Extracorporeal Membrane Oxygenation for Adult Respiratory Failure

David A Turner MD and Ira M Cheifetz MD FAARC

Extracorporeal membrane oxygenation (ECMO) is a form of cardiopulmonary bypass that is a mainstay of therapy in neonatal and pediatric patients with life threatening respiratory and/or cardiac failure. Historically, the use of ECMO in adults has been limited, but recent reports and technological advances have increased utilization and interest in this technology in adult patients with severe respiratory failure. As ECMO is considered in this critically ill population, patient selection, indications, contraindications, comorbidities, and pre-ECMO support are all important considerations. Once the decision is made to cannulate a patient for ECMO, meticulous multi-organ-system management is required, with a priority being placed on lung rest and minimization of ventilator-induced lung injury. Close monitoring is also necessary for complications, some of which are related to ECMO and others secondary to the patient's underlying degree of illness. Despite the risks, reports demonstrate survival > 70% in some circumstances for patients requiring ECMO for refractory respiratory failure. As the utilization of ECMO in adult patients with respiratory failure continues to expand, ongoing discussion and investigation are needed to determine whether ECMO should remain a "rescue" therapy or if earlier ECMO may be beneficial as a lung-protective strategy. *Key words: extracorporeal membrane oxygenation; ECMO; respiratory failure; adult; technology.* [Respir Care 2013;58(6):1038–1049. © 2013 Daedalus Enterprises]

Introduction

Extracorporeal membrane oxygenation (ECMO) is an important therapeutic strategy that was developed and first used to support an adult patient with refractory respiratory failure over 40 years ago.[1] Since introduction, ECMO has become a mainstay in the management of neonatal and pediatric patients with refractory respiratory and/or cardiac failure secondary to a wide range of diagnoses, in-

The authors are affiliated with the Division of Pediatric Critical Care Medicine, Department of Pediatrics, Duke Children's Hospital, Duke University Medical Center, Durham, North Carolina.

The authors have disclosed no conflicts of interest.

Correspondence: David A Turner MD, Division of Pediatric Critical Care, Department of Pediatrics, Duke University Medical Center, Box 3046 , Durham NC 27710. E-mail: david.turner@duke.edu.

DOI: 10.4187/respcare.02255

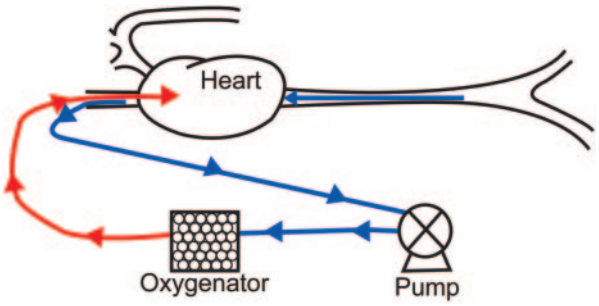

Fig. 1. Diagram of a typical veno-venous extracorporeal membrane oxygenation system. (Adapted from reference 28, with permission.)

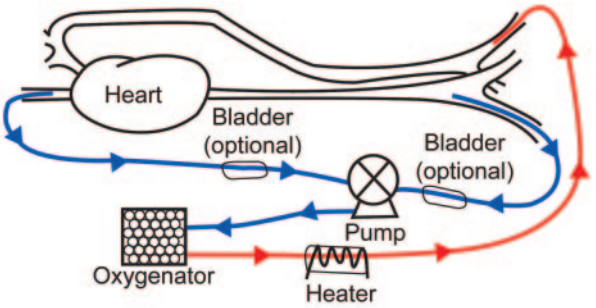

Fig. 2. Diagram of a typical veno-arterial extracorporeal membrane oxygenation system. (Adapted from reference 28, with permission.)

cluding meconium aspiration, pulmonary hypertension, pneumonia, myocarditis, cardiomyopathy, sepsis, and ARDS.[2-7] Despite widespread use in neonates and children, implementation of ECMO in the adult population has traditionally been limited,[8] but recent evidence suggests that ECMO may positively impact survival in adult patients with refractory respiratory failure.[9-16]

Recent reports, along with considerable advances in technology,[17,18] including advanced design double-lumen cannula, "respiratory dialysis," and pumpless veno-arterial extracorporeal gas support devices, have led to steadily increasing utilization of ECMO in adult patients.[8,19-25] Implementation of an adult ECMO program presents unique challenges related to patient selection, including age, weight, comorbid conditions, and degree of organ failure, which necessitate that both the risks and benefits associated with the decision to employ ECMO be carefully considered in each individual patient. While general guidelines are available to guide practitioners, ultimately, individualization and consideration of the specific clinical circumstances are important elements of patient selection and management.[26,27] This comprehensive review will examine the current data supporting the use of ECMO in adults as well as discuss patient selection parameters, complications, and benefits and risks of implementation of this potentially life-saving technology.

ECMO Basics

ECMO is a form of cardiopulmonary life-support, which can be 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 venous system of the patient (Fig. 1).[28] When adequate gas exchange can be achieved and there is no substantial compromise of cardiac function, VV ECMO, due to its generally lower risk of complications, is often the preferred approach over VA ECMO. Most patients with respiratory failure refractory to conventional therapies can be supported with VV ECMO as a mechanism to augment gas exchange while avoiding toxic ventilator settings. With VV ECMO, the level of mechanical ventilatory support is decreased to mitigate ventilator-induced lung injury (VILI). While carbon dioxide clearance with this approach is easily achieved, oxygenation may be somewhat less efficient. Gas exchange goals should be set as appropriate for the specific clinical circumstance. As with mechanical ventilation and most other modes of respiratory support, VV ECMO does not represent a cure for any underlying disease process(es), but simply a means to "rest" the lungs and allow for disease resolution and recovery of pulmonary function.

In VA ECMO, blood is drained from a central vein in a manner analogous to VV ECMO, but is returned to the arterial system, generally via the carotid artery in neonates and children, and the femoral artery in adults (Fig. 2). VA ECMO is essentially cardiopulmonary bypass for a period of days to weeks, and is extremely effective at both oxygenation and ventilation.

For adult respiratory failure, $>$ 80% of ECMO cases reported to the Extracorporeal Life Support Organization (ELSO) since 1986 have been VV ECMO, and the percentage of patients supported with VV ECMO continues to increase each year.[8] We will focus in this paper on the use of VV ECMO in the adult population.

Evidence for ECMO in Adults

Shortly after ECMO was first described for adults in the early 1970s,[1] the National Institutes of Health conducted a multicenter randomized trial comparing ECMO with conventional ventilation in adult patients with severe respiratory failure.[29] In this trial, 90 patients across 9 centers were randomized to either conventional ventilation or VA ECMO. The mortality in both groups exceeded 90%. The authors of this study concluded that support with ECMO may temporarily improve gas exchange in patients with severe respiratory failure but did not impact hospital or long-term survival.[29]

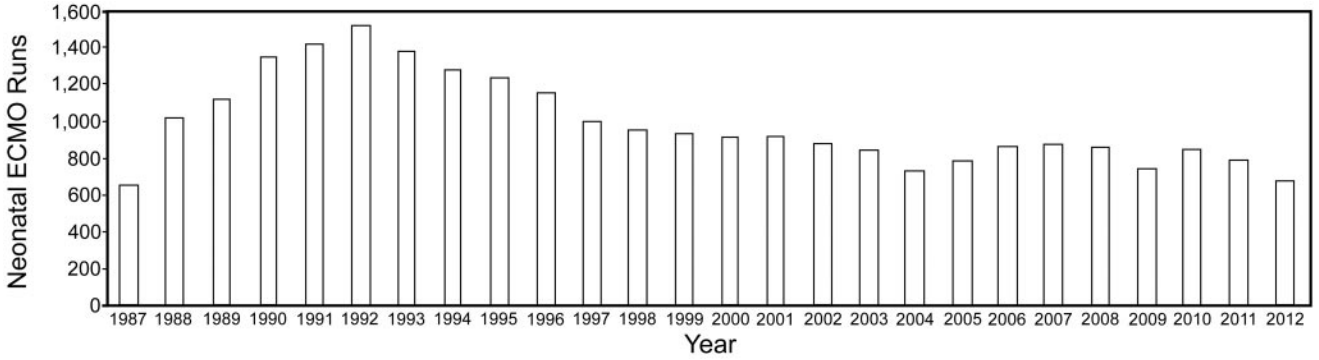

Fig. 3. Annual neonatal respiratory extracorporeal membrane oxygenation (ECMO) runs reported to Extracorporeal Life Support Organization (ELSO) since 1987. (From Reference 36, with permission.)

Over the next 10 years, case reports and small series in adults documented success using ECMO for refractory respiratory failure.[30-32] These data supported the notion that ECMO may have a role in a limited subset of critically ill adult patients, but there were no studies that demonstrated improvement in survival or other clinical outcomes in comparison to conventional mechanical ventilation. During this same time period in the late 1980s and early 1990s, neonatal ECMO became commonplace (Fig. 3), with multiple studies demonstrating improved outcomes in these patients.[8,33-36]

As successful use of ECMO in neonates continued to increase, a follow-up randomized trial was conducted to assess the impact of ECMO on adults with severe respiratory failure.[37] In this trial, Morris et al randomized 40 patients in a single center to either conventional ventilation or rescue with VV ECMO. This investigation demonstrated no significant outcome difference, with 42% survival in the conventional ventilation group, compared to 33% survival in the ECMO patients.[37] These data, in addition to the prior randomized trial that did not demonstrate superiority of ECMO in adult patients compared to conventional therapies, led to ECMO being used only sporadically in adults over the next 2 decades. Data reported to ELSO from 128 centers demonstrate that between 1986 and 2006 a mean of only 67 adult patients internationally were supported with ECMO annually for respiratory failure, compared to a mean of 1,207 neonatal and pediatric patients each year[36] (Fig. 4).

