Can the Outcome of Pediatric Extracorporeal Membrane Oxygenation after Cardiac Surgery be Predicted?

Ghassan Baslaim, MD, Jill Bashore, RN, Faiz Al-Malki, and Ahmed Jamjoom, MD

Purpose: The purpose of this study is to assess whether clinical and biochemical variables may be used to predict outcome in children treated with extracorporeal membrane oxygenation (ECMO) after cardiac surgery and to determine when to discontinue ECMO support.

Methods: We retrospectively reviewed the medical records of 26 children treated with ECMO after cardiac surgery at our institution from October 2000 to May 2004.

Results: Patients mean age was 16.4 months (range, two weeks to 144 months) and mean weight was 6.3 kg (range, 2.2-26 kg). Of the 26 children requiring ECMO support, 23 underwent biventricular repair, and 3 had single ventricle procedure. None of the single ventricle repair or the truncus arteriosus repair group survived the ECMO support. Twelve patients (46%) survived the ECMO support and were discharged from hospital. Four patients needed ECMO support after 45 min (mean) of cardiopulmonary resuscitation (CPR) time (range = 30-55 min) with 2/4 survived to discharge. All patients who survived to discharge showed no evidence of neurological deficit or disseminated intravascular coagulopathy (DIC) whereas 5 patients died following stroke, and 8 following DIC, respectively ($p=0.021$ and $0.002$). Renal failure developed in 8 cases (1 survivor and 7 nonsurvivors, $p=0.022$). Seventeen patients (65%) required re-exploration of the mediastinum for bleeding. Length of time on ECMO, although it was longer among the nonsurvivors, was not significantly different between the survivor (74.5 hours) and nonsurvivor (118.2 hours) groups ($p=0.41$). Inotrope score at ECMO initiation and serum lactate within 72 hours of ECMO were calculated and the difference between the two groups was not significantly related to survival ($p=0.29$ and 0.22 respectively).

Conclusion: Our findings suggest patients who develop renal failure, stroke and DIC during ECMO support have a high mortality. Patients with single ventricle physiology, and repaired truncus arteriosus may benefit less from ECMO support and have an increased risk of death. Elevated levels of lactate during the first 72 hours, high inotrope score at the initiation of ECMO and long ECMO support duration (more than 3 days) are all potential variables that can be used in determining when to discontinue ECMO support. (Ann Thorac Cardiovasc Surg 2006; 12: 21–7)

Key words: extracorporeal membrane oxygenation, congenital heart disease, cardiac surgery, outcome

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Introduction

Extracorporeal membrane oxygenation (ECMO) remains the standard pediatric technique used for extracorporeal life support (ECLS). Limitations in available therapeutic modalities, combined with the effectiveness and familiarity of ECMO support, have encouraged most pediatric
centers to use conventional ECMO for cardiac support and emergency resuscitation. However, mortality remains relatively high among patients who receive ECLS after cardiac surgery, and clinical measures that may be helpful in predicting outcomes have not been well quantified.1,2)

The progression of multiple organ system dysfunction or the development of a nosocomial infection has a significant negative impact on survival.3) Serious consideration should be given to discontinuing ECMO support and returning to more traditional support whenever there is a progressive increase in the number of abnormally functioning organ systems, development of nosocomial infection, or if the support has been provided for more than 250 hours and native cardiac function remains inadequate.

Despite identification of factors associated with hospital death, it is difficult to identify when further ECMO therapy is likely to be futile. The primary objectives of our review were to evaluate the length of time on ECMO, organ dysfunction, inotrope score and serum lactate level as predictors of survival for children treated with ECMO after cardiac surgery and to determine whether these variables may be used to influence when to discontinue ECMO support.

### Materials and Methods

Data were obtained retrospectively from 26 consecutive pediatric patients who required mechanical support after cardiac surgery from October 2000 to May 2004. Hospital records, operative reports, perfusion and intensive care unit data were used to obtain demographic information, operative and postoperative data. The patients requiring ECMO represented 4%, of a total of 664 children undergoing cardiopulmonary bypass for surgical correction of congenital heart diseases. The demographic makeup of patients in this review is described in Table 1.

Twenty-three patients had biventricular repair, and three had single ventricle repair (Table 2). The general indication for ECMO was inadequate cardiopulmonary function despite maximal conventional therapy. Specific indications for ECMO, as listed in Table 1, included ventricular dysfunction (Vd)(right, left, or both), pulmonary failure (Pf)(oxygenation, ventilation, or both), or others (pulmonary hypertensive crisis, allergic reaction to blood product, or postoperative pulmonary artery stenting). ECMO was initiated through the chest in all patients when the decision was made by the attending cardiothoracic surgeon in consultation with the anesthesiologist, pediatric intensivist and cardiologist. The decision was based, in general, on one of the following: 1) persistence of hypoxemia despite optimal blood gases, maximum ventilatory support with/out the use of the oscillator from the Pf point of view, 2) failure to maintain acceptable systemic blood pressure despite adequate filling pressure and appropriate escalation of inotropic support, and 3) combination of the above two conditions.

