

# Extracorporeal Membrane Oxygenation: Quo Vadis?

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- Introduction
- Extracorporeal Membrane Oxygenation Modalities
  - Venous-Arterial
  - Venous-Venous
  - Bi-Caval Venous-Venous
- The Extracorporeal Membrane Oxygenation System
  - Pumps
  - Circuits
  - Artificial Lungs
  - Technical Advances
- Extracorporeal Membrane Oxygenation for Respiratory Failure
  - Pre-ECMO Strategies
  - Patient Selection
    - Adults
    - CESAR Trial
    - Pediatrics
  - Pumpless Gas Exchange
    - Extracorporeal Removal of Carbon Dioxide
    - Interventional Lung Assist
    - Intravenous Gas Exchange
- Extracorporeal Membrane Oxygenation for Cardiac Failure
  - Extracorporeal Resuscitation
- Quo Vadis: Where Are We Going?

**Extracorporeal membrane oxygenation, a form of artificial circulatory support, continues to evolve beyond its well-established neonatal applications. It is often the most aggressive aspect of treatment algorithms in the management of severe respiratory and cardiac failure. While its use is relatively infrequent and executed in a small number of centers, it remains an important supportive measure while organ function is preserved and restored. Refinements in equipment and techniques continue to develop; patient-selection has changed, in adults and children, and cardiac applications have gained prominence. Key words: extracorporeal membrane oxygenation. [Respir Care 2009;54(7):948–957. © 2009 Daedalus Enterprises]**

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## Introduction

Despite a greater understanding of acute respiratory distress syndrome (ARDS), and improved approaches to mechanical ventilation and accompanying therapies, there remains a subset of patients who develop severe forms of ARDS for whom the clinician must consider nonconventional strategies. Similarly, advanced approaches to the management of patients in cardiac failure may also be required. Extracorporeal membrane oxygenation (ECMO), a modified form of cardiopulmonary bypass, is one such strategy that has been used to support organ function and provide time for the disease process to halt and, hopefully, reverse. Though early attempts at using ECMO in adults were unsuccessful,<sup>1</sup> the neonatal experience has led to a firm understanding of and improvement in ECMO techniques. The aim of this paper is to review ECMO techniques, to describe the application of ECMO in pediatric and adult cardiopulmonary failure, and to present an update in technology and patient applications.

### Extracorporeal Membrane Oxygenation Modalities

ECMO is an invasive technique in which blood is drained from the venous system, pumped through an artificial organ (oxygenator), and then re-infused to the patient.<sup>2</sup> This process augments the exchange of CO<sub>2</sub> and O<sub>2</sub> and permits the reduction of potentially injurious ventilator settings. There are 2 methods: venous-arterial, which supports both cardiac and pulmonary function; and venous-venous, which supports pulmonary function.

#### Venous-Arterial

In venous-arterial ECMO oxygen-depleted blood is drained from the right side of the heart and oxygenated blood is pumped back into the systemic side, which both augments gas exchange and supports cardiac function. Venous-arterial ECMO is more commonly used in neonates, particularly when both heart and lung function is compromised. This is accomplished via cannulation and ligation of the carotid artery, which is tolerated in neonates because collateral circulation develops. Venous-arterial ECMO is used to support patients in cardiac failure—a growing use of ECMO in neonates, pediatrics, and adults. The cannulation route may be transthoracic, as in patients who have undergone palliative and corrective cardiac surgery. In the immediate postoperative period the chest can be easily accessed, with the right atrium cannulated for drainage and the aorta for reinfusion.

#### Venous-Venous

Venous-venous ECMO is the preferred route for the management of severe respiratory failure, because carotid

blood flow is preserved.<sup>3</sup> The cannulation site depends on patient size. In older children and adults, the drainage of oxygen-depleted blood is from one or both femoral vessels, and the re-infusion of oxygenated blood is through the right-internal jugular vein.<sup>4</sup> The return of oxygenated blood to the right side of the heart, which then traverses the pulmonary system, provides sufficient gas exchange. Optimizing venous drainage is important to ensuring optimal ECMO flow. Adults may require drainage cannulas in both femoral vessels (the venous-venous-venous configuration). A double-lumen venous-venous cannula allows drainage and reinfusion through the right internal jugular vein. When properly placed, adequate gas exchange occurs and only one vessel is affected; however, weight and flow limitations exist.

#### Bi-Caval Venous-Venous

Until recently, ECMO via double-lumen venous-venous cannula was limited to infants and small children, but a series of double-lumen cannulas has been developed that may expand double-lumen venous-venous cannula applications to older children and adults.<sup>5</sup> The single cannula contains 2 channels, which provide simultaneous drainage of venous blood and reinfusion of arterial blood. The catheter is surgically placed into the internal jugular vein, and drainage occurs in 2 locations, with ports at upper and lower portions of the vena cava, thereby draining blood from the upper and lower body. The reinfusion port of the arterial channel is positioned such that oxygenated blood is streamlined into the venous system in the right atrium. In theory this cannula will better separate drainage and reinfusion, thereby allowing more oxygenated blood to be introduced to the systemic circulation. This new cannula is potentially easier to insert, requires the use of only one vessel, and eliminates the complications associated with femoral cannulation. It is anticipated that this catheter will further simplify the ECMO technique, and Food and Drug Administration approval is imminent.

### The Extracorporeal Membrane Oxygenation System

#### Pumps

ECMO systems are typically modified cardiopulmonary-bypass machines consisting of a single pump that is either centrifugal or occlusive. Centrifugal pumps propel blood forward through the ECMO circuit by means of a cone-shaped pump head that spins blood outward with centrifugal force.<sup>6,7</sup> An occlusive (roller) pump moves blood forward by compressing the tubing and thus propelling the blood. Centrifugal pumps, which were initially used as ventricular-assist devices, are being used at many ECMO centers. A centrifugal pump can result in a more compact

ECMO system and requires less circuitry, but older-generation centrifugal pump heads require periodic replacement. A roller-pump system requires more tubing because it requires a venous reservoir that receives gravity-fed blood, and the roller-head tubing is subject to wear and tear. Centrifugal pumps are less traumatic to blood cells.<sup>7</sup>

### Circuits

Customized circuits are used for ECMO, with the basic design consisting of a loop of tubing with designated drainage and reinfusion sides. The tubing dimensions are based on patient size. An artificial lung or diffusion membrane is positioned between the 2 sides and is composed of either silicone or a network of micro-porous polypropylene hollow-fibers, both with their advantages and disadvantages.