The Conventional Ventilation or ECMO for Severe Adult Respiratory Failure (CESAR) trial, a multicenter randomized trial, was published in 2009.[14] In this investigation by Peek et al, 180 adults with acute refractory respiratory failure were randomized to ECMO or treatment with conventional mechanical ventilation. This randomized controlled trial demonstrated a significant improvement in 6 month disability-free survival in the ECMO group (63%), when compared to the conventional ventilation patients (47%) ($P = .03$).[14] An important consideration in this study was that only 75% of the patients randomized and referred for ECMO were actually supported with ECMO, with the remaining 25% undergoing protocolized conventional mechanical ventilation at the ECMO referral center. While this percentage of ECMO referrals actually supported with ECMO is consistent with the 59–86% reported by other centers,[16,38] some experts would suggest that this investigation is a study of referral to an experienced quaternary ECMO center rather than a comparison of ECMO with conventional ventilation.[39,40] In addition, the conventional ventilation arm of the study was conducted at one of 92 different centers across England, without a specific ventilator management protocol.[14] Significantly fewer patients in the conventional ventilation group (70%) were treated with a "low-volume, low-pressure" ventilation strategy, when compared to the ECMO group (93%) ($P < .001$).[14] Despite the controversy associated with this study, these results likely contributed to the recent increased interest in ECMO worldwide as a therapeutic option in adult patients.

The results of the CESAR trial were published at a time when numerous reports were emerging that demonstrated successful utilization of ECMO to support critically ill adults infected with H1N1 influenza during the 2009–2010 international pandemic.[9,10,12,13,15,16,38,41-44] Survival in these reports consistently ranged from 68–83%, but most reports are single center experiences of < 15 patients.[9,12,13,15,16,38,41-44] The largest series of 68 patients was published by the Australia and New Zealand ECMO investigators.[10] This observational investigation compared 68 patients supported with ECMO as a rescue for refractory respiratory failure to 133 mechanically ventilated patients with H1N1 not supported with ECMO. In this study, survival to ICU discharge in the ECMO patients was 77%, compared to 91% in the non-ECMO group ($P = .01$).[10] Duration of ventilation and ICU stay were also longer in the ECMO group. These findings are not surprising, as ECMO was used in this study as a "rescue" therapy in those who failed more conventional management, and the

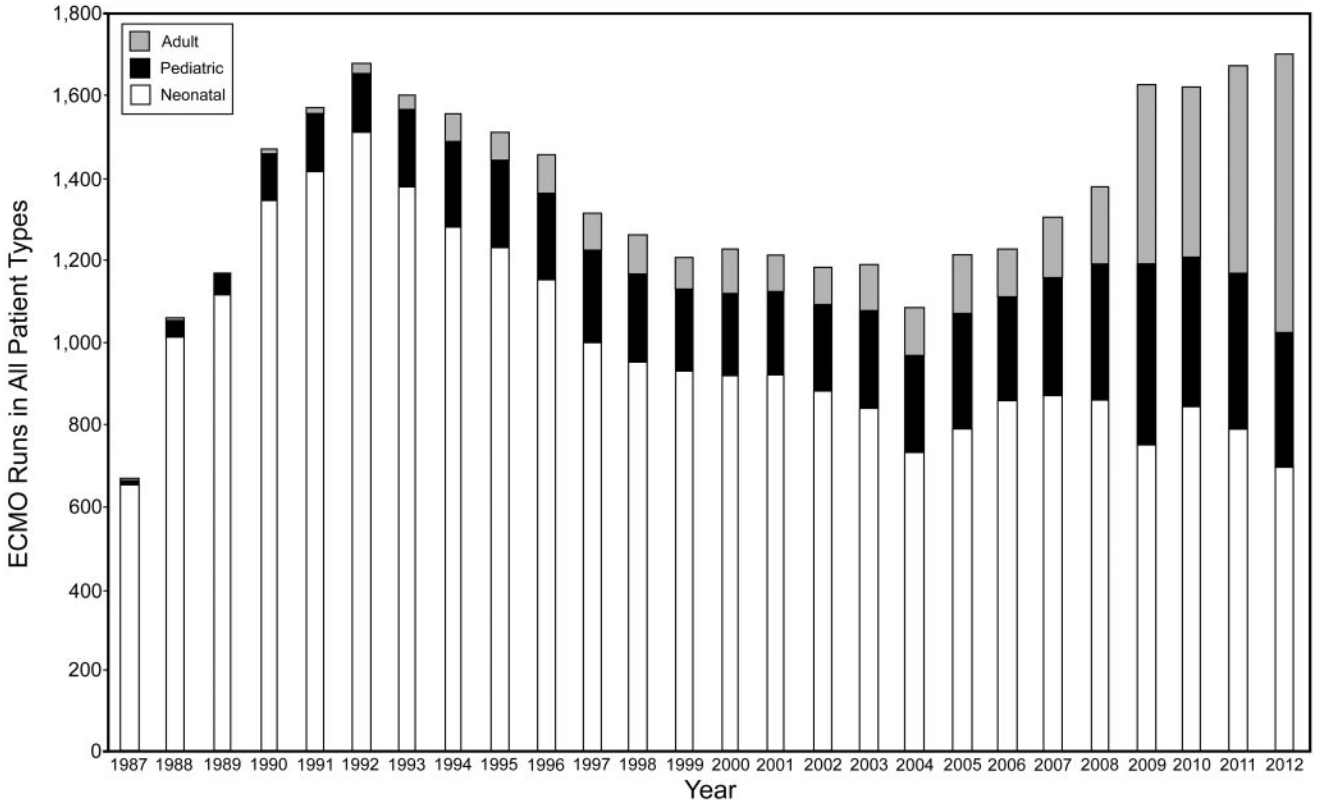

Fig. 4. Annual combined neonatal, pediatric, and adult respiratory extracorporeal membrane oxygenation (ECMO) runs reported to the Extracorporeal Life Support Organization since 1987. (From Reference 36, with permission.)

survival rates are consistent with the multiple case and single center reports of ECMO utilization in adults during the H1N1 pandemic.

The combination of these H1N1 data and the publication of the CESAR trial has substantially renewed interest in the utilization of ECMO in adults with refractory respiratory failure over the past 5 years. In 2008 the number of adult respiratory failure patients reported to the ELSO registry increased to 190, with further increases to 437 in 2009, 418 in 2010, and 507 in 2011[36] (Fig. 5). ECMO utilization for adult respiratory failure has exceeded pediatric respiratory cases annually for the past 2 years (see Fig. 4). Of note, the survival rates in adult patients supported with ECMO for respiratory failure in the past 5 years ranged from 53–61%, with 58% overall survival for adult respiratory failure ECMO patients in 2011.[8]

ECMO Patient Selection

ECMO Criteria

The increasing utilization of adult ECMO brings with it the challenge of patient selection and determination of ECMO candidacy. ECMO is primarily reserved for circumstances in which patients are refractory to escalating conventional therapies and have a "high" predicted mortality. The ELSO guidelines suggest that ECMO be considered in adult patients when predicted mortality exceeds 50%.[26,27] In those with severe hypoxemic respiratory failure, a combination of P_{aO_2}/F_{IO_2} and Murray score are often utilized to determine the potential need for ECMO, with a $P_{aO_2}/F_{IO_2} < 150$ mm Hg on an F_{IO_2} of > 0.9 and a Murray score of 2–3 being associated with a predicted mortality of 50%.[26,45] Other respiratory indications for ECMO in adults include respiratory acidosis refractory to conventional therapies and severe air leak.

As ECMO is being considered in an adult with progressive or refractory acute respiratory failure, the first question that must be answered for any potential ECMO patient is the reversibility of the underlying disease process. While lung injury and potential for pulmonary recovery is a crucial consideration, many other factors may impact a patient's potential for recovery. In adults, the risk generally increases with age, but this risk is likely related to comorbidities and other confounding factors rather than being directly age-related. Weight can also be a factor in patient selection, with morbid obesity contributing to potential difficulties with the cannulation procedure and/or achieving adequate ECMO blood flow. Limited data suggest that obesity may be an independent risk factor for

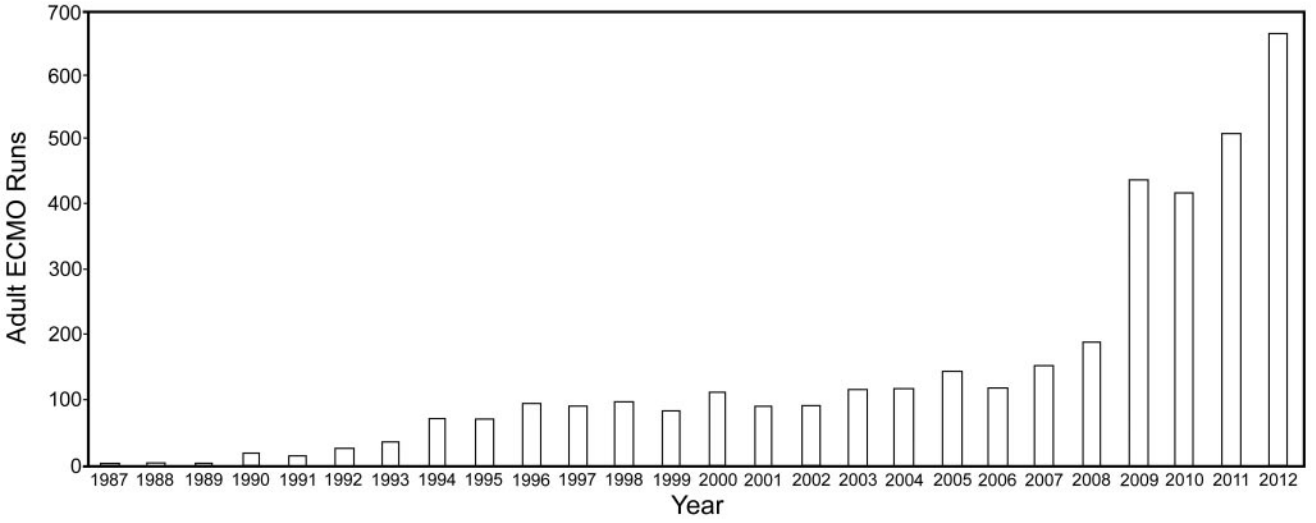

Fig. 5. Annual adult respiratory extracorporeal membrane oxygenation (ECMO) runs reported to the Extracorporeal Life Support Organization since 1987. (From Reference 36, with permission.)

