Extracorporeal Membrane Oxygenation in Pediatric Patients: Our Experience in the Last Ten Years

Lior Sasson MD[1], Ilan Cohen MD[2], Akiva Tamir MD[3], Alona Raucher Sternfeld MD[3], Yitzhak Berlowitz MD[4], Orit Lenczner CCP[1] and Sion Houri MD[2]

[1]Department of Cardiothoracic Surgery, [2]Pediatric Intensive Care Unit, [3]Pediatric Cardiology Unit, and [4]Directorate, Wolfson Medical Center, Holon, affiliated with Sackler Faculty of Medicine, Tel Aviv University, Ramat Aviv, Israel

ABSTRACT: **Background:** The use of extracorporeal membrane oxygenation (ECMO) in children after cardiac surgery is well established. ECMO support is becoming an integral tool for cardiopulmonary resuscitation in specified centers.

Objectives: To review our use of ECMO over a 10 year period.

Methods: All children supported with ECMO from 2000 to 2010 were reviewed. Most of these children suffered from cardiac anomalies. The patients were analyzed by age, weight, procedure, RACHS-1 when appropriate, length of support, and outcome.

Results: Sixty-two children were supported with ECMO; their median age was 3 months (range 0–216 months) and median weight 4.3 kg (range 1.9–51 kg). Thirty-four patients (52.3%) needed additional hemofiltration or dialysis due to renal failure. The children requiring ECMO support represented a wide spectrum of cardiac lesions; the most common procedure was arterial switch operation (27.4%, n=17). ECMO was required mainly for failure to separate from the heart-lung machine (n=55). The median duration of ECMO support was 4 days (range 1–14 days); 29 (46.7%) patients were weaned successfully from ECMO during this time period, and 5 of them died during hospitalization, yielding an overall hospital survival rate of 38.7%.

Conclusions: ECMO support has significant survival benefit for patients with post-cardiotomy heart failure. Its early deployment should be considered in cardiopulmonary resuscitation.

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KEY WORDS: extracorporeal membrane oxygenation (ECMO), cardiopulmonary resuscitation, cardiac anomalies, cardiac surgery

Extracorporeal life support has been used since 1973 [1,2]. Venoarterial extracorporeal membrane oxygenation is the most potent form of acute cardiorespiratory support available and has been widely used for circulatory support after cardiac surgery, with survival to hospital discharge reported at 40%–60% [2-4]. The traditional indications for use range from respiratory failure to a variety of cardiac medical conditions including hemodynamic collapse. ECMO became an integral part of treatment for pediatric cardiac surgeons both pre- and postoperatively [5-7]. However, its use is still associated with significant morbidity and mortality. The goal of treatment is to enable the heart to decrease its work so as to allow recovery of cardiac function from injury. ECMO is thus best used in patients with good potential for myocardial recovery in a matter of days. We present our experience with ECMO and demonstrate its benefit for survival in congenital heart anomalies.

PATIENTS AND METHODS

From 2000 to 2010, 62 patients with refractory cardiopulmonary failure requiring ECMO support were treated in the pediatric cardiothoracic department of Wolfson Medical Center through the "Save A Child's Heart" organization in Israel. The patients requiring ECMO represented 3.2% of a total of 1911 cardiac surgeries for correction of congenital heart defects. Retrospective data collection for the purpose of this study was approved by the Institutional Review Board at the Wolfson Medical Center, and the need for informed consent was waived.

Medical records were retrospectively reviewed (including hospital charts, operative reports, perfusion data and the pediatric intensive care unit records) to collect the data of the pediatric patients (0–18 years old) who were supported by the ECMO machine. These data were summarized for survivors and non-survivors and compared using the Mann-Whitney *U* test for continuous data and chi-square test for categorical data. P value < 0.05 was considered statistically significant.

Indications for ECMO support in this study included the inability to wean from cardiopulmonary bypass in the operating room (n=53) and hemodynamic instability in the PICU with clinical findings of refractory hypotension, acidosis, hypoxemia, pulmonary hypertension, and progressive decline in cardiac function despite maximal inotropic support or cardiopulmonary arrest (n=9).