Cannulation was performed either in the operating room or in the intensive care unit. Patients who failed to come off cardiopulmonary bypass after cardiac surgery had ECMO instituted with previously inserted single arterial and single venous cannulae. Five children who required ECLS in the postoperative period underwent transthoracic cannulation where the ascending aorta and the systemic venous atrium were cannulated after a period of a cardiopulmonary resuscitation (CPR) except for one. The neck was not the preferred site of cannulation in our

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**Table 1. Patient demographics**

<table>
<thead>
<tr>
<th>Variables</th>
<th>Survivors (n=12)</th>
<th>Nonsurvivors (n=14)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean, median age (range)</td>
<td>13.4, 5.1 mo (1.3-72)</td>
<td>18.9, 3.3 mo (0.5-144)</td>
<td>0.29</td>
</tr>
<tr>
<td>Mean, median weight (range)</td>
<td>6.7, 5.2 kg (2.9-19)</td>
<td>5.9, 3.3 kg (2.2-26)</td>
<td>0.06</td>
</tr>
<tr>
<td>Mean aortic cross clamp time (range)</td>
<td>172 min (32-330)</td>
<td>136 min (75-251)</td>
<td>0.09</td>
</tr>
<tr>
<td>Indication for ECMO (Vd/Pf/O)</td>
<td>7/3/2</td>
<td>10/3/1</td>
<td>0.45</td>
</tr>
<tr>
<td>Mean ECMO duration (range)</td>
<td>74.5 hr (12-189)</td>
<td>118.2 hr (5-331)</td>
<td>0.41</td>
</tr>
<tr>
<td>Mean inotrope score (range, n=25)</td>
<td>1,619.5 (250-2,810)</td>
<td>2,103.1 (700-4,015)</td>
<td>0.29</td>
</tr>
<tr>
<td>Mean serum lactate (range, n=22)</td>
<td>5.8 mmol/L (1.1-16.3)</td>
<td>9.3 mmol/L (0.9-24.7)</td>
<td>0.22</td>
</tr>
<tr>
<td>CPR time before ECMO (n=4)</td>
<td>30, 55 min</td>
<td>45, 50 min</td>
<td>0.87</td>
</tr>
</tbody>
</table>

ECMO, extracorporeal membrane oxygenation; Vd, ventricular dysfunction; Pf, pulmonary failure; O, others; CPR, cardiopulmonary resuscitation.
unit. Prophylactic antibiotics were routinely administered and maintained for a minimum of 72 hours after chest closure.


After assembly, the circuit was flushed with carbon dioxide, then primed with a total volume of 500-1,000 ml of Ringer’s lactate and completely de-bubbled. Meanwhile, one adult size unit of packed red blood cells was prepared (adding 100 IU/kg of heparin, 25 ml of sodium bicarbonate, 200 mg of calcium chloride, and 50 ml of fresh frozen plasma) and then infused to replace the crystalloid prime. The arterial and venous lines were handled in a sterile wrapper, clamped and transferred to the sterile field. The flow probe transducer and venous saturation monitor were attached and calibrated. The gas line and temperature probe were then attached to the oxygenator. The arterial and venous lines were connected to the appropriate cannulas. Venous drainage was achieved using a single straight wire reinforced cannula (DLP, Medtronic Inc., Minneapolis, MN, USA), and the oxygenated blood was returned into the ascending aorta through a DLP wire reinforced arterial cannula. The bypass bridge was clamped, bypass was initiated, and the flow rate gradually increased depending on patient size and blood flow requirement. The sweep gas was oxygen enriched air with the gas flow rate adjusted to maintain a PaCO2 of 4.5-5.5 kPa and FiO2 adjusted to keep the PaO2 between 20 and 30 kPa.

All patients were anticoagulated with heparin sulfate to achieve an activated clotting time (ACT) of 180-220 seconds, and a range of 160-180 seconds was accepted for bleeding patients. Hematocrit was maintained around 35 and 45% for acyanotic and cyanotic heart diseases, respectively. Platelet transfusion was provided to keep the platelet count greater than 100,000/mm³. A cell saving system was utilized as needed for rare blood group patients or when product availability in blood bank was at a critical level.