ECMO mortality.[19,46,47] Comorbid conditions, degree of non-pulmonary organ dysfunction, and neurologic status are other patient specific considerations that impact ECMO candidacy and outcome.[26,46-48]

The decision to proceed with ECMO is also impacted by the duration of mechanical ventilation prior to cannulation.[26,48-50] VILI is a key contributor to morbidity and mortality in patients with severe respiratory failure, and avoidance of VILI is a key priority in the management of patients with respiratory failure.[51-54] One approach to minimize VILI is early initiation of ECMO to maintain adequate gas exchange while "resting" the lungs. Older data suggest that mortality is increased in patients who required mechanical ventilation for greater than approximately 7 days prior to cannulation,[26,49,50] but in the era of lung-protective ventilation, it is likely that the "acceptable" pre-ECMO duration of ventilation is longer. A recent review of the ELSO registry by Zabrocki et al demonstrated that between 1993 and 2007, survival in pediatric patients supported with ECMO remained stable between 56% and 61% when they were ventilated for $\leq$ 14 days prior to cannulation.[48] In this study, survival fell to 38% in patients ventilated for $>$ 14 days prior to ECMO cannulation. While duration of mechanical ventilation must be considered in the potential ECMO patient, current data would suggest that support with lung-protective mechanical ventilation for up to 2 weeks prior to initiation of ECMO may be acceptable.

Special Considerations

As ECMO is being considered as a support modality in patients with refractory respiratory failure, comorbidities are other important considerations. In both pediatrics and adults, the complexity of patients supported with ECMO is increasing.[48,55] Zabrocki et al reported that 47% of pediatric respiratory ECMO patients reported to ELSO in 2007 had a comorbid condition, compared to only 19% in 1997.[48] Despite this increased complexity, survival remained unchanged at 57%.[48] However, survival in pediatric patients with isolated respiratory failure without a comorbid condition increased significantly, from 57% to 72%, between 1993 and 2007.[48] This increased survival for patients with isolated pediatric respiratory failure is consistent with recent data in adolescents and young adults with minimal comorbidities supported with ECMO during the H1N1 pandemic.[9,10,12,13,15,16,38,41-44]

Not surprisingly, Zabrocki et al also reported that the presence of comorbid conditions had a profound negative impact on overall survival in pediatric respiratory failure patients.[48] In the 3,213 children reviewed, renal failure was the most common comorbidity, present in 10% of patients prior to cannulation. Overall survival in the ECMO patients with preexisting renal failure was only 33%.[48] Other comorbidities were less common but also had a substantial impact on survival, as demonstrated by patients with malignancy, immunodeficiency, and history of solid organ transplantation having survival rates of 30%, 34%, and 16%, respectively.[48] As ECMO is being considered in the adult population, comorbid conditions and complications of critical illness are important considerations that may impact ECMO candidacy and anticipated outcome.

Another population of patients in which underlying comorbidity and organ dysfunction must be carefully considered are those with end-stage pulmonary disease awaiting lung transplantation. Outcomes for patients undergoing

Fig. 6. A patient ambulating on extracorporeal membrane oxygenation while being bridged to lung transplantation.

lung transplantation from ECMO traditionally have been poor,[56-62] but interest is growing in the utilization of "awake" ECMO as a bridge to lung transplantation[63-67] (Fig. 6). Some authors suggest that the morbidity and mortality in patients bridged to lung transplantation with ECMO may be related to weakness and deconditioning, with rehabilitation pre-transplant on ECMO having the potential to improve outcomes.[63-68] While there are a number of factors that must be considered when ECMO is being used as a bridge to lung transplantation, including institutional waiting lists, comorbid conditions, organ availability, and resource allocation, recent data would suggest that ECMO can be successfully implemented in select circumstances to bridge patients to lung transplantation.[63-68]

Techniques and Equipment

A given ECMO center may have single or multiple designs for ECMO circuits, depending on the resources available, institution preferences, and individual clinical circumstances. The basic components of a traditional ECMO circuit include the pump, oxygenator, cannula, circuit components, and various monitoring devices (Fig. 7). For large pediatric and adult patients there has been movement toward simplification and miniaturization of ECMO circuits[69] (Fig. 8). These simplified circuits increase the portability of ECMO systems and require less intensive maintenance and monitoring.[67-71] In addition, a number of recent advances have occurred in cannula, oxygenator, and pump technology that may contribute to improved outcomes.[17,28,72-77]

ECMO cannulae design in adults has improved substantially. Introduction of a double lumen VV ECMO cannula (Avalon Laboratories, Rancho Domingo, California) that drains blood from both the superior and inferior vena cava and directs the return of blood directly across the tricuspid

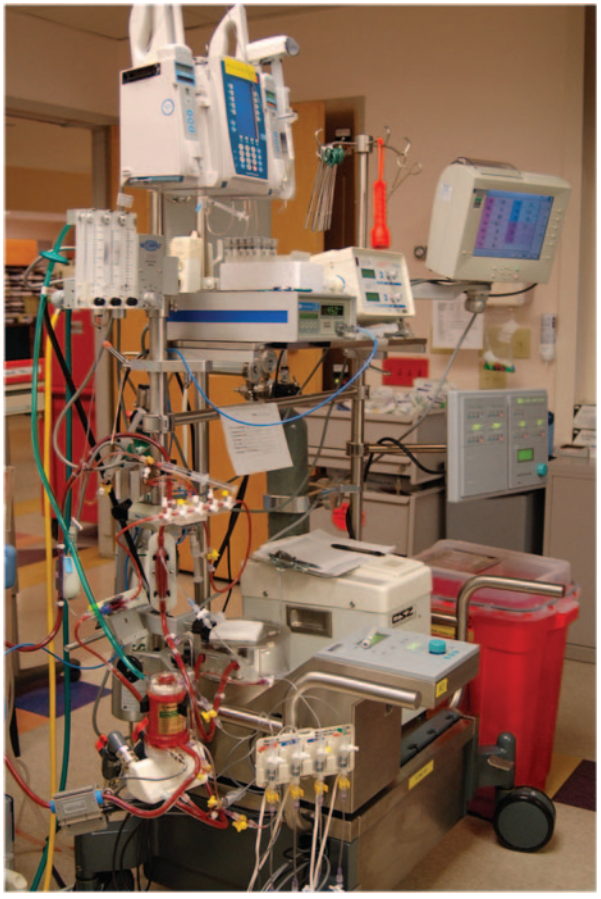

Fig. 7. A traditional extracorporeal membrane oxygenation system.

valve allows for single site percutaneous cannulation while minimizing recirculation through the ECMO system[64,67,78] (Fig. 9). These cannulae allow for avoidance of femoral venous cannulation and thus increase patient mobility and lower complication rates.[64,67,78-80] These factors, along with the ease of use associated with a percutaneous double lumen cannula, likely have contributed to the upswing in adult ECMO utilization over the past few years.[8]

ECMO pumps have traditionally involved a "roller-head" design in which 2 steel roller heads force blood forward through the tubing through sequential compression. However, the use of centrifugal pumps, which create flow via a magnet controlled, spinning motor, is increasing. In surveys of neonatal ECMO programs published by Lawson et al, use of roller head pumps decreased from 95% in 2002 to 53% in 2011.[81,82] The impact of centrifugal pumps in comparison to roller head pumps is uncertain. Although advantages generally include quicker pump assembly, shorter cannulation time, and a lower priming volume, it should be noted that concerns have been raised regarding a potential increased risk for hemolysis and complications in neonates supported with centrifugal pumps.[83,84] At this time, the impact of one pump type versus another in the

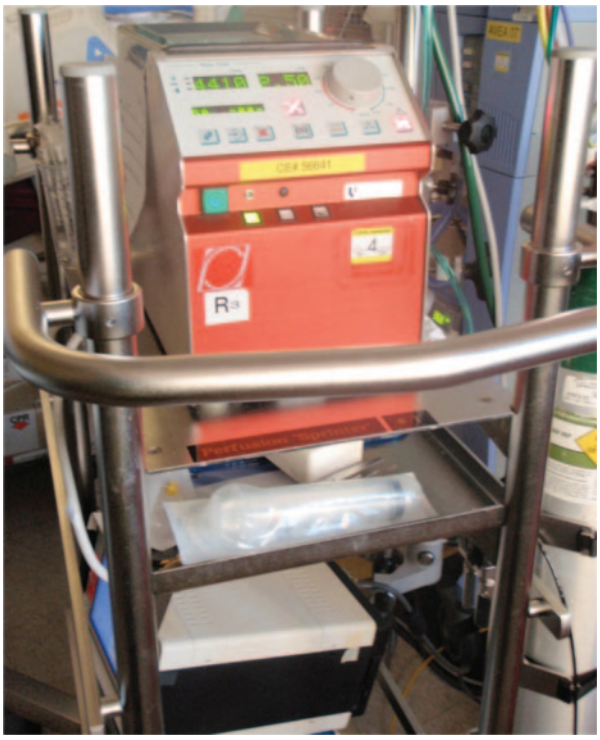

Fig. 8. A simplified extracorporeal membrane oxygenation system with improved portability and less monitoring.

