Extra-corporeal life support following cardiac surgery in children: analysis of risk factors and survival in a single institution

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Abstract

Objective: Application of extra-corporeal life support (ECLS) following pediatric cardiac surgery varies between different institutions based on manpower availability and philosophy towards ECLS utilization. We examined a large single institution experience with postoperative ECLS in children aiming to identify outcome predictors. Methods: Hospital records of all children who required postoperative ECLS at our institution were reviewed. Patients' demographics, cardiac anatomy, surgical and ECLS support details were entered into a multivariable regression analysis to determine factors associated with survival. Results: Between 1990 and 2007, 180 consecutive children, median age 109 days (range: 1 day–16.9 years), required postoperative ECLS. Sixty-nine children (38%) had undergone palliative treatment for single ventricle pathology. ECLS support was required for failure to separate from cardiopulmonary bypass (n = 83) or for postoperative low cardiac output state (n = 97). Forty-eight patients (27%) received rescue extra-corporeal membrane oxygenation (ECMO) support during active chest compression for refractory cardiac arrest. Under ECLS support, 37 patients required surgical revision and 20 received orthotopic heart transplantation. One hundred and nine patients (27%) received rescue extra-corporeal membrane oxygenation (ECMO) support during active chest compression for refractory cardiac arrest. Patients' survival could improve if renal and neurological complications are avoided.

Conclusion: ECLS plays a valuable role in children with low cardiac output state following cardiac surgery. More than one third of those patients, including young neonates, older children, patients with single ventricle, or those requiring rescue ECMO can be salvaged. Although prognosis worsens with prolonged ECLS duration, survival can be noted up to 16 days of support. Heart transplantation is often an important ECLS exit strategy and should be considered early in selected children.

Keywords: Congenital heart disease; Cardiac arrest; Extra-corporeal life support; Single ventricle

1. Introduction

Since extra-corporeal life support (ECLS) was used by Soeter and colleagues in 1973 for the first time in assisting the heart following surgical repair of tetralogy of Fallot [1]; the application of extra-corporeal membrane oxygenator (ECMO) for postoperative mechanical support achieved a great importance in the treatment of congenital heart disease, and became an invaluable tool in the postoperative management of patients at a majority of cardiac centers performing pediatric cardiac surgery [2–6].

ECLS is used in congenital heart surgery for several indications including failure to separate from cardiopulmonary bypass (CPB), postoperative low cardiac output, pulmonary hypertension, bridge to transplantation and for routine support following staged repair of hypoplastic left heart syndrome [7–10]. Moreover, the use of rescue ECMO (ECPR) to support patients having cardiac arrest that is refractory to conventional resuscitation measures has increased recently in the past decade following multiple reports showing hospital survival that is comparable to that of ECMO use for other cardiac indications [11–17].

Despite established efficacy in postoperative cardiac support, ECLS utilization varies between different institutions based on manpower availability and philosophy towards
ECLS use. Therefore, different series have reported various outcomes and different risk factors for death [2–6].

In the current report, we summarize our institutional experience with postoperative ECLS in children and analyze variables affecting hospital survival.

2. Patients and methods

From 1990 to 2007, 180 children under 18 years of age required postoperative ECLS. All the patients who required ECLS support at the same admission following surgical repair of congenital cardiac disease were included. Children who received ECLS support prior to surgical intervention were excluded. Patients were included in the ECPR group if venoarterial ECMO was used as part of the initial active resuscitation from a refractory cardiac arrest with the support initiated during active chest compression.

Patients were identified using the institutional ECLS and surgical database. Demographic, anatomic, surgical and ECLS details were abstracted from the medical records for analysis.

Approval of this study was obtained from the research ethics board at our institution and requirement for individual consent was waived for this observational study.

2.1. ECMO circuit and equipment

A standardized circuit is utilized. Since the majority of our patient cohort are neonates and infants who received ECMO support, we will briefly describe our ECMO circuit for this age group.