Vasoactive infusions were titrated to minimal levels once adequate blood pressure was achieved using ECMO and the flow was generally maintained between 80 and 110 ml/kg/min. Diuretics were used to enhance urine output, and hemofiltration was added to augment fluid removal in case of volume overload. Hemofiltration was performed using a Hemocor-HPH-400 filter (Minitech, Inc., Minneapolis, MN, USA) in line with ECMO circuit. Hemodialysis was instituted for anuria/oliguria renal failure (creatinine of >115 μmol/L). All patients were ventilated at low frequency (10 breaths/min) with a tidal volume of 8-12 ml/kg and positive end expiratory pre-
sure of 3-8 cmH₂O. All patients were sedated with benzodiazepine and narcotic analgesia, and neuromuscular blocking agents were used at the discretion of the attending physician.

In the event of diagnosed disseminated intravascular coagulopathy (DIC), coagulation profile was stabilized by fine titration of heparin infusion, ACT of 160-180 seconds was accepted, cell saver was avoided, and optimization of platelets and coagulation factors was exercised. Associated mediastinal bleeding was handled by surgical exploration and topical hemostasis. Electroencephalogram and head ultrasound were requested in case of a suspected stroke, if indicated by the neurologist, to complete the neurological assessment and to verify the brain death status. However, conservative management using a sedation, analgesia with/out anticonvulsant was practiced if there was no evidence of brain death.

The inotrope score which was adopted in our unit as a reference for acuity [dopamine + dobutamine + epinephrine + norepinephrine + amrinone (or milrinone ×15) all in microgram/kg/min ×100] was documented at the time of institution and just prior to the initiation of ECMO. Serum lactate level (mmol/L) was measured during the first 72 hours of ECMO support to reflect the adequacy of tissue perfusion (Table 1).

Weaning and separation of ECMO support was based on either adequate cardiopulmonary stability, or the development of one or more irreversible organ dysfunction precluding survival. Discontinuation was accomplished by maximizing inotropic and ventilator support and gradual decrease of ECMO flow rates in a fashion similar to weaning from cardiopulmonary bypass but over 12-24 hours. When flow rates were decreased to approximately 20% of maximal support, the bridge between the arterial and venous systems was unclamped and the circuit allowed to recirculate. The cannulas were subsequently removed after 1 hour of hemodynamic stability, and the chest closure was performed on the following day.

Cell saving system use and complications diagnosed while the patient was on ECMO were recorded and included: stroke, DIC, sepsis, renal failure, and bleeding (Table 3). Stroke was defined as the presence of intracranial infarct or hemorrhage, evidence of hypoxic insult, or brain death. The presence of decreased platelet count that is unresponsive to transfusion, increased activated clotting time despite decreasing heparin, the elevated prothrombin time three times normal, and evidence of clinical bleeding from surgical and/or other sites was defined as DIC. Sepsis was defined as the presence of one or more positive blood cultures and the requirement to change the antimicrobial therapy, with or without fever and raised white cell count. Renal failure was considered to be the need for hemodialysis for anuria, or oliguria with creatinine level >115 μmol/L. Bleeding was defined as intrathoracic bleeding or tamponade that required exploration.

Statistical analyses of the demographic and outcome data were done with a standard statistical package (SPSS 10.0 for Windows; SPSS Inc., Chicago, IL, USA). Data are presented as mean, median and range. Children who survived to hospital discharge are compared with those who died in the present cohort. Categorical data are compared with the χ² test, while continuous data are compared using the Mann-Whitney U test. A p value of 0.05 or less was considered to be significant.

<table>
<thead>
<tr>
<th>Complication</th>
<th>Survivors</th>
<th>Nonsurvivors</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stroke</td>
<td>0</td>
<td>5</td>
<td>0.021</td>
</tr>
<tr>
<td>DIC</td>
<td>0</td>
<td>8</td>
<td>0.002</td>
</tr>
<tr>
<td>Sepsis</td>
<td>3</td>
<td>1</td>
<td>0.208</td>
</tr>
<tr>
<td>Renal failure</td>
<td>1</td>
<td>7</td>
<td>0.022</td>
</tr>
<tr>
<td>Bleeding</td>
<td>6</td>
<td>11</td>
<td>0.127</td>
</tr>
<tr>
<td>Cell saving use</td>
<td>5</td>
<td>7</td>
<td>0.488</td>
</tr>
</tbody>
</table>

DIC, disseminated intravascular coagulopathy.