### Artificial Lungs

The silicone membrane has been the principal device used for ECMO for many years, and functions well for prolonged periods. These devices take longer to prime and de-air, and a selection of graduated size and surface area has to be maintained to support the full range of patient sizes. Hollow-fiber membranes are easier to de-air and prepare for clinical application but have not had the longevity of silicone-membrane oxygenators because of their tendency to “wet-out” or become saturated to the point that plasma leaks. Gas exchange takes place via diffusion across the fibers.<sup>8</sup>

The adjunct equipment that completes the ECMO system includes a water pump, which is connected to the heat-exchanger for temperature regulation, and monitors that measure flow, venous and arterial saturation, hematocrit, and other variables. ECMO systems also integrate monitors that measure circuit pressures that indicate changes in circuit resistance. Additional safety features include continuous monitoring of venous drainage and air detection, both with direct feedback to the pump. ECMO systems have battery supplies and are portable so that patients can be transported for diagnostic and interventional procedures.

### Technical Advances

Cardiopulmonary-bypass systems modified for ECMO support have improved over the years, and newer generations continue to be developed.<sup>9</sup> Though roller pump designs have not changed much, centrifugal systems have been refined. The main focus in modifying centrifugal technology has been to further reduce blood-cell trauma and hemolysis. Newer systems have better designed pump heads and better flow dynamics.<sup>10,11</sup> There is less turbulence and stagnancy, and the transfer of power from the

magnetic driver is greatly improved, resulting in less blood-cell trauma. Other purported benefits include improved longevity and relatively compact and portable consoles.

Hollow-fiber membrane technology has improved with the development of nonmicroporous membranes.<sup>10,11,12</sup> The fibers in these devices are coated with polymethylpentene, which greatly reduces plasma leakage.<sup>13,14</sup> They are arranged in a unique network: blood flow, gas flow, and flow through the heat-exchanger occur perpendicular to each other for maximum efficiency. Polymethylpentene membranes have low hemodynamic resistance and high flow capability.<sup>11</sup> A wide range of patients can be supported with these membranes, and the need to maintain a series of devices for different-size patients is eliminated. Additional benefits include easy preparation and de-airing, smaller circuit volume, and longevity.<sup>14</sup>

## Extracorporeal Membrane Oxygenation for Respiratory Failure

### Pre-ECMO Strategies

Because of the invasive nature of ECMO and associated risks, the decision to initiate ECMO is judiciously considered after other clinical strategies and therapies have been attempted and optimized.<sup>15</sup> ECMO has provided critical-care clinicians somewhat of a “safety net” as an adjunctive strategy in the management of severe ARDS. Inhaled nitric oxide, prone positioning, high-frequency oscillatory ventilation and other advanced ventilator modes, lung-recruitment methods, and pharmacologic agents have all been trialed, with various success, and are considered part of pre-ECMO management.<sup>16</sup> Hemmila and Napolitano comprehensively reviewed treatment options in the care of the patient with severe respiratory failure.<sup>17</sup>

### Patient Selection

There is no definitive consensus on when ECMO should be initiated in the care of children and adults with severe ARDS. If advanced treatments fail, ECMO is often the only remaining option and ECMO has to be factored into treatment decisions to avoid delayed transfer to an ECMO center. A ratio of  $P_{aO_2}$  to fraction of inspired oxygen ( $P_{aO_2}/F_{IO_2}$ )  $< 200$  mm Hg is one criteria used to identify ARDS, and in severe cases the  $P_{aO_2}/F_{IO_2}$  may be  $< 75$  mm Hg and mortality risk exceeds 80%—a point when ECMO is considered.<sup>18</sup> It is important to note that ECMO is supportive and not therapeutic, and that the most important criteria when considering ECMO are that the underlying disease process is reversible and that the risks associated with ECMO do not worsen the patient’s condition.

There continues to be deliberation regarding contraindications to ECMO, and some experienced ECMO centers

are willing to “push the envelope.” The decision to initiate ECMO is not an easy one, as death is often the alternative. Nonetheless, fundamental contraindications exist. The outcome is likely to be poor if ECMO is used in a patient who has had a protracted ventilator course with constant high inflation pressure (ie, a less lung-protective approach). However, ventilation modes and alveolar-recruitment strategies continue to evolve and provide the clinician with more options. The likelihood of hospital survival lessens if ECMO is used in patients with incurable diseases and existing neurologic impairment, and in elderly patients with marginal general health.<sup>19</sup> Since ECMO requires anticoagulation, patients who are prone to hemorrhage or who may have other incompatibilities to anticoagulation therapy may not be suitable candidates.

As advances in the medical and surgical management of critically ill children and adults have evolved, intensive care units have been presented with more complex cases that prompt the clinician to explore all options. The advent of alternative ECMO modalities, such as pumpless ECMO and ECMO during cardiopulmonary resuscitation (discussed below), will probably result in an ongoing deliberation as to which patients should be offered ECMO.

## Adults

The use of ECMO to support adults with severe respiratory failure is infrequent and done in a relatively small number of centers, so randomized controlled trials have been difficult to conduct and much of the evidence has come from case series. The earliest clinical trials to determine if ECMO was beneficial in adults with ARDS were undertaken when ECMO technology was in its early development, there was not a firm understanding of ARDS pathophysiology, and the studies yielded poor results.<sup>1</sup>

A 14-year review of ECMO, conducted at the University of Michigan,<sup>19</sup> described 255 adults who received ECMO, among 405 patients identified as having severe ARDS by set criteria, including a  $P_{aO_2}/F_{IO_2} < 100$  mm Hg, and who were considered to have an 80–100% mortality risk. In this group of patients 138 had primary lung injury, 117 had secondary lung injury, 67% were successfully transitioned off ECMO, and 52% survived to discharge. Those researchers identified pre-ECMO variables that greatly influenced survival, including age, sex,  $pH < 7.10$ ,  $P_{aO_2}/F_{IO_2}$ , and days of mechanical ventilation. The study affirmed that ECMO should be included in the treatment algorithm for ARDS in adults, and that it preserves life while the body repairs and restores organ functions. Other observations included that ECMO technology and ventilator strategies were evolving during that period and continue to improve.