The circuit is composed of (1/4) inch internal diameter poly-vinyl chloride (PVC) tubing with Carmeda® (Medtronic, Minneapolis, MN) heparin-bonded biocompatible surface coating. Total prime is approximately 400 mls. The main components are the Jostra Rotaflow centrifugal pump (Maquet, Hirrlingen, Germany) and Hilite® 2400 LT oxygenator (Medos, Stolberg, Germany). This system can support patients up to 20 kg (Fig. 1).

Cannulation site is dependent on clinical situation. In children having postoperative cardiac arrest within the first 5—7 days following surgery, direct aortic and atrial cannulation through the chest is usually done as it provides the most expeditious means of instituting support while allowing the performance of effective open cardiopulmonary resuscitation (CPR) if needed. In those who require ECMO support later than the early postoperative period, neck cannulation is performed. Femoral cannulation is occasionally considered as an alternative peripheral cannulation site in older children and adolescents. Left heart decompression via a left atrial vent or the creation of an atrial septostomy is employed when poor decompression of the left ventricle is noted despite adequate perfusion flows.

2.2. Critical care unit management

Pump flow is started initially at 100 ml/kg/min and adjusted to maintain end organ perfusion, normalization of arterial blood gases, increase in systemic venous saturation and clearance of lactic acidosis. Higher flows are needed for infants with single ventricle physiology and an open shunt [18]. Cardiac inotropes are adjusted as needed to maintain left heart function and pulsatility. High doses of inotropes are
avoided to minimize tachycardia and myocardial oxygen demand. Vasopressors are used to maintain a mean blood pressure of approximately 40–50 mmHg. Afterload reducing agents such as phenoxybenzamine and nitroprusside are often utilized to improve cardiac performance. Similarly, nitric oxide (INO therapeutics, Clinton, NJ), beginning at 20–40 ppm and weaned according to protocol, is used in children with pulmonary hypertension.

Mechanical ventilation is adjusted to maintain oxygenation of blood generated by the native cardiac output and to prevent lung atelectasis. The usual ventilation rate is 10–12 breaths/min, with fraction inspired oxygen of 0.21—0.35, and positive end-expiratory pressure of 5–10 cm H2O to maintain peak inspiratory pressure less than 20 cm H2O. Flow rate and oxygen concentration of the sweep gas are adjusted to maintain arterial blood gases at the desired levels.

Anticoagulation is achieved by continuous heparin infusion maintaining an activated clotting time of 180–200 s. Heparin doses are also monitored and adjusted as per protocol. Hematocrit is kept at 30–35% and platelet count greater than 100 000/mm3. Transfusions of packed cells and platelet concentrates are given as required. In the presence of persistent significant mediastinal bleeding, other blood products such as cryoprecipitate or fresh frozen plasma and anti-fibrinolytic agents such as epsilon amino caproic acid or tranexamic acid can be administered. We have used aprotinin infusion on multiple occasions in patients with excessive mediastinal hemorrhage. More over, activated factor seven concentrates (rVII a) have been safely used in multiple cases with refractory mediastinal bleeding while on ECMO.

Broad-spectrum prophylactic antibiotics are appropriately given to patients with an open chest and dosages are adjusted as necessary. Nutrition is commenced 24–48 h after institution of ECMO. Enteral route is used preferentially unless the feed is poorly absorbed; then parenteral nutrition is started alternatively.

When urine output falls below 2 and 3 ml/kg/h, diuretics are given to promote diuresis. In patients who are persistently oliguric or anuric, slow continuous ultrafiltration (SCUF) or peritoneal dialysis is utilized for extra volume removal.

Assessment of adequacy of surgical repair and the underlying cause leading to low cardiac output state or cardiac arrest is begun soon after patient stabilization and further intervention is considered to address and treat the underlying cause and optimize the patient for future weaning.

Follow-up echocardiography is done up to a daily interval to estimate cardiac recovery, detect residual lesions, thrombus formation in the left ventricle, and to assess the need for orthotopic heart transplantation (OHTX) in case of failure of heart recovery. Cardiac catheterization is occasionally considered for further diagnostic delineation or interventional management of residual lesions.

Timing of weaning is dependent on the clinical scenario, hemodynamics while on ECMO support, correction of the underlying cause and the presence of any residual lesions. In general, weaning for post-cardiotomy patients begins approximately 72 h following ECMO support. Transesophageal echocardiography is frequently used to assess myocardial function during the weaning process.