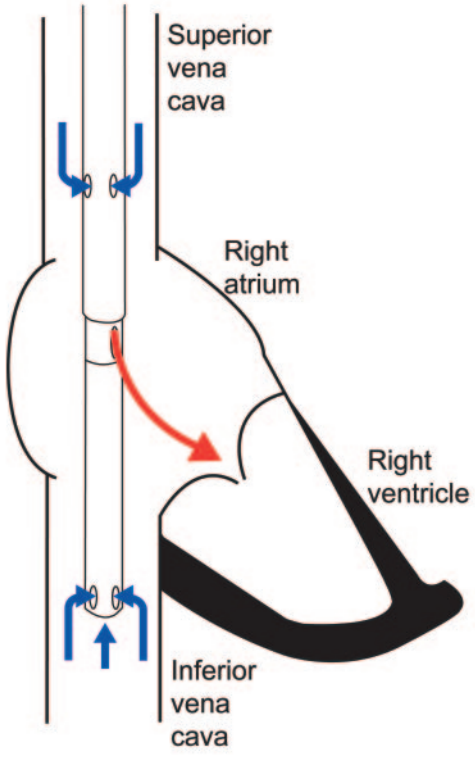

Fig. 9. Diagram of an appropriately positioned Avalon double-lumen VV ECMO cannula. (From reference 28, with permission.)

Fig. 10. CardioHelp system. (Courtesy of Maquet.)

adult population remains uncertain, and there is no specific recommendation or guideline available to direct selection of pumps for developing ECMO programs.

Oxygenator selection also has evolved with improved technology. In neonatal ECMO, silicone oxygenator use has fallen from 95% in 2002 to 25% in 2011, in association with an increase in application of polymethylpentine hollow fiber oxygenators.[81,82] Hollow fiber oxygenators are associated with decreased inflammation, improved gas exchange, and decreased need for replacement (ie, last longer in clinical use) compared to the prior generation of oxygenators and are becoming standard in most ECMO centers.[17,75,77,85]

Additional technological advances beyond "traditional" systems have enhanced the ability to provide extracorporeal support to patients with severe respiratory failure.[22,70,71,86-90] One important technological advance is the miniaturization of ECMO technology into a small self-contained system with an oxygenator, a pump, and all of the components necessary to provide ECMO support.[70,71,86] An example of this miniaturized technology is the CardioHelp system (Maquet, Wayne, New Jersey), which has been used to provide ECMO for transport, as a bridge to lung transplantation, and as a bridge to recovery for respiratory failure[70,71,86] (Fig. 10).

Another important advance in technology is the ability to provide "pumpless" support to patients, using an arterial-venous system.[22,87-90] This system uses the patient's arterial pressure as the driving pressure through the membrane. The Novalung (Novalung, Heilbronn, Germany) is a device that has been successfully used as a bridge to both

recovery and lung transplantation.[22,87-90] Additional investigation is warranted using these new devices to determine their optimal application, their impact on outcomes, and potential complications.

Complications

As discussed previously, the decision to support a patient with ECMO involves a number of crucial considerations. Patients in need of ECMO support have a high predicted mortality, and implementing an invasive therapy that requires central venous or arterial cannulation, systemic anticoagulation, and exposure to an extracorporeal bypass circuit involves substantial risk. While the data regarding complications for VV versus VA ECMO are not definitive, a number of studies in adults have demonstrated increased complication rates with VA ECMO.[79,80,91,92] In addition, the potential impact of an embolic or thromboembolic event may be more catastrophic when it occurs in the arterial system.

The most common complication encountered in ECMO patients is bleeding.[8] Cannula and other surgical site bleeding are 2 of the most frequent hemorrhagic complications in patients reported to ELSO, occurring in approximately 17% and 16% of adult patients, respectively.[8] While cannula and surgical site bleeding can usually be readily controlled, bleeding in other locations can have severe consequences. Pulmonary hemorrhage occurs in approximately 8% of adult ECMO patients, with a 36% overall survival rate in these patients.[8] Intracranial bleeding is of particular concern, given the devastating consequences, with an overall 17% survival rate. Fortunately, only approximately 4% of adult ECMO patients develop central nervous system bleeding complications.[8] Other bleeding complications include gastrointestinal bleeding and disseminated intravascular coagulation, occurring in 5% and 4% of patients respectively.

Along with bleeding risk, there are a numerous other potential complications associated with supporting patients with refractory respiratory failure with ECMO (Table). It is unclear whether complications are related specifically to ECMO as a support apparatus or to the degree of overall illness and organ dysfunction in these patients, but the etiology of the complications encountered during ECMO are likely multifactorial. For example, renal dysfunction is common, with 12% of adult respiratory ECMO patients developing a serum creatinine $>$ 3.0 mg/dL, and 13% requiring dialysis.[8] In addition, over half of adult respiratory patients require inotropic support during ECMO for capillary leak and myocardial dysfunction. Also of note, despite the lung-protective approach employed in most circumstances, 13% of adult ECMO patients develop a pneumothorax requiring intervention. While support with ECMO may be a contributor to this multi-organ dysfunction, it is likely that degree of illness is a substantial contributor.

Table. Adult Respiratory ECMO Complications Reported to the Extracorporeal Life Support Organization

Complication	Incidence (%)
Arrhythmia	15.2
Bleeding	
Cannula site	17.2
Central nervous system	3.9
Gastrointestinal	5.2
Surgical site	16.7
Central nervous system infarction	2.1
Infection (culture proven)	20.4
Mechanical	
Air in circuit	1.7
Clotting	2.3–12.6*
Oxygenator failure	16.1
Tubing rupture	1.4
Pneumothorax requiring intervention	13.0
Renal failure requiring dialysis	13.3
Seizures	1.1

* Incidence of clotting varies for individual extracorporeal membrane oxygenation (ECMO) circuit components.
(Data from reference 8.)

Infection is also relatively common, with culture proven infections occurring in approximately 20% of adult respiratory ECMO patients.[8] Interestingly, adult patients appear to have a significantly increased risk for infection while being supported with ECMO, when compared to pediatric and neonatal patients.[8,93] Newer techniques that avoid the need for femoral cannulation may improve the risk for infection in adult ECMO patients, but there are currently no available data.

Finally, mechanical complications during ECMO are another important consideration. Clotting related to ECMO is a well reported mechanical complication, ranging from 2–12% for the various ECMO circuit components.[8] Other mechanical complications include circuit air, connection cracks, and failure of circuit components. Devastating complications, including tubing/circuit rupture, are rare, occurring in $<$ 1.5% of patients, but a critical aspect of any ECMO program must be preparedness for potential complications.

Patient Management

As the utilization of ECMO in adult patients with life threatening respiratory failure continues to grow, an increasing emphasis will likely be placed on development of clear guidelines and standards. One important area of management in ECMO patients is mechanical ventilation strat-

egy. Lung-protective strategies have become a mainstay in the treatment for respiratory failure, with evidence supporting limitation of tidal volume and inspiratory pressure to decrease VILI and improve outcomes.[51-54,94-96] In patients on ECMO, ventilator support is decreased substantially from pre-ECMO levels, and the potential for VILI can be minimized. Some patients on ECMO may even be placed on tracheostomy collar or extubated without the need for mechanical ventilation.[60,63,67]

Additional areas of management in patients supported with ECMO are largely driven by underlying pathophysiology and disease process. Cardiovascular management includes vasoactive medications in more than half of respiratory adult VV ECMO patients,[8] but the decision to use these agents is largely determined by underlying degree of illness rather than ECMO support. Fluids, diuretics, antibiotics, sedation, and management of other organ systems and dysfunction are similarly dictated by the underlying clinical status of these critically ill patients.

Specific guidelines for clinical management of the ECMO patient are limited, but the ELSO published guidelines include considerations for patient selection, contraindications, and general management approaches.[26] Additionally, other publications are available to help guide practitioners in patient management and program development.[26,69,97-99] However, data are lacking on the efficacy of the various techniques and adjunctive therapies involved in the management of ECMO patients. Further investigation is needed to better clarify optimal approaches to support ECMO patients and potentially improve outcomes. Until then, clinical judgment and careful case by case consideration are needed to guide practitioners in decisions regarding supporting adults with life-threatening respiratory failure with ECMO.