Another review, from the University of Freiberg, Germany,<sup>20</sup> described similar survival rates in adults with

ARDS supported with ECMO. That 9-year review described 62 (of 245 patients with ARDS) who were supported with ECMO. The ECMO group had a 55% survival rate, and the non-ECMO group had a 61% survival rate. Those authors proposed that ECMO is an important adjunct in the care of selected patients with ARDS and should be maintained as an option.

ECMO has also been an important aid in managing severe graft dysfunction and failure following lung transplantation. In a series by Mason et al,<sup>21</sup> ECMO was used in 22 post-lung-transplant patients, of 427 lung-transplant recipients in a 15-year period. The principal need for ECMO was early postoperative failure of the graft, and the survival rate at one year was around 40%.

The Extracorporeal Life Support Organization (ELSO), an association of health-care professionals concerned with the care of patients supported with ECMO, maintains an international registry.<sup>22</sup> The number of adults supported with ECMO for respiratory failure reported in the ELSO registry is about 80 cases annually, with an overall survival rate of 50%. In the most recent 10-year period the number of cases reported has gradually increased, to about 100 cases annually, and the survival rate is slightly over 50% (Fig. 1).

## CESAR Trial

Long-awaited results from the Conventional Ventilatory Support Versus ECMO for Severe Respiratory Failure (CESAR) trial, will, hopefully, clarify the utility of ECMO in ARDS and its impact on outcomes.<sup>23</sup> The CESAR trial, a thoughtfully designed and ambitious randomized controlled trial conducted in the United Kingdom, aims to determine whether, “for patients with potentially reversible respiratory failure, ECMO: (1) will increase the rate of survival without disability by 6 months post-randomization, and (2) will be cost-effective from the viewpoints of the National Health System and society when compared to conventional ventilatory support.”<sup>23</sup> Severe respiratory failure and entry criteria for the study were defined as a Murray score  $> 3.0$  or uncompensated hypercapnia ( $pH < 7.20$ ). The study has concluded, and preliminary data presented at critical-care and ECMO forums suggest that ECMO may validate the first hypothesis and be superior to conventional ventilation in improving outcomes.<sup>24</sup> It remains to be seen if this will warrant an increase in ECMO utilization for respiratory failure in adults, and a need for more ECMO centers.

## Pediatrics

The position of ECMO in the treatment algorithm for severe ARDS in children is even less clear than in adults. Again, there have been few studies, and most have been

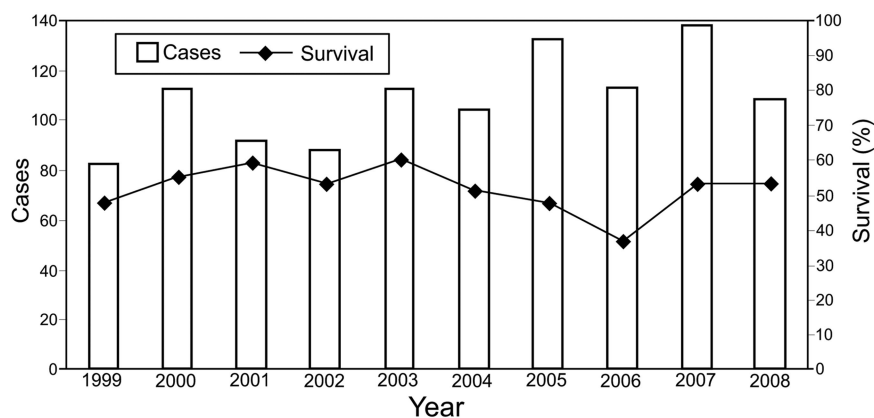


Fig. 1. Ten-year trend in the use of extracorporeal membrane oxygenation in adults with respiratory failure. (From Reference 22, with permission.)

retrospective reviews. The Pediatric Study Group set out to identify the role of ECMO in children with severe respiratory failure.<sup>25</sup> They compared an ECMO group to a non-ECMO group, based on the Pediatric Risk of Mortality score, and the ECMO cohort had better survival. Thirty-two centers contributed to the study, which included 331 patients. Only 50% of the centers had ECMO capabilities, and only 38 patients were supported with ECMO. The intention of the research was to set the stage for a randomized controlled trial, but none has been conducted.

In a small series by Masiakos et al,<sup>26</sup> 34 patients, with a mean age of 22 years and with severe ARDS ( $P_{aO_2}/F_{IO_2} < 70$  mm Hg) were supported with ECMO. The overall survival rate was 53%, and patients with isolated pulmonary processes and without other organ involvement had the best survival.

Maclaren et al<sup>27</sup> reported the use of ECMO in 45 children with refractory septic shock; the overall survival rate was 47%. Eighteen patients had cardiac arrest, and ECMO was initiated during cardiopulmonary resuscitation.

ECMO use has increased in children with life-threatening methicillin-resistant *Staphylococcus aureus*. In a retrospective study,<sup>28</sup> 45 children (median age 2.4 y) were supported with ECMO. Fifty percent of those cases occurred after 2005. Survival was related to age; children in the 1–4 year-old group had the best survival (65%). No common pre-ECMO assessments were associated with a higher risk of death.

Respiratory failure associated with hematopoietic stem-cell transplantation continues to challenge critical-care teams, and the decision to utilize extreme measures such as ECMO is very difficult to reach. A review of ECMO use in this population suggested that it is infrequently used, survival is quite poor, and its use should be considered cautiously.<sup>29</sup> Similarly, children in respiratory failure who have pre-existing immune-compromised conditions do not have better survival with ECMO.<sup>30</sup>

Though the decision to use ECMO in pediatrics may be difficult, whether to offer a second course of ECMO is even more of a dilemma. In a review by Fisher et al,<sup>31</sup> children who underwent a second course of ECMO had a survival rate similar to those who completed only one course. The incidence of a repeat course was only 3% in that study, and no specific characteristics were identified as more amenable to a second course. However, it was suggested that younger patients without renal dysfunction or other complications had a better chance of survival.

Data from the ELSO registry suggest that the use of ECMO for pediatric respiratory failure has had a slight annual increase.<sup>22</sup> On average about 230 cases have been reported annually in the last 10 years, and the survival rate has remained consistent at 50–55% (Fig. 2). The patients in this category of the registry have a more heterogeneous group of diagnoses and a broad age range (> 30 months to < 18 years). It is unlikely that a CESAR-like trial could be conducted in children, so reliance on trends identified in the ELSO registry and reported case series will have to suffice.