Weaning and separation from ECMO assist is accomplished with optimal ventilator and inotropic support, preferably with epinephrine requirements ≤0.02 mcg/kg/min. ECMO flow rates are gradually decreased. When flow rates are approximately 25% of maximal support, the arterial and venous lines are clamped and the bridge between the arterial and venous systems is opened, allowing the circuit to recirculate.

Following successful separation from ECMO, the cannulas are usually left in place for 1–3 h, flushed every 10–15 min and subsequently removed if hemodynamic stability is maintained. Purse-string sutures are usually left in place and re-snared with the chest left open following cannula removal in all post-cardiotomy patients. In patients who have had neck canulation, the vessels are repaired if the tissue was of good quality and the patient required ≤1 week of ECMO support.

2.3. Rescue ECMO protocol

A pre-assembled, pre-primed ECMO circuit and trained personnel are available in the critical care unit (CCU) at all times. The circuit system described above is utilized. For patients larger than 20 kg, that system provides temporary support until a 3/8 in. circuit with an increased surface area oxygenator can be substituted. The circuit is primed with Plasmalyte 148 (Baxter Corp., Toronto, Canada), an unbuffered electrolyte solution and is usable for 30 days.

When ECPR is requested, the blood bank is notified to prepare blood products. However, due to time limitations it is often necessary to initiate ECMO support with a clear prime. Heparin, 1 U/ml of prime, sodium bicarbonate, 35 meq., 25% albumin, 200 mls and calcium chloride, 250 mg, are added to the clear prime prior to cannulation. Additionally, systemic heparin is administered to the patient at a dose of 50 U/kg body weight to maintain an activated clotting time of 180–200 s.

Once the patient is stable on ECMO, the crystalloid volume is removed and packed red blood cells are added on a one-for-one syringe exchange transfusion process. Platelets and cryoprecipitate are given to correct the inherent coagulation deficiency.

A complete description of our rescue ECMO protocol has been described in length in a previous publication [14].

3. Statistical analysis

Descriptive statistics were reported as median, range and inter quartile range (IQR) for continuous variables and as frequencies and percentages for categorical variables. Unrelated two-group comparisons were done with unpaired, 2-tailed t-tests for continuous variables and χ² or Fisher’s exact test for categorical data. Potential patient demographic, anatomic, operative and ECMO risk factors were analyzed with a multivariable logistic regression model. The response variable was hospital survival. In all multivariable models the normality and linearity of continuous variables were assessed and appropriate transformations were utilized where necessary. A p value of 0.05 was considered significant. All analyses were done using the R statistical package.
4. Results

4.1. Patients’ characteristics

A total of 180 children (91 males) required postoperative ECLS. Patients ranged in age from 1 day to 16.9 years, with a median age of 109 days (IQR: 14—465). Median weight was 4.3 kg (range: 1.7—75, IQR: 3.2—7.8). Sixty-nine children (34%) had a single ventricle cardiac pathology while 111 (66%) had a two ventricle pathology.

ECLS was initiated in the operating room (OR) for failure to successfully wean off cardiopulmonary bypass support in 83 patients (46%), or later for low cardiac output and/or cardiopulmonary collapse in the CCU in 92 patients (51%) or the cardiac catheterization laboratory in 5 patients (3%). Forty-eight children (27%) required ECPR.

Cannulation sites were intrathoracic (n = 168) and neck cannulation (n = 12). Twenty patients were initially managed without an oxygenator for left or single ventricular support (LVAD) however eleven of them were converted later to full ECMO support. Specific patient characteristics are listed in Table 1.

4.2. Early results

ECLS was successfully discontinued (i.e. children survived and were able to maintain adequate hemodynamics >24 h following ECLS termination) in 109 patients (61%). This was accomplished by successful wean (n = 91) or by OHTX (n = 18). Eighteen patients required repeat ECMO runs during the same admission with one of them requiring two additional ECMO runs. One hundred patients (56%) required re-exploration for bleeding. Additional major complications included but were not limited to: neurological complications such as ischemic brain injury or intracranial hemorrhage (n = 32), renal dysfunction (n = 18), pulmonary hemorrhage (n = 9), in addition to mechanical problems requiring ECMO circuit component changes (n = 68).