Future Directions

With increasing ECMO experience and the potential for improved outcomes, some experts have begun to suggest early implementation of ECMO as a lung-protective strategy.[10,16,39,100] As VILI continues to be recognized as an important element of the morbidity and mortality of patients with acute respiratory failure, early initiation of ECMO represents an intriguing option to potentially improve outcomes and protect the lungs of these critically ill patients. Obviously, further data and investigation are needed to determine the impact of early implementation of ECMO on outcome, but, given recent data, clinical equipoise may exist for a large scale study to investigate this issue.

Summary

ECMO is a form of cardiopulmonary bypass utilized in select patients with a high expected mortality. While ECMO may be life-saving, the data to support the use of ECMO in adult patients are limited. A growing number of reports have been recently published that demonstrate survival rates $> 70\%$ in adult respiratory ECMO patients, but most studies do not have a comparison group and are not definitive. Despite limited data and lack of clear management guidelines, ECMO utilization in the adult population continues to rise, with survival rates remaining stable over time despite increasing complexity and more comorbid conditions. Bleeding remains the most common complication, but there are a number of other important potential complications, including renal dysfunction, infection, and mechanical problems.

Risks for complications may decrease as technology continues to improve, but data are limited and practitioners should carefully evaluate and investigate the various component options to further optimize the provision of ECMO. Although some general guidelines exist for the management of patients and the development of ECMO programs, practitioners are generally left to determine the appropriate approach for these most critically ill patients on a case by case basis. Finally, the difficult decision of the optimal timing of ECMO initiation remains unclear. Future investigation is needed to determine the overall impact of ECMO, and potentially earlier intervention with this support as a lung-protective strategy, on VILI and outcomes in adult patients with acute respiratory failure.

REFERENCES

1. Hill JD, O'Brien TG, Murray JJ, Dontigny L, Bramson ML, Osborn JJ, et al. Prolonged extracorporeal oxygenation for acute post-traumatic respiratory failure (shock-lung syndrome). Use of the Bramson membrane lung. N Engl J Med 1972;286(12):629-634.
2. Bahrami KR, Van Meurs KP. ECMO for neonatal respiratory failure. Semin Perinatol 2005;29(1):15-23.
3. Green TP, Moler FW, Goodman DM. Probability of survival after prolonged extracorporeal membrane oxygenation in pediatric patients with acute respiratory failure. Extracorporeal Life Support Organization. Crit Care Med 1995;23(6):1132-1139.
4. Hansell DR. Extracorporeal membrane oxygenation for perinatal and pediatric patients. Respir Care 2003;48(4):352-362; discussion 363-356.
5. Mehta NM, Turner D, Walsh B, Zurakowski D, Betit P, Wilson J, et al. Factors associated with survival in pediatric extracorporeal membrane oxygenation: a single-center experience. J Pediatr Surg 2010;45(10):1995-2003.
6. Mugford M, Elbourne D, Field D. Extracorporeal membrane oxygenation for severe respiratory failure in newborn infants. Cochrane Database Syst Rev 2008;(3):CD001340.
7. Pettignano R, Fortenberry JD, Heard ML, Labuz MD, Kesser KC, Tanner AJ, et al. Primary use of the venovenous approach for extracorporeal membrane oxygenation in pediatric acute respiratory failure. Pediatr Crit Care Med 2003;4(3):291-298.
8. Extracorporeal Life Support Organization. Registry report: international summary. Ann Arbor: ELSO; July 2012.
9. Chan KK, Lee KL, Lam PK, Law KI, Joynt GM, Yan WW. Hong Kong's experience on the use of extracorporeal membrane oxygen-

ation for the treatment of influenza A (H1N1). Hong Kong Med J 2010;16(6):447-454.
10. Davies A, Jones D, Bailey M, Beca J, Bellomo R, Blackwell N, et al. Extracorporeal membrane oxygenation for 2009 influenza A(H1N1) acute respiratory distress syndrome. JAMA 2009;302(17): 1888-1895.
11. Forrest P, Ratchford J, Burns B, Herkes R, Jackson A, Plunkett B, et al. Retrieval of critically ill adults using extracorporeal membrane oxygenation: an Australian experience. Intensive Care Med 2011;37(5):824-830.
12. Freed DH, Henzler D, White CW, Fowler R, Zarychanski R, Hutchison J, et al. Extracorporeal lung support for patients who had severe respiratory failure secondary to influenza A (H1N1) 2009 infection in Canada. Can J Anaesth 2010;57(3):240-247.
13. Nair P, Davies AR, Beca J, Bellomo R, Ellwood D, Forrest P, et al. Extracorporeal membrane oxygenation for severe ARDS in pregnant and postpartum women during the 2009 H1N1 pandemic. Intensive Care Med 2011;37(4):648-654.
14. Peek GJ, Mugford M, Tiruvoipati R, Wilson A, Allen E, Thalanany MM, 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):1351-1363.
15. Turner DA, Rehder KJ, Peterson-Carmichael SL, Ozment CP, Al-Hegelan MS, Williford WL, et al. Extracorporeal membrane oxygenation for severe refractory respiratory failure secondary to 2009 H1N1 influenza A. Respir Care 2011;56(7):941-946.
16. Noah MA, Peek GJ, Finney SJ, Griffiths MJ, Harrison DA, Grieve R, et al. Referral to an extracorporeal membrane oxygenation center and mortality among patients with severe 2009 influenza A(H1N1). JAMA 2011;306(15):1659-1668.
17. Dalton HJ. Extracorporeal life support: moving at the speed of light. Respir Care 2011;56(9):1445-1453; discussion 1453-1446.
18. Sivarajan VB, Best D, Brizard CP, Shekerdemian LS, D'Udekem Y, Horton SB, et al. Improved outcomes of paediatric extracorporeal support associated with technology change. Interact Cardiovasc Thorac Surg 2010;11(4):400-405.
19. Batchinsky AI, Jordan BS, Regn D, Necsoiu C, Federspiel WJ, Morris MJ, et al. Respiratory dialysis: reduction in dependence on mechanical ventilation by venovenous extracorporeal CO_2 removal. Crit Care Med 2011;39(6):1382-1387.
20. Fischer S, Hoeper MM, Tomaszek S, Simon A, Gottlieb J, Welte T, et al. Bridge to lung transplantation with the extracorporeal membrane ventilator Novalung in the veno-venous mode: the initial Hannover experience. ASAIO J 2007;53(2):168-170.
21. Hamid IA, Hariharan AS, Shankar NR. The advent of ECMO and pumpless extracorporeal lung assist in ARDS. J Emerg Trauma Shock 2011;4(2):244-250.
22. Johnson P, Frohlich S, Westbrook A. Use of extracorporeal membrane lung assist device (Novalung) in H1N1 patients. J Card Surg 2011;26(4):449-452.
23. Jung C, Lauten A, Pfeifer R, Bahrmann P, Figulla HR, Ferrari M. Pumpless extracorporeal lung assist for the treatment of severe, refractory status asthmaticus. J Asthma 2011;48(1):111-113.
24. Ricci D, Boffini M, Del Sorbo L, El Qarra S, Comoglio C, Ribezzo M, et al. The use of CO_2 removal devices in patients awaiting lung transplantation: an initial experience. Transplant Proc 2010;42(4): 1255-1258.
25. Zimmermann M, Bein T, Arlt M, Philipp A, Rupprecht L, Mueller T, et al. Pumpless extracorporeal interventional lung assist in patients with acute respiratory distress syndrome: a prospective pilot study. Crit Care 2009;13(1):R10.
26. Extracorporeal Life Support Organization (ELSO). Patient specific guidelines. http://www.elsonet.org/index.php/resources/guidelines.html. *Accessed March 21, 2013.*
27. Extracorporeal Life Support Organization (ELSO) Guidelines. http://www.elsonet.org/index.php/resources/guidelines.html. *Accessed March 21, 2013.*
28. Rehder KJ, Turner DA, Bonadonna D, Walczak RJ Jr, Rudder R, Cheifetz IM. Technological advances in extracorporeal membrane oxygenation for respiratory failure. Expert Rev Respir Med 2012; 6(5):513-521.
29. Zapol WM, Snider MT, Hill JD, Fallat RJ, Bartlett RH, Edmunds LH, et al. Extracorporeal membrane oxygenation in severe acute respiratory failure. A randomized prospective study. JAMA 1979; 242(20):2193-2196.
30. Egan TM, Duffin J, Glynn MF, Todd TR, DeMajo W, Murphy E, et al. Ten-year experience with extracorporeal membrane oxygenation for severe respiratory failure. Chest 1988;94(4):681-687.
31. Gattinoni L, Pesenti A, Mascheroni D, Marcolin R, Fumagalli R, Rossi F, et al. Low-frequency positive-pressure ventilation with extracorporeal CO_2 removal in severe acute respiratory failure. JAMA 1986;256(7):881-886.
32. MacDonnell KF, Moon HS, Sekar TS, Ahluwalia MP. Extracorporeal membrane oxygenator support in a case of severe status asthmaticus. Ann Thorac Surg 1981;31(2):171-175.
33. UK Collaborative ECMO Trail Group. UK collaborative randomised trial of neonatal extracorporeal membrane oxygenation. Lancet 1996; 348(9020):75-82.
34. Bartlett RH, Roloff DW, Cornell RG, Andrews AF, Dillon PW, Zwischenberger JB. Extracorporeal circulation in neonatal respiratory failure: a prospective randomized study. Pediatrics 1985;76(4): 479-487.
35. O'Rourke PP, Crone RK, Vacanti JP, Ware JH, Lillehei CW, Parad RB, et al. Extracorporeal membrane oxygenation and conventional medical therapy in neonates with persistent pulmonary hypertension of the newborn: a prospective randomized study. Pediatrics 1989;84(6):957-963.
36. Extracorporeal Life Support Organization. Registry report: international summary. Ann Arbor: ELSO; January 2013.
37. Morris AH, Wallace CJ, Menlove RL, Clemmer TP, Orme JF Jr, Weaver LK, et al. Randomized clinical trial of pressure-controlled inverse ratio ventilation and extracorporeal CO_2 removal for adult respiratory distress syndrome. Am J Respir Crit Care Med 1994; 149(2 Pt 1):295-305.
38. Patroniti N, Zangrillo A, Pappalardo F, Peris A, Cianchi G, Braschi A, et al. The Italian ECMO network experience during the 2009 influenza A (H1N1) pandemic: preparation for severe respiratory emergency outbreaks. Intensive Care Med 2011;37(9):1447-1457.
39. Checkley W. Extracorporeal membrane oxygenation as a first-line treatment strategy for ARDS: is the evidence sufficiently strong? JAMA 306(15):1703-1704.
40. Jones A, Barrett N, Scales D, Beale R. Ventilatory support versus ECMO for severe adult respiratory failure (letter). Lancet 2010; 375(9714):550-551; author reply 551.
41. Beurtheret S, Mastroianni C, Pozzi M, D'Alessandro C, Luyt CE, Combes A, et al. Extracorporeal membrane oxygenation for 2009 influenza A (H1N1) acute respiratory distress syndrome: single-centre experience with 1-year follow-up. Eur J Cardiothorac Surg 2012;41(3):691-695.
42. Mitchell MD, Mikkelsen ME, Umscheid CA, Lee I, Fuchs BD, Halpern SD. A systematic review to inform institutional decisions about the use of extracorporeal membrane oxygenation during the H1N1 influenza pandemic. Crit Care Med 2010;38(6):1398-1404.