## Pumpless Gas Exchange

### Extracorporeal Removal of Carbon Dioxide

Extracorporeal  $CO_2$  removal (also known as pumpless arteriovenous  $CO_2$  removal and pumpless extracorporeal lung assist) is an adaptation of traditional ECMO in which the pump is eliminated. The technique involves the creation of an extrapulmonary arterial-venous shunt in which blood is directed through a membrane.<sup>32</sup> The patient's native cardiac output is the pump in this simplified extracorporeal circuit, and gas exchange is augmented by diffusion.

The hypothesis of pumpless arteriovenous  $CO_2$  removal is that gas exchange can be greatly augmented in patients

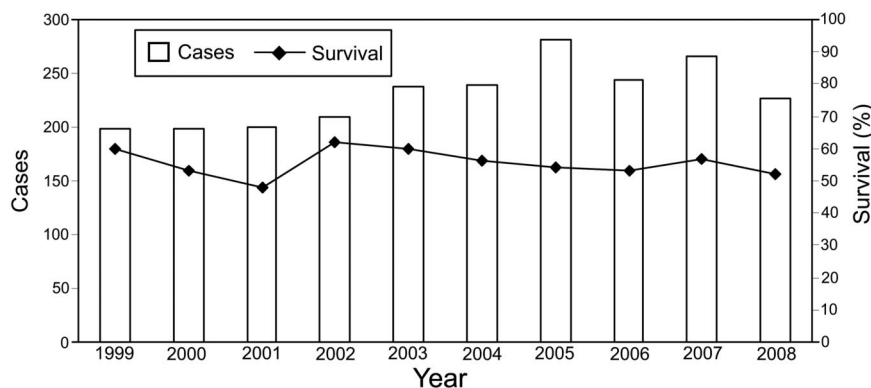


Fig. 2. Ten-year trend in the use of extracorporeal membrane oxygenation in children with respiratory failure age > 30 months to 18 years. (From Reference 22, with permission.)

with respiratory failure so that a less injurious and more protective mechanical ventilation strategy can be employed.<sup>33</sup> Earlier studies, though they demonstrated effective CO<sub>2</sub> removal, failed to show a significant advantage over a protocolized approach to mechanical ventilation, and bleeding complications were common.<sup>34</sup>

Extracorporeal CO<sub>2</sub> removal has been applied in patients with profound hypercarbia and respiratory acidosis refractory to conventional therapies. One benefit of pumpless arteriovenous CO<sub>2</sub> removal is the simplification of the ECMO system by elimination of the pump and large mechanized systems, which reduces the interaction of blood and foreign surfaces and minimizes the associated technical complications and other risks, such as hemolysis.

Conrad et al<sup>35</sup> used pumpless CO<sub>2</sub> removal to manage extreme hypercarbia (P<sub>aCO<sub>2</sub></sub> 90–186 mm Hg) and respiratory acidosis (pH 6.96–7.09) in 4 children with life-threatening asthma, and found that it obviated injurious ventilator pressure and allowed time for aggressive treatment of airflow obstruction.

### Interventional Lung Assist

Recently a pumpless CO<sub>2</sub> removal technique, described as interventional lung assist, was developed, based on a device brand-named the iLA (interventional lung assist) membrane ventilator (Novalung, Talheim, Germany),<sup>36</sup> which uses polymethylpentene to seal the hollow fibers. Gas exchange occurs via diffusion. The low resistance properties make it ideal for pumpless extracorporeal CO<sub>2</sub> removal.

The technique, well described by Meyer et al,<sup>37</sup> begins with vascular access via percutaneous cannulation of the femoral vessels: usually an artery in one leg and a vein in the other. Blood flow is passive and moves from the arterial cannula to the inlet of the membrane, and is directly influenced by the arterial blood pressure. Approximately 20% of the cardiac output is diverted through the device.

An average 70 mm Hg driving pressure is required. Blood exiting the membrane, with improved P<sub>CO<sub>2</sub></sub> and P<sub>O<sub>2</sub></sub>, is reinfused into the femoral vein, where it rejoins the remaining 80% of the circulation in the venous system. The principal objective is CO<sub>2</sub> removal, which can be regulated by titrating the gas flow rate supplied to the membrane. Improvements in oxygenation are variable and are affected by the inlet P<sub>aO<sub>2</sub></sub> and its subsequent mixing with venous blood, and the contribution of the patient's lung physiology.

An 8-year observational study conducted by Bein and colleagues<sup>38</sup> examined the application of interventional lung assist in 90 patients with severe respiratory failure who failed conventional interventions. The patients had P<sub>aO<sub>2</sub></sub>/F<sub>IO<sub>2</sub></sub> < 55 mm Hg, severe hypercarbia, and respiratory acidosis. Two hours after initiation of interventional lung assist there was significant improvement in P<sub>aO<sub>2</sub></sub>/F<sub>IO<sub>2</sub></sub>, P<sub>aCO<sub>2</sub></sub>, pH, and overall hemodynamic function, which allowed a decrease in vasopressor therapy. The survival rate was 41%, and poor outcomes were attributed to patient selection, because the study included patients with irreversible cancer and patients with poor hemodynamic profiles. There was a 24% complication rate, and compromised limb perfusion was the main culprit. The study demonstrated that interventional lung assist improves gas exchange, particularly CO<sub>2</sub> removal. The complications prompted an evaluation of cannula size to minimize limb damage. Successful application of interventional lung assist has also been described in other small case series, including as a bridge to lung transplantation<sup>39</sup> and in ARDS.<sup>40</sup>

Though interventional lung assist offers a simplified approach to ECMO, it is unclear what use it may have in severe respiratory failure or if it is superior to traditional ECMO or other modes of mechanical ventilation.<sup>41</sup> Severe hypercarbia without hypoxemic respiratory failure seems to be the primary indication for interventional lung assist, but few respiratory-failure scenarios present in that man-

ner, and a stable and fairly robust cardiac output is needed to propel the blood through the interventional-lung-assist membrane.