Median ECLS duration for the whole group was 4 days (range: 1—22, IQR: 2—6). Sixty-eight patients (38%) survived to hospital discharge. The causes for mortality overlapped but included a combination of problems including failure of cardiac recovery (n = 82), sepsis and multi-organ dysfunction (n = 30), ischemic brain injury (n = 22), and intracranial hemorrhage (n = 5).

4.3. Risk factors for death

Multiple variables were analyzed to test if they were significant predictors of adverse outcome. Those factors included age, weight and gender of the patients, cardiac anatomy, timing of ECLS initiation in the OR versus in the CCU or cath lab, ECPR during active chest compression, cannulation site, support type (ECMO vs LVAD), ECLS duration, repeat ECMO run at the same admission, surgical revision, OHTX, and the emergence of ECLS complications.

Survival in patients in whom ECLS was initiated in the OR for failure to separate from cardiopulmonary bypass was 40% and was not significantly different from survival of 37% when ECLS was started in the CCU or in the cath lab for low cardiac output and hemodynamic deterioration (p = 0.62).

Median ECLS duration for survivors was 3 days (IQR: 2.8—4.2) compared to 5 days (IQR: 2—7) in non-survivors (p = 0.05). ECLS was often terminated early within 1—3 days in patients with severe irreversible neurologic injury detected early following ECLS initiation, especially in those receiving ECPR. Although patients were less likely to survive if they required prolonged support durations, survival was observed following up to 16 days of ECLS support (up to 13 days without heart transplantation) (Figs. 2 and 3).

Repeat ECMO run at the same admission was a poor predictor of outcome with only one child surviving out of 18 patients (p = 0.02).

During the study period, there were 48 patients who received ECPR with ECMO support initiated for refractory cardiac arrest unresponsive to conventional cardiopulmonary resuscitation measures. Survival in this group was 46%, which compared favorably to survival of 35% in non-ECPR patients.

Thirty-seven patients required revision of cardiac repair while on ECLS support and 24% survived. In addition, 20...
patients received orthotopic heart transplantation and 60% survived.

Patients who had single ventricle palliative repair had survival of 45% while patients who underwent a biventricular repair had survival of 33%.

One hundred patients required exploration of the chest and 31% survived. Development of renal failure while receiving ECLS was associated with 11% survival and the emergence of major neurologic complications were associated with 9% survival.

Results of the logistic regression analysis are presented in Table 2. On multivariable regression analysis, factors associated with hospital death included development of renal failure ($p = 0.046$), neurological complications ($p = 0.0007$), longer ECLS duration ($p = 0.003$), repeat ECMO run ($p = 0.02$) and not performing heart transplantation ($p = 0.04$) (Table 2).

5. Discussion

There has been an exponential increase in ECLS utilization for cardiac support in children following surgical repair of congenital heart defects. Its employment has expanded to a complex array of postoperative illnesses.

5.1. ECLS use for single ventricle patients

Many recent series reported increased ECLS use to successfully salvage neonates with a functional single ventricle from refractory postoperative low cardiac output syndrome [2,7,8,19–21]. Indications for ECLS in these children include inability to separate from cardiopulmonary bypass, low cardiac output, cardiac arrest, thrombosis of the shunt, and elective support [2,7,8,19–21]. In single ventricle patients with shunts, the shunt is left open and ECLS flows are increased to maintain both pulmonary and systemic perfusion. This has been found to improve survival and decrease pulmonary ischemia and dysfunction [18].

Routine LVAD use to support patients after the Norwood stage 1 reconstruction has been described by some groups in an attempt to facilitate postoperative care, improve survival and neurologic outcome; however we have not adapted that elective policy at our institution [9,10].

In our current series, survival in patients with single ventricle pathology was 45% compared to 33% of those with two ventricle pathology. These results are not uniform in all patients with functional single ventricle. While the results have significantly improved in neonates with blocked shunts and following the Norwood operation, outcomes remain poor in other subgroups with single ventricle physiology such as patients with right atrial isomerism and obstructed pulmonary veins who continue to be a challenge and are associated with poor survival when ECLS use is needed postoperatively [20].