ECMO was initiated through the chest in all patients except for two who had respiratory failure on the ward and

ECMO = extracorporeal membrane oxygenation
PICU = pediatric intensive care unit

subsequent neck cannulation in the PICU. All the patients were connected to the same ECMO machine, Biomedicus pump 550 Bio-Console® manufactured by Medtronic, USA.

The cannulation sites were right atrium for venous outflow and the aorta for arterial inflow. The cannulas were attached to the circuit, which consisted of a centrifugal pump and a hollow-fiber or membrane oxygenator. Sternums were left open and covered with a Bogota bag sewn onto the skin. The flow rate was slowly increased up to 120 ml/kg/min depending on hemodynamic stability, blood gas samples, serum lactate levels, urine output, and mixed venous oxygen saturation reflecting the affectivity of tissue perfusion. The patients were cooled slightly (34–35°C) during mechanical circulatory support.

Anticoagulation was administered by a heparin infusion, maintaining activated clotting times in the range of 160–200 seconds. Activated clotting times and arterial blood gas parameters were usually checked hourly. Mechanical ventilation was set at 7–8 ml/kg and positive end-expiratory pressure at around 8–10, aiming to keep the lungs inflated with plateau pressure < 30–32. Inotropic drugs were administered to support cardiac function and prevent left ventricle distension. Nitric oxide was used in children with refractory pulmonary hypertension. Blood product administration during ECMO was based on our institutional guidelines for management of ECMO patients; this included packed red blood cells to maintain hematocrit above 40% and platelets to maintain their count above 100,000.

Echocardiography was performed once a day in all patients to assess heart function and to determine if any potentially correctable cardiac defects were present. Once the hemodynamic status improved, indicated by recovered ventricular function by echocardiography, normal blood pressure, lactate levels (≤ 2 mmol/L) and mixed venous saturation (≥ 65), weaning was attempted. Before weaning, ventilator support, fluid status, and inotrope and vasodilator treatment were optimized.

Separation from ECMO was accomplished by optimizing inotropic and ventilator support and gradually decreasing ECMO flow rates slowly within 12 hours to minimum (approximately 100 ml/min); a bridge between the arterial and venous system was then connected. The arterial and venous limbs above the bridge were clamped to isolate the patient from the ECMO, allowing the circuit to recirculate with cannula flushing every 15 minutes. After 6 hours of hemodynamic stability, the cannulas were removed. Chests were closed in the PICU at a later date.

STATISTICAL ANALYSIS

Analysis of data was carried out using SPSS 11.0 statistical analysis software (SPSS Inc., Chicago, IL, USA). Normality of distribution of continuous variables was assessed using the Kolmogorov-Smirnov test (cutoff at $P = 0.01$). Continuous variables such as days on ECMO and patient age were described as mean ± standard deviation and median (min-max). Categorical variables such as type of surgery were described using frequency distributions and are presented as frequency (%). Continuous variables were compared by survival status using the *t*-test for independent variables or the Mann-Whitney U test. Categorical variables were compared by survival status using the chi-square test. All tests are two-sided and considered significant at $P < 0.05$.

RESULTS

The demographic data are shown in Table 1. The patients treated with ECMO suffered from different types of heart disease with varying severity [Table 1]. Two patients (3.3%) required preoperative ECMO therapy due to significant hemodynamic instability. Fifty-three patients (85.4%) were treated after several failed attempts to wean them from the heart-lung machine. In the remaining seven patients (11.3%) the therapy was initiated in the PICU after resuscitation.

Males constituted 66% of the patients (n=41). Median age was 3 months (range 0–216 months). At the time of cannulation, 41 patients were less than 1 year old and eight patients were less than 1 month old. Median weight was 4.3 kg (range 1.9–51 kg). Thirty-four patients (52.3%) needed additional hemofiltration or dialysis, based on urine output and electrolyte balance. Twenty-nine (46.7%) patients were weaned successfully from ECMO during this period, presenting an overall rate of 38.7%.