### Intravenous Gas Exchange

Another device for enhancing gas exchange is the Hatler Catheter (ALung Technologies, Pittsburgh, Pennsylvania), which is an intravascular catheter that contains a hollow fiber membrane that removes carbon dioxide and increases oxygenation.<sup>42</sup> The catheter has a pulsating balloon that guides red blood cells through the fibers where gas exchange occurs.<sup>43</sup> This respiratory-assist catheter is controlled by a console that inflates and deflates the balloon and supplies oxygen. The goal is to improve gas exchange by providing 50% of the gas-exchange requirement, so that a gentle ventilatory approach may be employed.

An earlier device, the intravenacaval oxygenator and carbon-dioxide removal device (IVOX) had a similar architecture. It can remove 30% of CO<sub>2</sub> produced.<sup>44</sup> Safety and efficacy trials of the IVOX were favorable.<sup>45</sup>

The above-described devices are innovative but are still experimental, and it is uncertain whether they will fit into the treatment pathway for severe respiratory failure.

### Extracorporeal Membrane Oxygenation for Cardiac Failure

Despite advances in medical treatment and surgical intervention in patients with cardiac disease, they are sometimes insufficient and warrant a more aggressive approach. The use of extracorporeal devices in the management of cardiac failure is evolving rapidly; new circulatory-assist devices are being refined and becoming available for adult and pediatric patients. ECMO continues to play an important role in the management of the failing heart, as it tends to be readily available, is proven technology, and aids in restoring and stabilizing organ function.<sup>46</sup> However, ECMO has its limitations: it cannot be used for extensive periods, the patient has to remain in bed and often motionless, and there are associated complications.

ECMO has been used as an extension of cardiopulmonary bypass in adults who have undergone open-heart surgery but had persistent postoperative myocardial dysfunction.<sup>47</sup> Small cases series have reported survival rates of around 50%.<sup>48</sup> ECMO has also been used preoperatively and to support patients with fulminant myocarditis.<sup>49</sup>

A prominent use of ECMO is as a bridge to other forms of mechanical circulatory support and subsequent bridge to heart-transplant evaluation (“bridge-to-decision”) or directly to transplantation (“bridge-to-transplant”).<sup>48,50,51</sup> ECMO can stabilize the patient while an appropriate and more long-term mechanical circulatory device or other in-

tervention is selected. Mechanical circulatory-support devices have become more readily available and understood in adults, and with the right selection criteria can be initiated without interim ECMO. However, ECMO can be deployed fairly quickly and can rapidly stabilize a patient with acute unanticipated heart failure.

ECMO differs from ventricular-assist devices in that an oxygenator is present and the vascular access is via peripheral vessels. ECMO is a modification of cardiopulmonary bypass and requires adjunct equipment. A ventricular-assist system is simpler: it consists of a pump and driver, and has a substantially shorter circuit. Whereas ECMO can support heart and lung function, the main role of a circulatory-assist device is to compensate for the heart’s inability to pump. The earliest ventricular-assist device was a centrifugal pump that required intracardiac cannulation. This technique is still used, and centrifugal-pump technology has greatly improved.<sup>7</sup> Other forms of cardiac mechanical support include volume-displacement pumps and axial-flow pumps,<sup>52</sup> an extensive discussion of which is beyond the scope of this paper.

ECMO has been used in the management of cardiac dysfunction associated with congenital heart disease, and it continues to be a vital tool while newer circulatory devices are being developed and evaluated in this population.<sup>53</sup> ECMO has been used in the preoperative period, as a bridge to circulatory assist and transplant,<sup>54,55</sup> and during interventional procedures.<sup>56</sup> The survival rates in case series have been as high as 65%, and early ECMO initiation seems to improve outcomes.<sup>54-56</sup>

There has been a steady rise in the number of cardiac cases reported to the ELSO registry, and in all age groups.<sup>22</sup> In the period 1999 to 2008 there was an average of 126 pediatric cardiac cases per year reported, as compared to the previous 10-year period, in which the average was 72, and the survival rate has steadily improved to the current level of 60% (Fig. 3). Adult cases have also increased: there was an average of 115 cases reported annually in the most recent 5-year period, as compared to the previous 5-year period, in which there were an average of 50 cases per year.

### Extracorporeal Resuscitation

ECMO as an adjunct to CPR (E-CPR) has gained considerable footing in critical-care units and emergency settings. E-CPR is the rapid deployment of ECMO to patients undergoing CPR or who have marginally responded to standard resuscitation measures. E-CPR is often used when the cause of the cardiac arrest is unknown and there is a reasonable assumption that the overall condition is treatable and reversible. Successful E-CPR outcomes are in large part related to patient selection, but also to the immediate availability of the ECMO system, the ECMO spe-

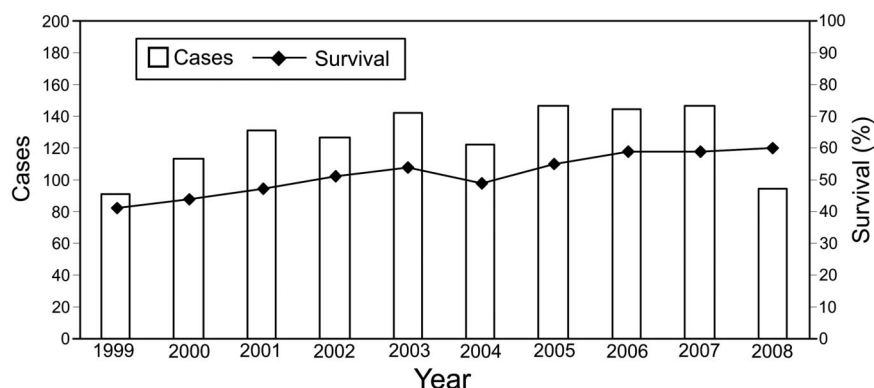


Fig. 3. Ten-year trend in the use of extracorporeal membrane oxygenation in children (1–16 y old) with cardiac failure. (From Reference 22, with permission.)