Patients following bidirectional cavopulmonary connection and the Fontan operations constitute another complicated group of patients due to technical difficulties, the requirement for placement of multiple venous canulas to adequately drain the disconnected venous circulation, and finally due to ineffective conventional resuscitation in those requiring ECPR as the intrathoracic and central venous pressures increase during CPR which limit the amount of blood going to the lungs and brain, respectively and therefore increase the risk of severe neurologic damage due to brain hypoxia following CPR [14,20,21]. Our institutional experience with those patients is limited although similar poor outcomes were noted in this subgroup of patients.

Table 2

<table>
<thead>
<tr>
<th>Univariate analysis</th>
<th>Multivariable analysis</th>
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<tbody>
<tr>
<td></td>
<td>OR (95% CI)</td>
</tr>
<tr>
<td>Age</td>
<td>1.06 (0.96–1.16)</td>
</tr>
<tr>
<td>Weight</td>
<td>1.02 (0.99–1.05)</td>
</tr>
<tr>
<td>Male gender</td>
<td>0.59 (0.32–1.08)</td>
</tr>
<tr>
<td>Single ventricle</td>
<td>0.61 (0.33–1.14)</td>
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<tr>
<td>ECMO started in OR</td>
<td>0.85 (0.47–1.56)</td>
</tr>
<tr>
<td>ECPR</td>
<td>0.63 (0.32–1.24)</td>
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<tr>
<td>ECMO duration</td>
<td>1.09 (1.00–1.19)</td>
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<tr>
<td>Surgical revision</td>
<td>2.19 (0.96–4.97)</td>
</tr>
<tr>
<td>ECMO exit by OHTX</td>
<td>0.36 (0.14–0.93)</td>
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<tr>
<td>Repeat ECMO run</td>
<td>12.0 (1.36–92.2)</td>
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<tr>
<td>Mechanical complications</td>
<td>0.88 (0.47–1.63)</td>
</tr>
<tr>
<td>Bleeding complications</td>
<td>1.92 (1.04–3.53)</td>
</tr>
<tr>
<td>Neurological complications</td>
<td>7.57 (2.21–26.0)</td>
</tr>
<tr>
<td>Renal dysfunction</td>
<td>5.47 (1.22–24.6)</td>
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<tr>
<td>Pulmonary hemorrhage</td>
<td>5.15 (0.63–42.2)</td>
</tr>
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5.2. Indication for ECLS

Unlike other previous reports, we have found no difference in survival between patients who required ECLS for failure to separate from cardiopulmonary bypass and those who required ECLS for low cardiac output following a period of hemodynamic stability [3,4]. While mediastinal hemorrhagic complications may be increased in the first group, re-exploration for bleeding was not associated with increased death risk.

Our policy is to utilize chest cannulation in patients requiring ECLS support within the first 5–7 days following cardiac surgery while neck cannulation is often used if ECLS support is required more than a week postoperatively. Advantages of neck cannulation include decreased mediastinal hemorrhage and potentially decreased risk of mediastinitis; while advantages of chest cannulation is the ease of access especially in patients requiring ECLS for failure to separate from cardiopulmonary bypass and those with open chest who require ECLS support within the first hours to days following cardiac surgery. Moreover, chest approach allows increased opportunity to place larger cannulas, multiple cannulas or decompress the left ventricle as required by patient anatomy and ECLS physiology. While repair of neck vessels is usually attempted in all cases, it is often not possible in smaller neonates and those who require ECLS for a prolonged duration. In our series, the two approaches had similar outcomes with regards to overall survival, risk of stroke or mediastinitis. Although bleeding complications were more common with chest cannulation, probably related to the fact that many of those patients required ECLS immediately after surgery, exploration for bleeding was not identified as a risk factor for hospital survival.