The children requiring ECMO mechanical support represented a wide spectrum of cardiac lesions [Table 2]: 17 patients (27.4%) had transposition of the great arteries, 10 (16.1%) had

Table 1. Demographic data of patients

Total no. of patients	62
Age (mos), median (range)	3 (0–217)
Weight (kg), median (range)	4.3 (1.9–51)
Male	41 (66%)
Indication for ECMO	
Failure weaning from cardiopulmonary bypass	53
Cardiopulmonary resuscitation	9
Procedures (N)	
Arterial switch operation	17
Tetralogy of Fallot repair	10
Total anomalous pulmonary venous return	5
Ventricular septal defect closure	3
Truncus arteriosus	3
Interrupted aortic arch repair	3
Double outlet right ventricle repair	3
Complete atrioventricular canal repair	3
Rastelli operation	2
Aortic or mitral valve replacement/repair	3
Blalock-Taussig shunt and pulmonary artery banding	1
Pulmonary artery embolectomy	1
Hypoplastic left heart syndrome status after stage I repair (Norwood)	2
HLHS status after stage I repair (Damus-Kaye-Stansel)	2
Other	4

Table 2. Survival as a function of diagnosis

Diagnosis/Procedures	No. of patients	Survival (%)
Arterial switch operation	17	30
Tetralogy of Fallot repair	10	60
Total anomalous pulmonary venous return	5	100
Ventricular septal defect closure	3	100
Truncus arteriosus	3	33
Interrupted aortic arch repair	3	33
Double outlet right ventricle repair	3	100
Complete atrioventricular canal repair	3	0
Aortic or mitral valve replacement/repair	3	33
Other	12	33

Table 3. Survival by RACHS-1

RACHS-1	No. of patients	Survival (%)
Risk category 1	0	N/A
Risk category 2	18	77.8
Risk category 3	10	50
Risk category 4	25	32
Risk category 5	0	N/A
Risk category 6	4	0

RACHS = risk adjustment in congenital heart surgery

tetralogy of Fallot, 5 (8%) had total anomalous pulmonary venous return, 3 (4.8%) had truncus arteriosus, 3 (4.8%) had interrupted aortic arch, 3 (4.8%) had double outlet right ventricle, 3 (4.8%) had complete atrioventricular canal, 2 (3.2%) had transposition of the great arteries combined with a ventricular septal defect and pulmonary stenosis requiring a Rastelli operation, 3 (4.8%) had aortic or mitral valve disorders, 4 (6.4%) had hypoplastic left heart syndrome, and 6 (9.6%) had other diagnoses.

The patients were also categorized according to the risk adjustment for congenital heart disease, RACHS-1 [8], as shown in Table 3. Complications during ECMO included mediastinal bleeding, brain hemorrhage, pulmonary bleeding, sepsis, and multi-organ failure. According to years, this represents 51.85% successful weaning in the first 5 years compared to 41.8% in the last 5 years. This difference can be explained by the younger age and lower weight of the non-survivors in the last 5 years: 1 month and 3.2 kg respectively, versus 19 months and 8.5 kg in the first 5 years.

DISCUSSION

The use of ECMO for circulatory support has been studied and published by many centers. The published ECMO support for patients with congenital heart defect undergoing cardiac surgery is 2.6– 4% [1,4,5] and the reported survival rate ranged between 40 and 60% [9-16]. This is consistent with our finding of 47%. It is clear that myocardial dysfunction after complex congenital cardiac surgery is often reversible. It is accepted that the time that ECMO support is begun is directly related to its successful outcome [6,9,13,15,17,18]. A poorer prognosis is reported when patients were placed on ECMO in the operating room as compared to patients who were connected in the PICU [11]. Our data did not show significant difference in survival between the groups, 52.8% and 55.6% respectively; this finding is consistent with other reports [5,9].

Based on the anatomical diagnosis, Balasubramanian et al. [19] and Chaturvedi et al. [3] reported a decreased survival of 37% and 21%, respectively, in tetalogy of Fallot patients compared to other operative procedures. This is contrary to our findings of 60% survival, which may be related to aggressive relief of pulmonary artery obstruction and routine monocusp implantation in patients with small pulmonary valve annulus.

