. A new pumpless extracorporeal interventional lung assist in critical hypoxemia/hypercapnia. Crit Care Med. 2006;34(5):1372–7.
27. Bein T, et al. Lower tidal volume strategy (approximately 3 ml/kg) combined with extracorporeal CO2 removal versus 'conventional' protective ventilation (6 ml/kg) in severe ARDS: the prospective randomized Xtravent-study. Intensive Care Med. 2013;39(5):847–56.
28. Elliot SC, et al. Pumpless extracorporeal carbon dioxide removal for life-threatening asthma. Crit Care Med. 2007;35(3):945–8.
29. Burki NK, et al. A novel extracorporeal CO(2) removal system: results of a pilot study of hypercapnic respiratory failure in patients with COPD. Chest. 2013;143(3):678–86.
30. Kluge S, et al. Avoiding invasive mechanical ventilation by extracorporeal carbon dioxide removal in patients failing noninvasive ventilation. Intensive Care Med. 2012;38(10):1632–9.
31. Abrams DC, et al. Pilot study of extracorporeal carbon dioxide removal to facilitate extubation and ambulation in exacerbations of chronic obstructive pulmonary disease. Ann Am Thorac Soc. 2013;10(4):307–14.
32. Singer JP, et al. The impact of pretransplant mechanical ventilation on short- and long-term survival after lung transplantation. Am J Transplant. 2011;11(10):2197–204.
33. Lang G, et al. Primary lung transplantation after bridge with extracorporeal membrane oxygenation: a plea for a shift in our paradigms for indications. Transplantation. 2012;93(7):729–36.
34. Hammainen P, et al. Usefulness of extracorporeal membrane oxygenation as a bridge to lung transplantation: a descriptive study. J Heart Lung Transplant. 2011;30(1):103–7.
35. Mason DP, et al. Should lung transplantation be performed for patients on mechanical respiratory support? The US experience. J Thorac Cardiovasc Surg. 2010;139(3):765–73 e1.
36. Toyoda Y, et al. Efficacy of extracorporeal membrane oxygenation as a bridge to lung transplantation. J Thorac Cardiovasc Surg. 2013;145(4):1065–70; discussion 1070–1.
37. Fuehner T, et al. Extracorporeal membrane oxygenation in awake patients as bridge to lung transplantation. Am J Respir Crit Care Med. 2012;185(7):763–8.
38. Mohite PN, et al. Extracorporeal life support in "awake" patients as a bridge to lung transplant. Thorac Cardiovasc Surg. 2015;63:699–705.
39. Tsao NW, et al. Extracorporeal membrane oxygenation-assisted primary percutaneous coronary intervention may improve survival of patients with acute myocardial infarction complicated by profound cardiogenic shock. J Crit Care. 2012;27(5):530 e1–11.
40. Sheu JJ, et al. Early extracorporeal membrane oxygenator-assisted primary percutaneous coronary intervention improved 30-day clinical outcomes in patients with ST-segment elevation myocardial infarction complicated with profound cardiogenic shock. Crit Care Med. 2010;38(9):1810–7.
41. Asaumi Y, et al. Favourable clinical outcome in patients with cardiogenic shock due to fulminant myocarditis supported by percutaneous extracorporeal membrane oxygenation. Eur Heart J. 2005;26(20):2185–92.
42. Diddle JW, et al. Extracorporeal membrane oxygenation for the support of adults with acute myocarditis. Crit Care Med. 2015;43(5):1016–25.
43. Brechot N, et al. Venoarterial extracorporeal membrane oxygenation support for refractory cardiovascular dysfunction during severe bacterial septic shock. Crit Care Med. 2013;41(7):1616–26.
44. Huang CT, et al. Extracorporeal membrane oxygenation resuscitation in adult patients with refractory septic shock. J Thorac Cardiovasc Surg. 2013;146(5):1041–6.
45. Maggio P, et al. Extracorporeal life support for massive pulmonary embolism. J Trauma. 2007;62(3):570–6.
46. Pokersnik JA, et al. Have changes in ECMO technology impacted outcomes in adult patients developing postcardiotomy cardiogenic shock? J Card Surg. 2012;27(2):246–52.
47. Khan MS, et al. Is mechanically bridging patients with a failing cardiac graft to retransplantation an effective therapy? Analysis of the United Network of Organ Sharing database. J Heart Lung Transplant. 2012;31(11):1192–8.
48. Chen YS, et al. Cardiopulmonary resuscitation with assisted extracorporeal life-support versus conventional cardiopulmonary resuscitation in adults with in-hospital cardiac arrest: an observational study and propensity analysis. Lancet. 2008;372(9638):554–61.
49. Shin TG, et al. Extracorporeal cardiopulmonary resuscitation in patients with inhospital cardiac arrest: a comparison with conventional cardiopulmonary resuscitation. Crit Care Med. 2011;39(1):1–7.