Table 1. Summary of Case Series of Extracorporeal Membrane Oxygenation During Cardiopulmonary Resuscitation

First Author	Population	Cases (n)	Hospital Survival (%)	Study Period (y)
Alsoufi <sup>58</sup>	Pediatric	18	30	5
Mégarbone <sup>59</sup>	Adult	17	24	2
Thourani <sup>60</sup>	Pediatric	15	75	3
Hannan <sup>61</sup>	Pediatric	103	55	9
Huang <sup>62</sup>	Pediatric	27	41	3
Chen <sup>63</sup>	Adult	135	34	13

cialist to operate it, the surgical infrastructure (including personnel and equipment to rapidly gain vascular access), and the supporting intensive-care staff that ensure quality CPR is maintained while ECMO is initiated.<sup>57</sup>

The ELSO registry began including the category E-CPR in 1992, and since then over 1,600 cases have been reported across all age categories, and the overall survival-to-discharge rate has been around 36%. The evidence supporting E-CPR has mainly been reported by single centers, and the survival rate range has been 30–40% (Table 1).

Chan and colleagues conducted a critical look at E-CPR in infants and children with heart disease.<sup>64</sup> They used ELSO data to identify risk and survival trends, and found that overall hospital survival was 42%, and pre-ECMO factors including severe acidosis, renal dysfunction, and low systemic perfusion throughout the ECMO course were associated with lower survival. Chan et al did not identify a clear set of criteria for E-CPR, but suggested that early use prior to arrest, rapid deployment of resources, and the quality of the CPR are important factors in maximizing the chance of survival without disability.

It is unclear how predominant E-CPR will become and if specific indications for its use will emerge.<sup>65</sup> The American Heart Association Guidelines for Cardiopulmonary Resuscitation and Emergency Cardiovascular Care<sup>66</sup> include consideration of E-CPR for in-hospital cardiac arrest if the arrest period is brief and the condition is reversible and amenable to other interventions.

It remains to be seen if E-CPR will become a standard in certain cardiovascular or emergency programs. A hospital survival rate of 30–40% from conditions that would probably result in death is somewhat compelling.<sup>67</sup>

Well-established ECMO centers can adapt existing equipment and resources for rapid deployment, and can refine the process and improve the response time of E-CPR.<sup>68</sup> Though standard ECMO systems are mobile, they tend to be bulky and heavy. Some centers have devised systems that are more portable, lightweight, and very compact, and include a centrifugal pump and membrane oxygenator.<sup>69</sup> More compact and portable devices that can be easily deployed to most settings are also in development. The Cardiohelp (Maquet, Bridgewater, New Jersey) is one such device; it consists of an all-inclusive hybrid pump/oxygenator that is useful in most ECMO situations, including transport.<sup>70</sup> As portable systems become clinically tested and readily available, they may be suitable for E-CPR. The ideal scenario would be to have a rapidly deployable system that aids resuscitation and then provides the necessary support while additional interventions are contemplated.

### Quo Vadis: Where Are We Going?

ECMO continues to be an important rescue modality in the management of severe cardiopulmonary failure in chil-



dren and adults, and the hospital survival rate is favorable. Clinicians can explore the boundaries of advanced interventions and techniques with ECMO. Research on improving ECMO technology will focus on streamlining systems that permit rapid initiation with enhanced safety and flexibility.