43. Kumar A, Zarychanski R, Pinto R, Cook DJ, Marshall J, Lacroix J, et al. Critically ill patients with 2009 influenza A (H1N1) infection in Canada. JAMA 2009;302(17):1872-1879.
44. Power CA, Van Heerden PV, Moxon D, Martindale G, Roberts B. Extracorporeal membrane oxygenation for critically ill patients with influenza A (H1N1) 2009: a case series. Crit Care Resusc 2011; 13(1):38-43.
45. Murray JF, Matthay MA, Luce JM, Flick MR. An expanded definition of the adult respiratory distress syndrome. Am Rev Respir Dis 1988;138(3):720-723.
46. Dolch ME, Frey L, Buerkle MA, Weig T, Wassilowsky D, Irlbeck M. Transesophageal echocardiography-guided technique for extracorporeal membrane oxygenation dual-lumen catheter placement. ASAIO J 2011;57(4):341-343.
47. Rastan AJ, Dege A, Mohr M, Doll N, Falk V, Walther T, 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): 302-311, 311.e1.
48. Zabrocki LA, Brogan TV, Statler KD, Poss WB, Rollins MD, Bratton SL. Extracorporeal membrane oxygenation for pediatric respiratory failure: survival and predictors of mortality. Crit Care Med 2011;39(2):364-370.
49. Masiakos PT, Islam S, Doody DP, Schnitzer JJ, Ryan DP. Extracorporeal membrane oxygenation for nonneonatal acute respiratory failure. Arch Surg 1999;134(4):375-379; discussion 379-380.
50. Pranikoff T, Hirschl RB, Steimle CN, Anderson HL, 3rd, Bartlett RH. Mortality is directly related to the duration of mechanical ventilation before the initiation of extracorporeal life support for severe respiratory failure. Crit Care Med 1997;25(1):28-32.
51. Ferguson ND, Frutos-Vivar F, Esteban A, Anzueto A, Alia I, Brower RG, et al. Airway pressures, tidal volumes, and mortality in patients with acute respiratory distress syndrome. Crit Care Med 2005;33(1): 21-30.
52. Gajic O, Dara SI, Mendez JL, Adesanya AO, Festic E, Caples SM, et al. Ventilator-associated lung injury in patients without acute lung injury at the onset of mechanical ventilation. Crit Care Med 2004;32(9):1817-1824.
53. Gajic O, Frutos-Vivar F, Esteban A, Hubmayr RD, Anzueto A. Ventilator settings as a risk factor for acute respiratory distress syndrome in mechanically ventilated patients. Intensive Care Med 2005;31(7):922-926.
54. Acute Respiratory Distress Syndrome Network. Ventilation with lower tidal volumes as compared with traditional tidal volumes for acute lung injury and the acute respiratory distress syndrome. N Engl J Med 2000;342(18):1301-1308.
55. 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):2105-2114.
56. Hammainen P, Schersten H, Lemstrom K, Riise GC, Kukkonen S, Sward K, et al. Usefulness of extracorporeal membrane oxygenation as a bridge to lung transplantation: a descriptive study. J Heart Lung Transplant 2011;30(1):103-107.
57. Jackson A, Cropper J, Pye R, Junius F, Malouf M, Glanville A. Use of extracorporeal membrane oxygenation as a bridge to primary lung transplant: 3 consecutive, successful cases and a review of the literature. J Heart Lung Transplant 2008;27(3):348-352.
58. Mason DP, Thuita L, Nowicki ER, Murthy SC, Pettersson GB, Blackstone EH. Should lung transplantation be performed for patients on mechanical respiratory support? The US experience. J Thorac Cardiovasc Surg 2010;139(3):765-773, e761.
59. Nosotti M, Rosso L, Palleschi A, Lissoni A, Crotti S, Marenghi C, et al. Bridge to lung transplantation by venovenous extracorporeal membrane oxygenation: a lesson learned on the first four cases. Transplant Proc 2010;42(4):1259-1261.
60. Olsson KM, Simon A, Strueber M, Hadem J, Wiesner O, Gottlieb J, et al. Extracorporeal membrane oxygenation in nonintubated patients as bridge to lung transplantation. Am J Transplant 2010; 10(9):2173-2178.
61. Puri V, Epstein D, Raithel SC, Gandhi SK, Sweet SC, Faro A, et al. Extracorporeal membrane oxygenation in pediatric lung transplantation. J Thorac Cardiovasc Surg 2010;140(2):427-432.
62. Russo MJ, Davies RR, Hong KN, Iribarne A, Kawut S, Bacchetta M, et al. Who is the high-risk recipient? Predicting mortality after lung transplantation using pretransplant risk factors. J Thorac Cardiovasc Surg 2009;138(5):1234-1238 e1231.
63. Fuehner T, Kuehn C, Hadem J, Wiesner O, Gottlieb J, Tudorache I, et al. Extracorporeal membrane oxygenation in awake patients as bridge to lung transplantation. Am J Respir Crit Care Med 2012 Apr 1;185(7):763-8.
64. Garcia JP, Iacono A, Kon ZN, Griffith BP. Ambulatory extracorporeal membrane oxygenation: a new approach for bridge-to-lung transplantation. J Thorac Cardiovasc Surg 2010;139(6):e137-e139.
65. Hayes D Jr, Kukreja J, Tobias JD, Ballard HO, Hoopes CW. Ambulatory venovenous extracorporeal respiratory support as a bridge for cystic fibrosis patients to emergent lung transplantation. J Cyst Fibros 2012;11(1):40-45.
66. Mangi AA, Mason DP, Yun JJ, Murthy SC, Pettersson GB. Bridge to lung transplantation using short-term ambulatory extracorporeal membrane oxygenation. J Thorac Cardiovasc Surg 2010;140(3): 713-715.
67. Turner DA, Cheifetz IM, Rehder KJ, Williford WL, Bonadonna D, Banuelos SJ, et al. Active rehabilitation and physical therapy during extracorporeal membrane oxygenation while awaiting lung transplantation: a practical approach. Crit Care Med 2011;39(12):2593-2598.
68. Rehder KJ, Turner DA, Hartwig MG, Williford WL, Bonadonna D, Walczak RJ, et al. Active rehabilitation during ECMO as a bridge to lung transplantation. Respir Care 2012 [Epub ahead of print] doi:10.4187/respcare.02155.
69. Turner DA, Williford WL, Peters MA, Thalman JJ, Shearer IR, Walczak RJ, Jr., et al. Development of a collaborative program to provide extracorporeal membrane oxygenation for adults with refractory hypoxemia within the framework of a pandemic. Pediatr Crit Care Med 2011;12(4):426-430.
70. Haneya A, Philipp A, Foltan M, Camboni D, Mueller T, Bein T, et al. First experience with the new portable extracorporeal membrane oxygenation system Cardiohelp for severe respiratory failure in adults. Perfusion 2012;27(2):150-155.
71. Roncon-Albuquerque R Jr, Basílio C, Figueiredo P, Silva S, Mergulhão P, Alves C, et al. Portable miniaturized extracorporeal membrane oxygenation systems for H1N1-related severe acute respiratory distress syndrome: a case series. J Crit Care 2012;27(5):454-463.
72. Curtis JJ, Walls JT, Wagner-Mann CC, Schmaltz RA, Demmy TL, McKenney CA, et al. Centrifugal pumps: description of devices and surgical techniques. Ann Thorac Surg 1999;68(2):666-671.
73. Horton S, Thuys C, Bennett M, Augustin S, Rosenberg M, Brizard C. Experience with the Jostra Rotaflow and QuadroxD oxygenator for ECMO. Perfusion 2004;19(1):17-23.
74. Khan S, Vasavada R, Qiu F, Kunselman A, Undar A. Extracorporeal life support systems: alternative vs conventional circuits. Perfusion 2011;26(3):191-198.
75. Khoshbin E, Roberts N, Harvey C, Machin D, Killer H, Peek GJ, et al. Poly-methyl pentene oxygenators have improved gas exchange capability and reduced transfusion requirements in adult extracorporeal membrane oxygenation. ASAIO J 2005;51(3):281-287.