Results

ECMO was used in 26 pediatric patients after cardiac surgery. Patients ranged in age from two weeks to 144 months, with a mean and median age of 16.4 and 4.3 months respectively. Mean and median weight was 6.3 and 3.7 kg respectively, with a range of 2.2-26 kg. Indications for ECMO were as follows: Vd (n=17; 65%), Pf (n=6; 23%), or others (n=3; 12%); 1 had pulmonary hypertensive crisis in the intensive care unit, 1 had allergic reaction to blood products immediately postcardiopulmonary bypass, and 1 had required postoperative distal pulmonary artery stenting. Twelve patients survived the ECMO support and were discharged from the hospital (46%). Of the 5 children who required ECMO support in the postoperative period, 4 patients received an average period of 45 min of CPR (range = 30-55 min). Two of the CPR group survived to discharge.

The children requiring ECMO support represented a
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Wide spectrum of cardiac lesions. Of the 26 patients, 23 underwent biventricular repair, and 3 had single ventricle procedure. Five patients had dextro-transposition of great arteries (d-TGA) and intact ventricular septum (IVS), 3 had total anomalous pulmonary venous drainage (TAPVD), 3 had truncus arteriosus, 3 had complete atrioventricular canal (CAVC) defect, 3 had d-TGA and ventricular septal defect (VSD), 2 had d-TGA and IVS with subpulmonic stenosis (Sub-PS), 1 had d-TGA and IVS who underwent pulmonary artery banding and construction of Blalock-Taussig (BT) shunt for left ventricular training, 2 had pulmonary atresia (PA) and VSD with multiple aortopulmonary collaterals (MAPCAs), 2 had hypoplastic left heart complex (HLHC) who underwent modified Norwood repair, 1 had double-outlet right ventricle (DORV), and 1 had thrombosed conduit of the extracardiac (EC) Fontan connection who underwent urgent revision of the connection. Table 2 expresses survival as a function of anatomic diagnosis. None of the single ventricle repair or the truncus arteriosus group survived the ECMO support.

Complications are listed in Table 3. All patients who survived to discharge showed no evidence of neurological deficit or DIC whereas 5 and 8 patients developed stroke and DIC among the nonsurvivors, respectively (p=0.021 and 0.002). Four patients required modification of antibiotic therapy for positive blood and/or other body fluid cultures (3 survivors and 1 nonsurvivor, p=0.208). Renal failure requiring hemodialysis occurred in 8 cases (1 survivor and 7 nonsurvivors, p=0.022). Seventeen patients (65%) required re-exploration of the mediastinum for bleeding (6 survivors and 11 nonsurvivors, p=0.127), with 12 of them (71%) requiring the use of a cell saving system (5 survivors and 7 nonsurvivors, p=0.488).

Although the length of time on ECMO was longer among the nonsurvivors, it was not significantly different between the survivor (74.5 hours) and nonsurvivor (118.2 hours) groups (p=0.41). Inotrope score was calculated just prior to initiation of ECMO support, and the score records were available for 25 patients. However, the difference between the two groups was not significantly related to survival. Similarly, serum lactate levels within 72 hours of ECMO initiation were not significantly different between the two groups, and the serum lactate levels were available for 22 patients (Table 1).

**Discussion**

ECMO after cardiac surgery is most commonly used for support after failing to wean off of cardiopulmonary bypass and for delayed postcardiotomy cardiorespiratory failure. Trying to determine the point at which ECMO becomes futile has not been well established in postcardiotomy patients. Reversibility of heart dysfunction is a key determinant to the success of ECMO. A number of recent reports on the use of ECMO after cardiac surgery for myocardial or Pf have shown encouraging results. Survival rates of greater than 50% have been reported in children requiring mechanical support with ECMO.

The decision to place a child on ECLS is determined by the treating team’s judgment and is affected by many factors including ventricular function, magnitude of conventional inotropic support, and pulmonary function. We believe that increased experience with ECLS would improve our results, just as it has at other centers. However, our use of ECMO is 4% according to this study. A relatively higher usage than in most series is reported by Raithel et al. in which 8.4% of pediatric patients required ECLS following cardiac surgery. This highlights the difficulties of direct comparison between series.

Our center does currently offer rapid resuscitation ECLS for patients with ongoing CPR using a crystalloid primed circuit. In a series of 11 children with congenital heart disease who underwent cardiac operation and subsequently suffered postoperative cardiac arrest, del Nido et al. reported that the mean duration of CPR was 65±9 min until ECMO flow was initiated. They concluded that the success of resuscitation depends largely on the speed and recognition of the arrest event and establishment of effective respiratory and circulatory support. The experience with rapid resuscitation in the current cohort was appreciated in 4 cases requiring CPR before the initiation of ECLS. The mean CPR time was 45 min (less than 1 hour), and the range was 30-55 min. Two out of those 4 patients survived to discharge (50% mortality).