## REFERENCES

- Zapol WM, Snider MT, Hill JD, Fallat RJ, Bartlett RH, Edmunds LH, et al. Extracorporeal membrane oxygenation in severe acute respiratory failure. *JAMA* 1979;242(2):2193-2196.
- Skinner SC, Hirschl RB, Bartlett RH. Extracorporeal life support. *Semin Pediatr Surg* 2006;15(4):242-250.
- 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.
- Rich PB, Awad SS, Crotti S, Hirschl RB, Bartlett RH, Schreiner RJ. A prospective comparison of atrio-femoral and femero-arterial flow in adult venovenous extracorporeal life support. *J Thorac Cardiovasc Surg* 1998;116(4):628-632.
- Avalon Laboratories. Avalon elite bi-caval dual lumen catheter (product information sheet). [http://www.avalonlabs.com/downloads/infosheets/bicaval\\_dl\\_product\\_sheet.pdf](http://www.avalonlabs.com/downloads/infosheets/bicaval_dl_product_sheet.pdf). Accessed May 15, 2009.
- Ichikawa S, Nosé Y. Centrifugal blood pumps for various clinical needs. *Artif Organs* 2002;26(11):916-918.
- Curtis J, Walls JT, Wagner-Mann CC, Schmaltz RA, Demmy TL, McKenney CA, Mann FA. Centrifugal pumps: description for devices and surgical techniques. *Ann Thorac Surg* 1999;68(2):666-671.
- Jegger D, Tevaearai HT, Mallabiarrena I, Horisberger J, Seigneul I, von Segesser LK. Comparing oxygen transfer performance between three membrane oxygenators: effect of temperature changes during cardiopulmonary bypass. *Artif Organs* 2007;31(4):290-300.
- Wang S, Kunselman AR, Meyers J, Ündar A. Comparison of two different blood pumps on delivery of gaseous microemboli during pulsatile and nonpulsatile perfusion in simulated infant CPB model. *ASAIO J* 2008;54(5):538-541.
- 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.
- Formica F, Avalli L, Martino A, Maggioni E, Muratore M, Ferro O, et al. Extracorporeal membrane oxygenation with a poly-methylpentene oxygenator (Quadrox D). The experience of a single Italian centre in adult patients with refractory cardiogenic shock. *ASAIO J* 2008;54(1):89-94.
- Thiara APS, Noel TN, Kristiansen F, Karlsen HM, Fiane AE, Svennevig JL. Evaluation of oxygenators and centrifugal pumps for long-term pediatric extracorporeal membrane oxygenation. *Perfusion* 2007;22(5):323-326.
- Khosbin E, Westrope C, Pooboni S, Machin D, Killer H, Peek GJ, et al. Performance of polymethyl pentene oxygenators for neonatal extracorporeal membrane oxygenation: a comparison with silicone membrane oxygenators. *Perfusion* 2005;20(3):129-134.
- Koshbin E, Roberts N, Harvey C, Machin D, Killer H, Peek GJ, et al. Poly-methyl pentene oxygenators have improved gas exchange capability and reduce transfer requirements in adult extracorporeal membrane oxygenation. *ASAIO J* 2005;51(3):281-287.
- Beiderlinden M, Eikermann M, Boes T, Breitfeld C, Peters J. Treatment of severe respiratory distress syndrome: role of extracorporeal gas exchange 2006;32(10):1627-1631.
- Kopp R, Kuhlen R, Max M, Rossaint R. Evidence-based medicine in the therapy of the acute respiratory distress syndrome. *Intensive Care Med* 2002;28(2):244-255.
- Hemmila MR, Napolitano LM. Severe respiratory failure: Advanced treatment options. *Crit Care Med* 2006;34(9 Suppl):S278-S290.
- Lewandowski K. Extracorporeal membrane oxygenation for severe acute respiratory failure. *Crit Care* 2000;4:156-168 doi:10.1186/cc689.
- Hemmila MR, Rowe SA, Boules TN, Miskulin J, McGillicuddy JW, Schuerer DJ, et al. Extracorporeal life support for severe acute respiratory distress syndrome in adults. *Ann Surg* 2004;240(4):595-607.
- Mols G, Loop T, Geiger K, Farthmann E, Benzig A. Extracorporeal membrane oxygenation: a ten-year experience. *Am J Surg* 2000;180(2):144-154.
- Mason DP, Boffa DJ, Murthy SC, Gildea TR, Budev MM, Mehta AC, et al. Extended use of extracorporeal membrane oxygenation after lung transplantation. *J Thorac Cardiovasc Surg* 2006;132(4):954-960.
- Extracorporeal Life Support Organization. Annual international registry. January 2009. <http://www.else.med.umich.edu/registry.htm>. Accessed May 12, 2009.
- Peek GJ, Clemens F, Elbourne D, Firmin R, Hardy P, Hibbert C, et al. CESAR: conventional ventilatory support vs extracorporeal membrane oxygenation for severe adult respiratory failure. *BMC Health Services Research* 2006;6:163.
- Hitt EP. CESAR trial: extracorporeal membrane oxygenation improves survival in patients with severe respiratory failure. *Medscape Medical News*, February 5, 2008.
- Green TP, Timmons OD, Fackler JC, Moler FW, Thompson AE, Sweeney MF. The impact of extracorporeal membrane oxygenation on survival in pediatric patients with acute respiratory failure. *Crit Care Med* 1996;24(2):323-329.
- Masiakos PT, Islam S, Doody DP, Schnitzer JJ, Ryan DP. Extracorporeal membrane oxygenation for nonneonatal acute respiratory failure. *Arch Surg* 1999;134(4):375-380.
- Maclaren G, Butt W, Best D, Donath S, Taylor A. Extracorporeal membrane oxygenation for refractory septic shock in children: one institution's experience. *Ped Crit Care Med* 2007;8(5):498-499.
- Creech BC, Johnson GB, Bartilson RE, Yang E, Barr FE. Increasing use of extracorporeal life support in methacillin-resistant *Staphylococcus aureus* in children. *Pediatr Crit Care Med* 2007;8(3):231-235.
- Gow KW, Wulkan ML, Heiss KF, Haight AE, Heard ML, Rycus P, Fortenberry JD. Extracorporeal membrane oxygenation for support of children after hematopoietic stem cell transplantation; the extracorporeal life support organization experience. *J Pediatr Surg* 2006;41(4):662-667.
- Gupta M, Stanley TP, Moler FW. Extracorporeal life support for severe respiratory failure in children with immune compromised conditions. *Pediatr Crit Care Med* 2008;9(4):380-385.
- Fisher JC, Stolar CJH, Cowles RA. Extracorporeal membrane oxygenation for cardiopulmonary failure in pediatric patients: is a second course justified? *J Surg Res* 2008;148(1):100-108.
- Zwischenberger JB, Conrad SA, Alpard SK, Grier LR, Bidani A. Percutaneous extracorporeal arteriovenous CO<sub>2</sub> removal for severe respiratory failure. *Ann Thorac Surg* 1999;68(1):181-187.
- Conrad SA, Zwischenberger JB, Grier LR, Alpard SK, Bidani A. Total extracorporeal arteriovenous carbon dioxide removal in acute respiratory failure: phase I clinical trial. *Intensive Care Med* 2001;27(8):1340-1351.
- Morris AH, Wallace CJ, Menlove RL, Clemmer TP, Orme JF, Weaver LK, et al. Randomized clinical trial of pressure-controlled inverse ratio ventilation and extracorporeal CO<sub>2</sub> removal for adult respiratory distress syndrome. *Am J Respir Crit Care Med* 1994;149(2 Pt 1):295-305.