76. Mendler N, Podechtl F, Feil G, Hiltmann P, Sebening F. Seal-less centrifugal blood pump with magnetically suspended rotor: rot-a-flot. Artif Organs 1995;19(7):620-624.
77. Peek GJ, Killer HM, Reeves R, Sosnowski AW, Firmin RK. Early experience with a polymethyl pentene oxygenator for adult extracorporeal life support. ASAIO J 2002;48(5):480-482.
78. Bermudez CA, Rocha RV, Sappington PL, Toyoda Y, Murray HN, Boujoukos AJ. Initial experience with single cannulation for venovenous extracorporeal oxygenation in adults. Ann Thorac Surg 2010; 90(3):991-995.
79. Bisdas T, Beutel G, Warnecke G, Hoeper MM, Kuehn C, Haverich A, et al. Vascular complications in patients undergoing femoral cannulation for extracorporeal membrane oxygenation support. Ann Thorac Surg 2011;92(2):626-631.
80. Gander JW, Fisher JC, Reichstein AR, Gross ER, Aspelund G, Middlesworth W, et al. Limb ischemia after common femoral artery cannulation for venoarterial extracorporeal membrane oxygenation: an unresolved problem. J Pediatr Surg 2010;45(11):2136-2140.
81. Lawson DS, Walczak R, Lawson AF, Shearer IR, Ing R, Schulman S, et al. North American neonatal extracorporeal membrane oxygenation (ECMO) devices: 2002 survey results. J Extra Corpor Technol 2004;36(1):16-21.
82. Lawson S, Ellis C, Butler K, McRobb C, Mejak B. Neonatal extracorporeal membrane oxygenation devices, techniques and team roles: 2011 survey results of the United States' Extracorporeal Life Support Organization centers. J Extra Corpor Technol 2011;43(4):236-244.
83. Barrett CS, Thiagarajan RR. Centrifugal pump circuits for neonatal extracorporeal membrane oxygenation. Pediatr Crit Care Med 2012; 13(4):492-493.
84. Meyer AD, Wiles AA, Rivera O, Wong EC, Freishtat RJ, Rais-Bahrami K, et al. Hemolytic and thrombocytopathic characteristics of extracorporeal membrane oxygenation systems at simulated flow rate for neonates. Pediatr Crit Care Med 2012;13(4):e255-e261.
85. Khoshbin E, Dux AE, Killer H, Sosnowski AW, Firmin RK, Peek GJ. A comparison of radiographic signs of pulmonary inflammation during ECMO between silicon and poly-methyl pentene oxygenators. Perfusion 2007;22(1):15-21.
86. Haneya A, Philipp A, Mueller T, Lubnow M, Pfeifer M, Zink W, et al. Extracorporeal circulatory systems as a bridge to lung transplantation at remote transplant centers. Ann Thorac Surg 2011;91(1):250-255.
87. Matheis G. New technologies for respiratory assist. Perfusion 2003; 18(4):245-251.
88. Bartosik W, Egan JJ, Wood AE. The Novalung interventional lung assist as bridge to lung transplantation for self-ventilating patients - initial experience. Interact Cardiovasc Thorac Surg 2011;13(2):198-200.
89. Fischer S, Simon AR, Welte T, Hoeper MM, Meyer A, Tessmann R, et al. Bridge to lung transplantation with the novel pumpless interventional lung assist device NovaLung. J Thorac Cardiovasc Surg 2006;131(3):719-723.
90. Petzoldt M, Braune S, Bittmann I, Kluge S. Rescue therapy with a pumpless extracorporeal lung assist device in a patient with acute interstitial lung disease and severe refractory hypercapnia. Respir Care 2012;57(2):293-297.
91. Hartwig MG, Appel JZ 3rd, Cantu E 3rd, Simsir S, Lin SS, Hsieh CC, et al. Improved results treating lung allograft failure with venovenous extracorporeal membrane oxygenation. Ann Thorac Surg 2005;80(5):1872-1879; discussion 1879-1880.
92. Hermans G, Meersseman W, Wilmer A, Meyns B, Bobbaers H. Extracorporeal membrane oxygenation: experience in an adult medical ICU. Thorac Cardiovasc Surg 2007;55(4):223-228.
93. Bizzarro MJ, Conrad SA, Kaufman DA, Rycus P. Infections acquired during extracorporeal membrane oxygenation in neonates, children, and adults. Pediatr Crit Care Med 2011;12(3):277-281.
94. Albuali WH, Singh RN, Fraser DD, Seabrook JA, Kavanagh BP, Parshuram CS, et al. Have changes in ventilation practice improved outcome in children with acute lung injury? Pediatr Crit Care Med 2007;8(4):324-330.
95. Determann RM, Royakkers A, Wolthuis EK, Vlaar AP, Choi G, Paulus F, et al. Ventilation with lower tidal volumes as compared with conventional tidal volumes for patients without acute lung injury: a preventive randomized controlled trial. Crit Care 2010; 14(1):R1.
96. Pinheiro de Oliveira R, Hetzel MP, Dos Anjos Silva M, Dallegrave D, Friedman G. Mechanical ventilation with high tidal volume induces inflammation in patients without lung disease. Crit Care 2010;14(2):R39.
97. Dalton HJ, Butt WW. Extracorporeal life support: an update of Rogers' Textbook of Pediatric Intensive Care. Pediatr Crit Care Med 2012;13(4):461-471.
98. Mullany DV, Bull TN, Hunt W, Shekar K, Thomson B, Fraser JF, et al. Outcomes of the first 30 cases of an adult extracorporeal membrane oxygenation program: strategies to manage the "learning curve" and implications for intensive care unit risk adjustment models. Crit Care Resusc 2012;14(2):119-129.
99. Rehder KJ, Turner DA, Bonadonna D, Walczak RJ, Rudder RJ, Cheifetz IM. Technological advances in extracorporeal membrane oxygenation for respiratory failure. Expert Rev Respir Med 2012; 6(4):377-384.
100. Maclaren G, Combes A, Bartlett RH. Contemporary extracorporeal membrane oxygenation for adult respiratory failure: life support in the new era. Intensive Care Med 2012;38(2):210-220.

Discussion

Hess: How do you manage the ventilator when a patient is on ECMO?

Turner: Specific ventilator guidelines are difficult to offer, as every patient is different. However, a few key principles can help guide management. The overall goal of ECMO is to provide adequate gas exchange while avoiding "toxic" ventilator support, and thus minimizing the risk of VILI. A simplistic way of thinking about the VV ECMO system is as a "third lung" that's used for gas exchange while allowing the patient's lungs to "rest." Overall, you want to choose settings that provide adequate (not ideal) gas exchange and minimize injury. Ventilator support is a balance between adequate gas exchange, keeping the lungs open to potentially facilitate a shorter ECMO course, and avoiding "toxic" settings.

Hess: So why not just turn off the ventilator?

Turner: In most circumstances, clinicians manage the ventilator with the

goal of maintaining lung recruitment and keeping the lung open. For any given patient this may require minimal support, and in these patients some would advocate extubation instead of turning off the ventilator. In some circumstances it's feasible to extubate, with or without NIV [noninvasive ventilation].

MacIntyre: These VV ECMO systems are really good at clearing CO_2—you can manage CO_2 almost entirely—but VV ECMO is borderline on oxygenation support, so you may not be able to get the ventilator off. Oxygenation is probably going to be a bigger problem than CO_2.

Turner: I agree. With VV ECMO the lungs contribute to gas exchange, although to a variable degree, and many patients will have oxygen saturations in the mid-to-upper 80s. The amount you're able to decrease the ventilator depends on the balance between the patient's lungs and the ECMO flow characteristics. Our experience has been that, in most circumstances, VV ECMO patients do need the ventilator, but there have been reports of patients—especially patients being bridged to lung transplantation—who can tolerate tracheostomy collar or even extubation to NIV or room air.

Kallet: We have a fellow at University of California San Francisco who trained at Michigan and had a lot of ECMO experience during the H1N1 outbreak. An interesting thing she pointed out is that the younger patients who were hyperdynamic didn't seem to do as well in terms of oxygenation. That's basically what Neil said about CO_2 not being a problem. They're hyperdynamic so the pump machine couldn't keep up with the oxygenation demands, but older people whose hearts couldn't handle the pulmonary vascular resistance from ARDS had a lower cardiac output and seemed to do much better on ECMO.

Turner: Yes, oxygenation is sometimes an issue in VV ECMO patients who are hyperdynamic with good cardiac output. However, during the H1N1 pandemic most centers did not have important issues with oxygenation in the adolescent and young adult patients on VV ECMO, but those patients did remain on the ventilator during ECMO.[1-3] Also, recently we have had several otherwise healthy adolescents and young adults supported with VV ECMO as a bridge to lung transplantation who have done quite well with oxygenation. Some were even weaned to room air on tracheostomy collar while on ECMO and awaiting their transplants. But there are certainly situations in which the balance between flow limitation and cardiac output create difficulties with oxygenation. As with any ARDS patient, the team has to decide on the oxygenation target and how to achieve it.