Patients with an adequate two ventricle repair have significantly higher hospital survival as reported by Kolovos et al. In our series biventricular repair except for truncus arteriosus tented to have better survival compared with the other patients. The relatively small sample size limited finer comparison of survival by surgical diagnosis.

Also, because of the diversity of diagnoses and indications these differences were not statistically significant in our review.

There were five major complications in our series with bleeding being the most dominant one (65%). A cell saving system was used in 12 cases out of the 17 patients who required exploration for bleeding. Some series have
reported almost 70% of patients having bleeding complications. Meticulous hemostasis and close monitoring of the ACT and platelet count in addition to a high threshold utilizing cell saving system are essential in keeping this complication to a minimum. In this series, no thrombotic event was appreciated among the cohort, and significant clinical bleeding as a mediastinal hemorrhage was mainly appreciated among the DIC group. Complications such as, stroke, renal failure and DIC were significantly higher among the nonsurvivors in this series. Similar observation was made by others relating poor outcome to renal failure or multiorgan dysfunction. Some patients considered infected in our study may have been colonized rather than infected. We did not attempt to distinguish between colonization and infection. We chose to use a fairly liberal definition of sepsis, and any postcardiotomy ECMO patient with positive cultures, with or without change in white cell count, are usually considered septic and treated with specific antimicrobial therapy.

As previously reported, among postcardiotomy patients who survive, myocardial function returns within 3-5 days, and is very unlikely to improve sufficiently after 8-10 days of support. Several studies have shown that prolonged periods of mechanical support have a negative impact on survival. In our patient population 46% of patients requiring 75 hours (mean) of ECMO support were successfully discharged home compared with 54% who required 118 hours (mean) of support. Despite the poor results in patients who did not survive a long ECMO support we would advocate the use of ECLS for a period of up to 3 days providing improvement was realistically anticipated. If however, after this time there is no significant improvement in myocardial function we would not recommend its continued use.

The evolution of lactate concentration after therapeutic management is able to reflect tissue perfusion and predict more accurately the outcome. It has been suggested that serial blood lactate measurements may be an accurate predictor of death or the requirement for ECMO support for patients undergoing complex neonatal cardiac surgery. Support of the failing myocardium is initiated with inotropic agents. Progressive decline in clinical status despite maximal pharmacologic doses of inotropic therapy signals the need for mechanical assistance. We evaluated the level of serum lactate within 72 hours of the initial support and inotrope score at the time of ECMO institution, to determine whether the degree of hyperlactatemia and the score were associated with the outcome. Poor outcome was observed among the group with serum lactate more than 9 mmol/L and inotrope score more than 2000. In spite of our effort to identify more predictors for the ECMO outcome, the difference between the survivor and the nonsurvivor groups with respect to both inotrope score and the level of serum lactate did not reach the point of statistical significance.

Although other authors have reported that noncardiac complications negatively affect successful weaning from ECMO, the time frame for development or progression of organ system dysfunction and the relationship to mortality has not been described. We believe that strong consideration should be given to discontinuation of ECMO support in postoperative cardiac patients if there is progressive organ dysfunction, particularly at or beyond 75 hours. However, similar to findings in other studies, our variables recorded before ECMO and during ECMO were not statistically significant predictors of survival and were not greatly helpful in identifying when to discontinue ECMO support. We speculate that the lack of significant relationship between the predicting variables and outcome likely results from the relatively small number of cases in our study. Perhaps more specific measurements of cardiac function that are practical for routine use would provide better guidance for the duration of ECMO support.

In summary, ECMO provides effective support for postoperative cardiac and pulmonary dysfunction refractory to conventional medical management. Renal failure, stroke and DIC were all associated with high mortality. Mechanical support should be initiated before development of significant metabolic abnormalities. Patients with single ventricle physiology, repaired truncus arteriosus, elevated level of lactate during the first 72 hours of ECMO, high inotrope score at the initiation of ECMO and long ECMO support duration (more than 3 days), may benefit less from ECMO support and have an increased risk of death. Those with an adequate two ventricle repair who do not develop major organ dysfunction have higher hospital survival rates. Advances in patient selection may improve outcome.

Our study has limitations. The patients are from a single center and therefore, our findings may not be applicable to other clinical settings. Data were collected by chart review, and some laboratory data, such as lactate levels and inotrope scores, were not available for the entire cohort. These analyzed variables are frequently difficult to retrospectively determine by an audit of the medical records and have undisputable analysis and conclusions.
References