35. Conrad SA, Green R, Scott K. Near-fatal asthma managed with pumpless arteriovenous carbon dioxide removal. *Crit Care Med* 2007; 35(11):2624-2629.
36. iLA membrane ventilator (product information sheet). NovaLung. [http://www.novalung.com/eng/content/file/en\\_2008\\_01%20ila%20product%20information.pdf](http://www.novalung.com/eng/content/file/en_2008_01%20ila%20product%20information.pdf). Accessed May 15, 2009
37. Meyer A, Strüber M, Fischer S. Advances in extracorporeal ventilation. *Anesthesiology Clin* 2008;26(2):381-391.
38. Bein T, Weber F, Philipp A, Prasser C, Pfeifer M, Schmid F, et al. A new pumpless extracorporeal interventional lung assist in critical hypoxemia/hypercapnia. *Crit Care Med* 2006;34(5):1372-1377.
39. Fischer S, Simon AR, Welte T, Hoepfer MM, Meyer A, Tessenar R, et al. Bridge to lung transplantation with the novel pumpless interventional lung assist device Novalung. *J Thorac Cardiovasc Surg* 2008;131(3):719-723.
40. Zimmermann M, Bein T, Arlt M, Phillip A, Rupperecht 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.
41. Morris AH. Extracorporeal support and patient outcome: Credible causality remains elusive. *Crit Care Med* 2006;34(5):1551-1552.
42. Sim KM, Evans TW, Keogh BF. Clinical strategies in intravascular gas exchange. *Artif Organs* 1996;20(7):807-810.
43. Hattler BG, Lund LW, Golob J, Russian H, Lann MF, Merrill TL, et al. A respiratory gas exchange catheter: in vitro and in vivo tests in large animals. *J Thorac Cardiovasc Surg* 2002;124(3):529-530.
44. Mortenson JD. Intravascular oxygenator: a new alternative method for augmenting blood gas transfer in patients with acute respiratory failure. *Artif Organs* 1992;16(1):75-82.
45. Conrad SA, Bagley A, Bagley B, Schaap RN. Major findings from the clinical trials of the intravascular oxygenator. *Artif Organs* 1994; 18(11):846-863.
46. Smedira NG, Moazami N, Golding CM, McCarthy PM, Apperson-Hansen C, Blackstone EH, Cosgrove DM. Clinical experience with 202 adults receiving extracorporeal membrane oxygenation for cardiac failure: survival at five years. *J Thorac Cardiovasc Surg* 2001; 122(1):92-102.
47. Klotz S, Rukosujew A, Welp H, Schnid C, Tijan DT, Scheld HH. Primary extracorporeal membrane oxygenation versus primary ventricular assist device implantation in low cardiac output syndrome following cardiac surgery. *Artif Organs* 2007;31(5):390-394.
48. Bakhtiary F, Keller H, Dogan S, Dzemali O, Oezasalan F, Meininger D, et al. Venous extracorporeal membrane oxygenation for treatment of cardiogenic shock: Clinical experiences in 45 adult patients. *J Thorac Cardiovasc Surg* 2008;135(2):384-388.
49. Pages ON, Aubert S, Combes A, Luyt CE, Pavie A, Léger P, et al. Paracorporeal pulsatile biventricular assist device versus extracorporeal membrane oxygenation-extracorporeal life support in adult fulminant myocarditis. *J Thorac Cardiovasc Surg* 2009;137(1):194-197.
50. Davies RR, Russo MJ, Hong KN, O'Bryne ML, Cork DP, Moskowitz AJ, et al. The use of mechanical circulatory support as a bridge to transplantation in pediatric patients: analysis of the United Network of Organ Sharing database 2008;135(2):421-427.
51. Pagani FD, Lynch W, Swaniker F, Dyke DB, Bartlett R, Koelling T, et al. Extracorporeal life support to left ventricular assist device bridge to heart transplant. *Circulation* 1999;100(19 Suppl):II206-II210.
52. Baughman KL, Jarcho JA. Bridge to life—cardiac mechanical support. *N Engl J Med* 2007;357(9):846-848.
53. Duncan B. Mechanical circulatory support for infants and children with cardiac disease. *Ann Thorac Surg* 2002;73(5):1670-1677.
54. Chaturvedi RR, Macrae D, Brown L, Schindler M, Smith EC, Davis KB, et al. Cardiac ECMO for biventricular hearts after paediatric open heart surgery. *Heart* 2004;90(5):545-551.
55. Aharon AS, Drinkwater DC, Churchwell KB, Quisling SV, Reddy VS, Taylor M, et al. Extracorporeal membrane oxygenation in children after repair of congenital cardiac lesions. *Ann Thorac Surg* 2001;72(6):2095-2102.
56. Allan CK, Thiagarajan RR, Armsby LR, del Nido PJ, Laussen PC. Emergent use of extracorporeal membrane oxygenation during pediatric cardiac catheterization. *Pediatr Crit Care Med* 2006;17(3): 212-219.
57. Thiagarajan RR, Laussen PC, Rycus PT, Bartlett RH, Bratton SL. Extracorporeal membrane oxygenation to aid cardiopulmonary resuscitation in infants and children. *Circulation* 2007;116(15):1693-1700.
58. Alsoufi B, Al-Radi OO, Nazar RI, Gruenwald C, Foreman C, Williams WG, et al. Survival outcomes after rescue extracorporeal cardiopulmonary resuscitation in pediatric patients with refractory cardiac arrest. *J Thorac Cardiovasc Surg* 2007;134(4):952-959.
59. Mégarbone B, Leprince P, Deye N, Résière D, Guerrier G, Rettab S, et al. Emergency feasibility in medical intensive care unit of extracorporeal life support for refractory cardiac arrest. *Intensive Care Med* 2007;33(5):758-764.
60. Thourani VH, Kirshborn PM, Kanter KR, Sinsic J, Kogon BE, Wagoner S, et al. Venous extracorporeal membrane oxygenation (VA-ECMO) in pediatric cardiac support. *Ann Thorac Surg* 2006;82(1):138-145.
61. Hannan RL, Ojito JW, Ybarra MA, O'Brien MC, Rossi AF, Burke RP. Rapid cardiopulmonary support in children with heart disease; a nine-year experience. *Ann Thorac Surg* 2006;82(5):1637-1642.
62. Huang S, Wu E, Lin J, Chen Y, Chang C, Chiu I, et al. Extracorporeal membrane oxygenation rescue for cardiopulmonary resuscitation in pediatric patients. *Crit Care Med* 2008;36(5):1607-1613.
63. Chen Y, Yu H, Huang S, Lin J, Chi N, Wang C, et al. Extracorporeal membrane oxygenation support can extend the duration of cardiopulmonary resuscitation. *Crit Care Med* 2008;36(9):2529-2535.
64. Chan T, Thiagarajan RR, Frank D, Bratton SL. Survival after extracorporeal cardiopulmonary resuscitation in infants and children with heart disease. *J Thorac Cardiovasc Surg* 2008;136(4):984-992.
65. Topjian A, Nadkarni V. E-CPR...Is there E-nough E-evidence to reach a "tipping point" for rapid deployment? *Crit Care Med* 2008; 36(5):1679-1681.
66. American Heart Association. Guidelines for cardiopulmonary resuscitation and emergency cardiovascular care. *Circulation* 2005;112(24 Suppl):IV1-IV203.
67. Varon J, Acosta P. Extracorporeal membrane oxygenation in cardiopulmonary resuscitation: Are we there yet? (editorial) *Crit Care* 2008; 36(5):2685-2686.
68. Karimova A, Robertson A, Cross N, Smith L, O'Callahan M, Tuleau C, et al. A wet-primed extracorporeal membrane oxygenation circuit with hollow-fiber membrane oxygenator maintains adequate function for use during cardiopulmonary resuscitation after 2 weeks on standby. *Crit Care Med* 2005;33(7):152-1576.
69. Arlt M, Phillip A, Zimmerman M, Voelkel S, Hilker M, Hobbahn J, Schmid C. First experiences with a new miniaturised life support system for mobile percutaneous cardiopulmonary resuscitation. *Resuscitation* 2008;77(3):345-350.
70. Maquet. Cardiohelp (technical data sheet). <http://www.maquet-cardiohelp.com/index.php?id=61&L=1>. Accessed May 15, 2009.