5.3. ECMO use for rapid resuscitation in cardiac arrest

Cardiac arrest may complicate the postoperative course following surgical repair of congenital heart disease. Survival following pediatric cardiac arrest ranges between 14 and 44%. However, following CPR duration of >30 min, survival with conventional CPR measures decreases to 0–5% [22,23]. Cardiac arrest is a common indication for ECMO, comprising nearly 25% of all indications for ECMO in pediatric cardiac patients [11—17]. Several groups have developed systems that allow expeditious institution of ECMO after cardiac arrest that is refractory to conventional CPR. Reported hospital survival was comparable or higher than that of controls requiring elective ECLS [11—17].

We have recently reported our experience with ECPR in 80 children with various underlying pathologies including 39 postoperative patients. Hospital survival for the whole group was 34%. Median CPR duration before ECMO was 41 min [14]. In our current series, hospital survival in postoperative patients was 46%. In our experience, timing of ECPR initiation (weekdays vs weekends and weeknights) did not influence survival. Most importantly, the duration of CPR prior to ECMO institution did not correlate with survival and favorable neurological outcome was observed in patients following prolonged CPR duration up to 95 min [14].

A recent study from Philadelphia demonstrated similar findings. Hospital survival for ECPR in 66 children was 33%, higher for patients with cardiac pathology. They also reported that three out of the six children who had CPR longer than 60 min survived [13]. Another analysis of the data from the Extracorporeal Life Support Organization registry showed a comparable 38% survival to hospital discharge. Risk factors for death were pre-ECMO pH < 7.2, CPR during ECMO, non-cardiac pathology, renal, neurological and pulmonary hemorrhage complications [15].

While survival did not correlate with CPR duration prior to ECMO, the most common reason for death in ECPR patients was ischemic brain injury indicating the need for expeditious institution of ECMO in refractory cardiac arrest [14]. Special care should be made to avoid frequent interruption of chest compression during the dissection and cannulation process. In our series, we have noted that patients with blocked shunts have a worse prognosis and higher incidence of neurological injury likely due to persistent hypoxia despite adequate CPR and therefore ECPR should be considered early in this group of patients [14].

5.4. Surgical re-intervention and heart transplantation

Postoperative ECLS provides temporary stabilization of hemodynamics and perfusion of vital organs. Successful termination of ECLS relies on the absence of significant residual lesions that may have contributed to low cardiac output and/or hemodynamic collapse. Failure to correct postoperative residual lesions has been found to contribute to poor ECLS survival [4,6].

Trans-sternal echocardiography may be limited by poor acoustic windows and transthoracal echocardiography is often necessary. Cardiac catheterization can be safely performed while on ECLS and can aid in the diagnosis of residual lesions in addition to its intervention role such as defect closure, balloon dilatation, stent implantation, and coil placement [8,24,25].

In our current series, 37 patients underwent reoperations for residual lesions and 24% survived.

In patients in whom residual lesions are not amenable to surgical correction or in whom there is no evidence of cardiac recovery within 48–72 h following ECLS, heart transplantation becomes the only choice for successful ECLS exit strategy. Twenty patients in our series remained on ECLS until a suitable donor heart became available with eventual 90% ECLS wean and 60% survival which is an encouraging result considering that those patients are unlikely to survive otherwise. In the current series, the ability to receive heart transplantation was found to be associated with improved survival.

5.5. ECLS duration

Increased duration of ECLS was found in our study to correlate with decreased survival. Average ECLS duration was shorter in survivors compared to non-survivors. This difference may even be understated as a significant number of our patients required ECPR. ECMO support is often terminated early in those patients due to overwhelming neurological damage despite evidence of cardiac recovery.

Nonetheless, it should be noted that there were hospital survivors in our series up to 13 days of ECLS without OHTX and
up to 16 days with OHTX. Again, early consideration to enlist patients for transplantation should be made in appropriate patients with significant residual lesions or no evidence of cardiac recovery.

5.6. ECLS complications

Similar to multiple previous reports, ECLS complications were found to be significant predictors of poor outcome [2—9]. Ischemic brain injury was a common cause for early termination of ECLS; sometimes before any attempts were made to wean and assess for cardiac recovery. In our series, it was the most common cause for death in the ECPR group [14]. Efforts to maintain brain perfusion such as expedient institution of ECMO in cardiac arrest, avoidance of frequent interruption of CPR during ECMO cannulation, maintenance of stable flows, perfusion pressure and adequate decompression of the superior vena cava during mechanical support, and avoidance of additional damage due to intracranial bleeding are all important aspects to limit the extent of neurological injury. Furthermore, there may also be benefit in maintaining the children at cooler temperatures after arrest for higher likelihood of neurological recovery.