50. Shin TG, et al. Two-year survival and neurological outcome of in-hospital cardiac arrest patients rescued by extracorporeal cardiopulmonary resuscitation. Int J Cardiol. 2013;168(4):3424–30.
51. Halter J, et al. Evidence of systemic cytokine release in patients undergoing cardiopulmonary bypass. J Extra Corpor Technol. 2005;37(3):272–7.
52. Underwood MJ, et al. Changes in "inflammatory" mediators and total body water during extra-corporeal membrane oxygenation (ECMO). A preliminary study. Int J Artif Organs. 1995;18(10):627–32.
53. Noerr B. ECMO and pharmacotherapy. Neonatal Netw. 1996;15(6):23–31.
54. Dagan O, et al. Preliminary studies of the effects of extracorporeal membrane oxygenator on the disposition of common pediatric drugs. Ther Drug Monit. 1993;15(4):263–6.
55. Toomasian JM, Bartlett RH. Hemolysis and ECMO pumps in the 21st century. Perfusion. 2011;26(1):5–6.
56. Masiakos PT, et al. Extracorporeal membrane oxygenation for non-neonatal acute respiratory failure. Arch Surg. 1999;134(4):375–9; discussion 379–80.
57. Mehta U, et al. Extracorporeal membrane oxygenation for cardiac support in pediatric patients. Am Surg. 2000;66(9):879–86.
58. Rosenberg AA, et al. Prolonged duration ECMO for ARDS: futility, native lung recovery, or transplantation? ASAIO J. 2013;59(6):642–50.
59. Oliver WC. Anticoagulation and coagulation management for ECMO. Semin Cardiothorac Vasc Anesth. 2009;13(3):154–75.
60. Combes A, et al. Position paper for the organization of extracorporeal membrane oxygenation programs for acute respiratory failure in adult patients. Am J Respir Crit Care Med. 2014;190(5):488–96.
61. Barbaro RP, et al. Association of hospital-level volume of extracorporeal membrane oxygenation cases and mortality. Analysis of the extracorporeal life support organization registry. Am J Respir Crit Care Med. 2015;191(8):894–901.
62. Paden ML, et al. Extracorporeal life support organization registry report 2012. ASAIO J. 2013;59(3):202–10.
63. Schmidt M, et al. Predicting survival after extracorporeal membrane oxygenation for severe acute respiratory failure. The respiratory extracorporeal membrane oxygenation survival prediction (RESP) score. Am J Respir Crit Care Med. 2014;189(11):1374–82.
64. Cheng R, et al. Complications of extracorporeal membrane oxygenation for treatment of cardiogenic shock and cardiac arrest: a meta-analysis of 1,866 adult patients. Ann Thorac Surg. 2014;97(2):610–6.
65. Murray JF, et al. An expanded definition of the adult respiratory distress syndrome. Am Rev Respir Dis. 1988;138(3):720–3.
66. Steiner CK, et al. Predictors of acquiring a nosocomial bloodstream infection on extracorporeal membrane oxygenation. J Pediatr Surg. 2001;36(3):487–92.
67. Elerian LF, et al. Usefulness of surveillance cultures in neonatal extracorporeal membrane oxygenation. ASAIO J. 2001;47(3):220–3.

68. Rao AS, et al. A novel percutaneous solution to limb ischemia due to arterial occlusion from a femoral artery ECMO cannula. J Endovasc Ther. 2010;17(1):51–4.
69. Ijsselstijn H, van Heijst AF. Long-term outcome of children treated with neonatal extracorporeal membrane oxygenation: increasing problems with increasing age. Semin Perinatol. 2014;38(2): 114–21.
70. Linden VB, et al. ECMO in ARDS: a long-term follow-up study regarding pulmonary morphology and function and health-related quality of life. Acta Anaesthesiol Scand. 2009;53(4):489–95.
71. Schmidt M, et al. The PRESERVE mortality risk score and analysis of long-term outcomes after extracorporeal membrane oxygenation for severe acute respiratory distress syndrome. Intensive Care Med. 2013;39(10):1704–13.
72. Gravel MT, et al. Kidney transplantation from organ donors following cardiopulmonary death using extracorporeal membrane oxygenation support. Ann Transplant. 2004;9(1):57–8.
73. Ingemansson R, et al. Clinical transplantation of initially rejected donor lungs after reconditioning ex vivo. Ann Thorac Surg. 2009;87(1):255–60.
74. Posluszny J, Rycus PT, Bartlett RH, Engoren M, Haft JW, Lynch WR, Park PK, Raghavendran K, Napolitano L. Outcome of Adult Respiratory Failure Patients Receiving Prolonged (≥14 Days) ECMO. Ann Surg. 2016 Mar;263(3):573-81. doi: 10.1097/SLA.0000000000001176.