In our study as in others [10,19], the most common procedure associated with postoperative ECMO support was the arterial switch procedure (27.4%), with 30% successful weaning from ECMO.

Total anomalous pulmonary venous connection comprised 8.1% from the entire group with 100% successful weaning from ECMO. In this group, the left ventricle might have been too small in the immediate postoperative period; thus, ECMO support may be an integral part of the surgical treatment.

The review of the in-hospital course of the patients treated with ECMO in our institution demonstrated a survival rate of 47%. Age, weight, ECMO time, ECMO in the operating room or in the PICU, dialysis, or types of procedure were not predictive factors for survival in our study [Table 4] [20].

In some studies, survival was found to be greater when ECMO was instituted at some point after successful weaning from cardiopulmonary bypass [21], suggesting better cardiac performance than in patients who could not be weaned from cardiopulmonary bypass in the operating room. Duncan

Table 4. Comparison of survivor and non-survivor clinical variables

Variable	Non-survivors (n = 33)	Survivors (n = 29)	*P* value
Site of ECMO Operating room (N) PICU (N)	 28 5	 25 4	 0.88
Age (mos) (range) Weight (kg) (range) ECMO duration	1 (0–48) 3.7 (2.3–51) 5 (1–13)	3 (0–13) 4.6 (1.9–20) 3 (1–13)	0.78 0.42 0.12
Tetralogy of Fallot	4	6	0.36
Arterial switch operation	12	5	0.09
Total anomalous pulmonary venous return	0	5	0.018

and co-workers [15] suggested prompt establishment of an adequate cardiac output as the most important factor in successful resuscitation [9,22], and indeed in our practice the ECMO team is an integral component of a code protocol.

It was also found that incomplete repair carries the poorest prognosis, with a mortality rate of up to 100% [14]. A complete surgical repair should be a prerequisite for instituting ECMO.

In our study, 12 patients (19.3%) were treated with ECMO support for more than 6 days and 9 of them died. This is consistent with the report by Black and colleagues [14] of no survival in patients on support for more than 6 days [14]. It was shown that 48–72 hours on ECMO provides the most significant contractile function benefit with less advantage beyond that time [21].

The decompression of the left ventricle with active venting during ECMO is routine for many hospitals [9,23]. We, however, did not use left ventricular venting, which may be a contributing factor to the mortality in the arterial switch group. In those patients it is important to decompress the left ventricle and maintain low end-diastolic pressure to ensure sufficient coronary perfusion pressure to facilitate the muscle recovery.

This report has several limitations that are inherent in retrospective observational studies. Further study is needed to determine the most important factor in predicting the outcome.

CONCLUSIONS

ECMO support for post-cardiotomy failure carries significant survival benefit and should be an integral part of the pediatric cardiac surgeon's treatment tools. Improved outcomes can be achieved by eliminating any residual lesions, early deployment and using left ventricular venting.

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Corresponding author:
Dr. L. Sasson
Dept. of Cardiothoracic Surgery, Wolfson Medical Center, P.O. Box 5, Holon 58100, Israel
Phone: (972-3) 502-8723
Fax: (972-3) 502-8735
email: dawn@wolfson.health.gov.il