Intracranial hemorrhage was a serious morbidity in our population. Daily head ultrasound examinations should be performed, especially in the high-risk first few days. Aggressive early weaning from ECLS may be considered with early signs of bleeding.

Renal dysfunction was noted to be an important risk factor for death. Measures to decrease this morbidity include having low threshold for early institution of ECLS to preserve optimal renal perfusion, maintenance of stable flows and adequate perfusion pressures during mechanical support and meticulous attention to bleeding to avoid frequent interruptions of flows and tamponade. The use of agents such as dopamine and fenoldapam may have a role in the maintenance of renal perfusion. Diuretics, mannitol, peritoneal dialysis and continuous ultrafiltration should be employed to improve end organ perfusion and function. In addition, the use of anti-inflammatory mediators, methods to limit the inflammatory mediators while on ECLS, and establishment of pulsatile flow may be of potential benefit and represent areas for future research in an effort to improve organ perfusion during ECLS and prevent development of end organ dysfunction that significantly complicate patient’s course and lead to serious morbidity and high mortality.

6. Summary

ECLS plays a valuable role in cardiopulmonary support of a wide range of postoperative cardiac illnesses. More than one third of those patients, including young neonates, older children, patients with single ventricle, or those requiring rescue ECMO can be salvaged. Although prognosis worsens with prolonged ECLS duration, survival can be noted up to 16 days of support. Heart transplantation is an important ECLS exit strategy and should be considered early in patients showing no signs of cardiac recovery or having residual defects not amenable to repair. Renal and neurological complications continue to be a major source of morbidity; attention to methods to avoid those complications may improve patient survival.

Acknowledgment

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References


Appendix A. Conference discussion

Dr E. da Cruz (Aurora, Colorado, USA): I will ask a couple of questions and then I would like to bring up a philosophical note to share with the audience before we open the discussion. The first question concerns the survival of the patients with univentricular repair, which was better than that with patients with biventricular repair. Do you think this could have been due to the fact that with univentricular patients we might be more aggressive because we think they have less reserve? Which brings up the point also that maybe when the activation time for ECMO was shorter, we become more aggressive, maybe the results are a little better, the outcome of these patients. I don’t know if you want to answer that.

Dr Alsoufi: One of the limitations of this retrospective study is that we can’t comment on the role of certain variables such as clinical judgement and the decision making process. Nonetheless, the philosophy towards ECMO utilization in Toronto is aggressive and the threshold to initiate ECMO in patients with low cardiac output or circulatory collapse is low. This approach at SickKids is equally aggressive for patients with single or two ventricle pathologies.

Of note, I may not have presented all the data for the sake of time, but the improved results in single ventricle patients in our series were not uniform. For example, hospital survival in patients who required ECMO following the Norwood operation was around 50%, while survival in those who required ECMO following palliative surgery for right atrial isomerism with obstructed pulmonary veins was less than 30%. Likewise, survival following the Glenn procedure was around 30%. This goes along with other series that reported that ECMO in patients following Glenn or Fontan operation is challenging. Our experience with ECMO following the Fontan operation is limited.

Dr da Cruz: Did you apply any brain protection measures in some of your patients? In other words, if yes, this could have had an impact on the neurologic outcome as a predictor.

Dr Alsoufi: You mean following ECMO initiation?

Dr da Cruz: Following patients who arrested and are started on ECMO.

Dr Alsoufi: As presented, neurological complications were associated with poor survival. Any methods that decrease those complications may therefore be associated with improved outcomes. Efforts to maintain brain perfusion such as expeditious institution of ECMO in cardiac arrest, avoidance of frequent interruption of CPR during ECMO cannulation, maintenance of stable flows, perfusion pressure and adequate decompression of the superior vena cava during ECMO, and avoidance of additional damage due to intracranial bleeding are all important aspects to limit the extent of neurological injury. In patients who receive rescue ECMO or ECPR, we usually do core cooling and apply ice around the head. A study is currently underway in Toronto to assess the benefit of this approach in limiting neurological injury following cardiac arrest.