Gajic: You didn't mention VA ECMO much. In the context of ARDS, aside from transplantation, very few patients really need VV ECMO. However, the hype about ECMO in our institution facilitated the access of medical critically ill patients to life-saving VA ECMO in specific conditions, such as potentially reversible, severe biventricular failure from any cause where early VA ECMO might prevent multi-organ failure. What about adult VA ECMO? I think that's where the field should be going; VV ECMO could be a distraction, outside lung transplant.

Turner: You're right. The discussion has been primarily about VV ECMO for respiratory failure, but there are potentially important applications for VA ECMO in neonatal, pediatric, and adult patients. One of the benefits of developing an adult ECMO program, whether it starts as a VV or VA program, is that expansion to include other ECMO modalities is possible.

Schmidt: My question is about resource utilization. Right now for ARDS patients you need one nurse for two patients, one doctor for however many patients, and one RT [respiratory therapist] for a whole unit. Right now, at least at Massachusetts General Hospital, it's one-to-one RT coverage, and many providers concentrating on one patient. Can we do this with ECMO? How many patients can we really do? Or are we getting better results from the ECMO patients because we can't really take care of the rest?

Turner: Resource utilization is an important consideration. With some of the new and simplified ECMO systems, a single dedicated ECMO specialist for each ECMO pump may not be needed. In centers that use RTs as ECMO specialists, some are staffing these simplified ECMO systems with the RTs in the units. Obviously, an ECMO program requires an increase in staffing, but it doesn't necessarily have to be one ECMO specialist for every ECMO pump. As for nursing implications, most of these patients are already staffed one-to-one. One key difference is with awake and ambulatory ECMO patients. Substantial resources are required to ambulate these patients, including several members of the multidisciplinary team. However, preliminary data suggest that in some circumstances the improved outcomes from rehabilitation in these ECMO patients for a given hospitalization may actually decrease overall resources utilized.

Kacmarek: We still use a one-to-one RT-to-ECMO-patient ratio if there's only one ECMO system operational in the unit, but we do cohort patients, so if we have multiple patients on ECMO, one RT can easily take care of two patients, particularly with the new systems. It's made a difference,

but we have not yet gotten to the point where the RT who already manages 5 to 7 other patients in the unit is the only person responding to the ECMO patient. Is that what you're doing?

Turner: We use that same model for our simplified VV ECMO systems. An RT is assigned to the ECMO patient and potentially other patients in the same pod, but there are other RTs assigned to manage the remainder of the ICU.

Kacmarek: We have gotten to a point where now almost 25% of our RT staff is capable of manning the ECMO system. We're moving more into the management of cardiac patients. This year we will do about 35 patients, 30 of whom will be cardiac patients, with VA ECMO as the primary approach.

Turner: Our number of RTs trained to manage our ECMO systems also continues to grow, as do our number of annual ECMO patients. Overall, our patients are evenly distributed between cardiac and non-cardiac ECMO cases.

Kacmarek: We are doing so many fewer adult respiratory ECMO cases: 2 to 4 per year at most. And we're pretty much the same with pediatric respiratory failure cases. For respiratory failure in neonates, pediatrics, and adults our numbers have been going way down.

Turner: The data reported to ELSO show a downward trend in neonatal respiratory ECMO runs, but the annual number of pediatric respiratory ECMO runs has remained relatively stable following the increase in 2008-2009.[4] Most of the growth in respiratory ECMO over the past several years has been in adult patients.

MacIntyre: A few years ago there was a lot of interest in intracorporeal membrane oxygenation or ICMO, in which catheters are placed in the great vessels—the inferior vena cava—and you run O_2 through these tentacles. I think it was called the IVOX system, and there have been variations on it since. Where is that technology? Obviously, no pump is involved, and the membrane oxygenator is inside the body rather than outside.

Turner: There has been very little published on that in the past several years, but there are ongoing efforts to design smaller, simpler, and more efficient extracorporeal gas exchange devices.

Marini: The capacity of those systems is considerably less than the present-day ECMO systems. And the catheters, as Neil alluded to, have also been improved. But the big problem with those is diffusion: getting O_2 to cross the diffusion barrier near the catheter is difficult, so for oxygenation they lack efficiency. On the CO_2 side they're a bit better because you can strip off about as much CO_2 as needed. Usually clearance is sufficient to bring the patient off the cusp of intolerance. I think they have a potential role, but certainly attention has diverted away from them.

Berra: You showed that patients treated with ECMO after prolonged mechanical ventilation have worse outcomes. What causes the increased mortality, sepsis, or complications from ECMO?

Turner: Zabrocki[5] found that ECMO mortality was higher in pediatric patients mechanically ventilated for more than 14 days prior to ECMO cannulation. Overall survival in that study was 38% if the duration of pre-ECMO mechanical ventilation was greater than 14 days, in comparison to 56–61% in patients ventilated for less than 14 days prior to ECMO. These data suggest that the decision to use ECMO should be made prior to 2 weeks of mechanical ventilation.

Schmidt: That almost gets you into long-term ventilation: 3 weeks. If it's for 2 weeks on the ventilator, the mortality will increase. I think they're comparing apples and oranges; those are different patients. I'm not an ECMO believer, but I think it's unfair to ECMO to say that you shouldn't put somebody on it after 2 weeks of ventilation, because for someone on the ventilator for 3 weeks the mortality is also up at about 80% once they've stayed on the ventilator for 4 weeks. I think it's not a fair argument. It's not an argument against ECMO; it's an argument about ventilating too long.

Turner: An important issue here is that those data are from pediatric patients, and they also represent a change from prior studies[6,7] that found that mortality increased after approximately one week of pre-ECMO mechanical ventilation. Based on these recent data from Zabrocki,[5] it would appear that the "safe" duration of pre-ECMO mechanical ventilation may be longer than it was in the past, potentially related to our lung-protective approaches.

Kacmarek: I've recently heard in a number of presentations that in Europe they're using VV ECMO to support patients with COPD and acute respiratory failure. I have not heard of anybody in the United States who is transitioning patients from NIV to VV ECMO. Is anybody doing that in the United States?

Turner: There seems to be growing interest in earlier cannulation of selected patients, and there are people in the United States who feel that ECMO should be used earlier, especially with the newer systems, simplification of cannulation, and decreased complication rates.

Kallet: What is the infection rate, particularly from femoral-femoral cannulation? In my institution they're staying away from groin lines when-

ever possible, because of infection concerns. What are the infection stats for ECMO?

Turner: In adult patients, culture-proven infection occurs in about 20% of respiratory ECMO patients. Interestingly, infection rates in adults are higher than in neonates and pediatrics, which may be related to the traditional femoral-femoral cannulation approach in adult patients. Culture-proven infection is approximately 18% in pediatrics, and only 6% in neonates. However, our local experience has been substantially lower infection rates in our patients. For whatever reason, adults are at higher risk of culture-proven infection during ECMO, and patients with these infections have a survival of 45%, compared to 57% in those without infections.

Gajic: Have you had any experience with sterile inflammation, which can sometimes occur in these patients? We had a 20-year-old patient with acute interstitial pneumonia on ECMO who developed a leukemoid reaction, with a white blood cell count of 45,000, hyperinflammation, and fever, but he was clearly culture-negative and unlikely to be infectious. It happened toward the end of the need for ECMO support, and after the cannulas came out, 72 hours later the storm resolved. Steroids were given and all of that. Any thoughts?

Turner: The timing of the inflammatory response you describe is interesting. You certainly can have an inflammatory response related to exposure to the bypass circuit and all the foreign materials with ECMO, but usually this response follows cannulation or a circuit or component change, within 24 to 48 hours. The severity and duration of inflammatory response is difficult to predict for any given patient. However, anecdotally, this inflammatory response appears to be less with some of the newer available circuit components.

REFERENCES

1. Davies A, Jones D, Bailey M, Beca J, Bellomo R, Blackwell N, et al. extracorporeal membrane oxygenation for 2009 influenza A (H1N1) ARDS. JAMA 2009;302(17):1888-1895.
2. Turner DA, Rehder KJ, Peterson-Carmichael SL, Ozment CP, Al-Hegelan MS, Williford WL, et al. Extracorporeal membrane oxygenation for severe refractory respiratory failure secondary to 2009 H1N1 influenza A. Respir Care 2011;56(7):941-946.
3. Patroniti N, Zangrillo A, Pappalardo F, Peris A, Cianchi G, Braschi A, et al. The Italian ECMO network experience during the 2009 influenza A (H1N1) pandemic: preparation for severe respiratory emergency outbreaks. Intensive Care Med 2011;37(9):1447-1457.
4. Extracorporeal Life Support Organization. Registry report: international summary. ECMO registry of the Extracorporeal Life Support Organization (ELSO). Ann Arbor: ELSO; July 2012.
5. Zabrocki LA, Brogan TV, Statler KD, Poss WB, Rollins MD, Bratton SL. Extracorporeal membrane oxygenation for pediatric respiratory failure: survival and predictors of mortality. Crit Care Med 2011;39(2):364-370.
6. Masiakos PT, Islam S, Doody DP, Schnitzer JJ, Ryan DP. Extracorporeal membrane oxygenation for nonneonatal acute respiratory failure. Arch Surg 1999;134(4):375-379, discussion 379-380.
7. Pranikoff T, Hirschl RB, Steimle CN, Anderson HL 3rd, Bartlett RH. Mortality is directly related to the duration of mechanical ventilation before the initiation of extracorporeal life support for severe respiratory failure. Crit Care Med 1997;25(1):28-32.