References

1. Soeter JR, Mamiya RT, Sprague AY, McNamara JJ. Prolonged extracorporeal oxygenation for cardiorespiratory failure after tetralogy correction. *J Thorac Cardiovasc Surg* 1973; 66 (2): 214-18.
2. Langley SM, Sheppard SB, Tsang VT, et al. When is extracorporeal life support worthwhile following repair of congenital heart disease in children? *Eur J Cardiothorac Surg* 1998; 13: 520-5.
3. Chaturvedi RR, Macrae D, Brown KL, et al. Cardiac ECMO for biventricular hearts after pediatric open heart surgery. *Heart* 2004; 90: 545-51.
4. Delius RE, Bove EL, Meliones JN, et al. Use of extracorporeal life support in patients with congenital heart disease. *Crit Care Med* 1992; 20: 1216-22.
5. Alsoufi B, Shen I, Karamlou T, et al. Extracorporeal life support in neonates, infants, and children after repair of congenital heart disease: modern era results in a single institution. *Ann Thorac Surg* 2005; 80: 15-21.
6. Tajik M, Cardarelli MG. Extracorporeal membrane oxygenation after cardiac arrest in children: what do we know? *Eur J Cardiothorac Surg* 2008; 33: 409-17.
7. Allan CK, Thiagarajan RR, del Nido PJ, Roth SJ, Almodovar MC, Laussen PC. Indication for initiation of mechanical circulatory support impacts survival of infants with shunted single-ventricle circulation supported with extracorporeal membrane oxygenation. *J Thorac Cardiovasc Surg* 2007; 133: 660-7.
8. Jenkins KJ, Gauvreau K, Newburger JW, Spray TL, Moller JH, Iezzoni LI. Consensus-based method for risk adjustment for surgery for congenital heart disease. *J Thorac Cardiovasc Surg* 2002; 123 (1): 110-18.
9. Aharon AS, Drinkwater DC, Churchwell KB, et al. Extracorporeal membrane oxygenation in children after repair of congenital cardiac lesions. *Ann Thorac Surg* 2001; 72: 2095-102.
10. Loforte A, Delmo Walter EM, Stiller B, et al. Extracorporeal membrane oxygenation for intraoperative cardiac support in children with congenital heart disease. *Interact CardioVasc Thorac Surg* 2010; 10: 753-9.
11. Del Nido PJ. Extracorporeal membrane oxygenation for cardiac support in children. *Ann Thorac Surg* 1996; 61: 305-11.
12. Jaggers JJ, Forbess JM, Shah AS, et al. Extracorporeal membrane oxygenation for infant postcardiotomy support: significance of shunt management. *Ann Thorac Surg* 2000; 69: 1476-83.
13. Thiagarajan RR, Laussen PC, Rycus PT, Bartlett RH, Bratton SL. Extracorporeal membrane oxygenation to aid cardiopulmonary resuscitation in infants and children. *Circulation* 2007; 116: 1693-700.
14. Black MD, Coles JG, Williams WG, et al. Determinants of success in pediatric cardiac patients undergoing extracorporeal membrane oxygenation in children after cardiac surgery. *Ann Thorac Surg* 1995; 60: 133-8.
15. Duncan BW, Ibrahim AE, Hraska V, et al. Use of rapid-deployment extracorporeal membrane oxygenation for the resuscitation of pediatric patients with heart disease after cardiac arrest. *J Thorac Cardiovasc Surg* 1998; 116: 305-11.
16. Walters HL, Hakimi M, Rice MD, et al. Pediatric cardiac surgical ECMO: multivariate analysis of risk factors for hospital death. *Ann Thorac Surg* 1995; 60: 329-37.
17. Kane DA, Thiagarajan RR, Wypij D, et al. Rapid-response extracorporeal membrane oxygenation to support cardiopulmonary resuscitation in children with cardiac disease. *Circulation* 2010; 122: S241-8.
18. Ziomek S, Harrell JE, Fasules JW, et al. Extracorporeal membrane oxygenation for cardiac failure after congenital heart operation. *Ann Thorac Surg* 1992; 54: 861-8.
19. Balasubramanian SK, Tiruvoipati R, Amin M, et al. Factors influencing the outcome of pediatric cardiac surgical patients during extracorporeal circulatory support. *J Cardiothorac Surg* 2007; 2: 4.
20. Alsoufi B, Al Radi OO, Gruenwald C, et al. Extra-corporeal life support following cardiac surgery in children: analysis of risk factors and survival in a single institution. *Eur J Cardiothorac Surg* 2009; 35: 1004-11.
21. Ghez O, Horea F, Ughetto F, Fraisse A, Kreitmann B, Metras D. Postoperative extracorporeal life support in pediatric cardiac surgery: recent results. *ASAIO J* 2005; 51: 513-16.
22. 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: 1637-42.
23. Duncan BW, Hraska V, Jonas RA, et al. Mechanical circulatory support in children with cardiac disease. *J Thorac Cardiovasc Surg* 1999; 117: 529-42.

"When money speaks, the truth keeps silent"

Russian proverb