Most importantly, timely institution of ECMO support in patients with marginal hemodynamics may be the most vital means to prevent extensive neurological damage.

Dr da Cruz: Now, these predictors of death are so important, we’re talking patients who are already on ECMO. My concern also regards patients who suddenly become candidates for ECMO, urgent or emergent ECMO, in the context of ECPR, for instance, so in these patients it is more difficult to define predictor factors. And I’m asking this because the indications for ECMO are expanding beyond the boundaries of the intensive care units, particularly cardiac intensive care units, so my question to you, and to the audience also, is, if you think that there are criteria to follow when you are called to a patient who arrests in the ward or in the emergency department, do you assist all-comers? Do you have any other criteria to follow?

Dr Alsoufi: We have reported the Toronto experience with rescue ECMO at the STS meeting a year and a half ago: 80 patients with various underlying pathologies including post-cardiotomy patients received ECPR. In that study, we examined multiple variables that may have a significant effect on outcome. We were unable to identify major predictors of poor outcome. Our team in Toronto is aggressive with the utilization of rescue ECMO for all patients having cardiac arrest that is refractory to conventional resuscitation measures on the ward or in the emergency room. Those patients are promptly transferred, while receiving CPR, to the cardiac care unit where we are equipped to initiate ECMO. The only exception at our institution would be children with severe chromosomal anomalies or other severe conditions that would severely hinder their future lifestyle; those patients are usually identified at time of admission as non-candidates for ECMO.

Dr G. Sarris (Athens, Greece): I have two questions. First, in many studies duration of CPR prior to institution of ECMO is a very potent, independent predictor of mortality. Have measured and studied the effects of this factor?

My second question: Your most frequent complication and the one which we all clinically appreciate as very important is bleeding. In your large experience, do you have any suggestions for all of us as to how to minimize this rather serious complication which contributes to mortality?

Dr Alsoufi: In a previous paper, when we studied 80 consecutive patients who received ECPR during active chest compression, we found that the duration of CPR prior to ECMO initiation did not necessarily correlate with favorable outcome. In fact, survival with intact neurological status was observed in patients who received prolonged CPR up to 95 min. Nonetheless, a decision to utilize ECMO in the setting of cardiac arrest is usually made within the first 5–10 min of conventional CPR. We’ve also identified certain patients in whom resuscitation is challenging, such as those with blocked aortopulmonary shunts or Glenn bidirectional cavopulmonary anastomosis. Those patients may be at higher risk of developing neurological injury due to hypoxia and ineffective CPR during cardiac arrest.

As for the second question, in patients who require ECMO for post-cardiomyotomy support started in the operating room, if they give us the luxury of time, we attempt to wean off CPB, give protamine and blood products to secure hemostasis, then give heparin again and initiate ECMO. Otherwise, we apply the general principles of hemostasis and utilize all the means we have at our disposal. We rely heavily on transfusion of blood products such as platelets, FFP, cryoprecipitate to maintain anticoagulation parameters above transfusion thresholds per our protocol. We use local hemostatic products, anti-fibrinolytic agents and we’ve used aprotinin frequently. In many occasions, we’ve also used activated factor 7 without major incidents while on ECMO.

Mr W. B rawn (Birmingham, United Kingdom): Of the survivors, I think it’s about 28% or 30% at 1 year, what sort of morbidity did they exhibit? What sort of neurological problems did you encounter? They survived to 1 year, but what was their quality of life?

Dr Alsoufi: In terms of cardiopulmonary state, the follow-up hospital records indicate that the majority of survivors are within the expected functional status. As for the neurological state, detailed neurological exam was not performed in those patients to be able to answer your question. However, we have looked at that before in patients requiring rescue ECMO. In this group of patients that is at highest risk of developing ischemic neurological injury, 33% survived to hospital discharge including 3% with significant neurological damage while the remaining 30% had no gross deficit and their neurological exam was similar to that reported prior to their arrest and ECPR.