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Experience with Extracorporeal Life Support in Pediatric Patients after Cardiac Surgery

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Extracorporeal life support (ECLS) had been successfully used in neonatal respiratory failure, but cardiac ECLS has been used increasingly in recent years. The purpose of this study was to review our experience in pediatric patients supported by ECLS for postoperative circulatory failure and to analyze the factors associated with mortality. Between January 1999 and December 2004, 68 pediatric patients (< 18 years old) who received ECLS within 7 days after cardiac surgery at the National Taiwan University Hospital were included in this study. The overall survival rate of this cohort was 32.4%. Age and gender did not affect survival. Patients with separate biventricular physiology had a higher probability of survival than those with systemic-pulmonary shunt or cavopulmonary anastomosis (41.3% *vs.* 13.6%, $p < 0.05$). Acute renal failure during ECLS was significantly associated with mortality (83% *vs.* 33.5%, $p < 0.001$). After ECLS initiation, the lowest lactate levels on the second to fourth days were lower in survivors than in nonsurvivors (2.4 *vs.* 3.3 mmol/L, $p < 0.05$). There was a trend toward a better survival in the most recent 2 years in comparison with the previous 4 years (47.6% *vs.* 25.5%, $p = 0.07$), although this trend did not reach statistical significance. In conclusion, nonbiventricular physiology, acute renal failure, and high blood lactate levels after ECLS increased the risk of mortality for pediatric patients requiring ECLS for postoperative cardiac support. *ASAIO Journal* 2005; 51:517–521.

Many patients have a depressed cardiac function during early postcardiac surgical periods.[1,2] Supporting the failing heart with extracorporeal life support (ECLS) may be life-saving when other conventional managements fail to maintain adequate cardiac output.[3] The use of ECLS for cardiac failure had been steadily increased over the past 15 years, with the overall survival rate remaining at approximately 40%.[4] There is still some controversy about the timing of ECLS initiation, duration of ECLS, and prognostic factors for patients receiving ECLS after cardiac surgery.[2,5,6] We have reported our previous experience in adult patients with ECLS for postcardiotomy shock,[7] and in the current article we report our experience with pediatric ECLS patients and try to identify factors associated with the outcomes.

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Materials and Methods

Study Population

The Investigational Review Board of National Taiwan University Hospital approved the study. In our institute, data regarding all ECLS patients, including diagnosis, ECLS indication, treatment course, and outcome, have been prospectively collected for quality assurance since 1999. Records of pediatric patients (aged < 18 years) who received ECLS after cardiac surgery between January 1999 and December 2004 were retrieved from the database for this study.

Patient Classification

The patients were divided into two groups according to cardiac physiology after surgery. Group I consisted of patients with separate biventricular physiology after surgery, including three patients who received a heart transplant. Group II consisted of patients whose cardiac physiology were not biventricular, for example, single ventricle, systemic-pulmonary shunt, cavopulmonary anastomosis, or Fontan physiology.

Indications for ECLS were: 1) failure to separate from cardiopulmonary bypass, thus ECLS was initiated in the operating room; 2) deterioration in the intensive care unit (ICU) because of postoperative low-output syndrome; or 3) cardiac arrest in the ICU with ECLS used for cardiopulmonary resuscitation (so-called extracorporeal cardiopulmonary resuscitation, ECPR).

ECLS Technique

The ECLS circuit consists of a centrifugal pump and a hollow-fiber microporous membrane oxygenator with an integrated heat exchanger, with all surfaces heparin-bound (Medtronic Inc., Anaheim, CA). There was no bridge between the arterial and venous lines.[7] The pre- and postoxygenator blood oxygen saturation was continuously monitored by an MX-2 trioptic measurement cell (Medtronic Inc.). We used a servo-regulated roller pump (COBE International, Arvada, CO) and silicone membrane oxygenator for ECLS (n = 7) only in cases when ECLS was required for longer duration (more than 4–7 days), because this system requires more anticoagulation and may increase postoperative bleeding. In addition, the ECLS with centrifugal pump and hollow-fiber oxygenator is easier to prime.

Almost all patients were cannulated through the ascending

aorta and the right atrium. The sternum wound was kept open with a syringe bridge. Only two patients (weight > 30 kg) received cannulation through the femoral vessels. Decompression of the left ventricle by left atrial (LA) cannulation was done when signs of severe pulmonary edema or left ventricular distension could not be managed by increasing the bypass flow. The systemic-pulmonary shunt was usually kept open during ECLS.

ECLS blood flow was generally maintained between 80 and 120 $ml \cdot kg^{-1} \cdot min^{-1}$. Vasoactive infusions were gradually tapered if adequate blood pressure was achieved using ECLS. Diuretics were administered in cases of fluid overload and a peritoneal dialysis catheter was usually used to augment fluid removal. Hemofiltration could be performed using a hemofilter (FH22; Gambro, Hechigen, Germany) on the ECLS circuit, if needed.

In patients receiving ECLS immediately after surgery, we usually started heparin infusion on the second postoperative day when the risk of bleeding was lower. Patients were anticoagulated to achieve an activated clotting time of 160–180 seconds; in cases with excessive bleeding, the goal was lowered to 140 seconds. We did not use aprotinin or antifibrinolytic agents during ECLS. Platelets were transfused to keep the platelet count above 50,000/mm^3, and red blood cells were generally transfused to maintain a hematocrit between 35% and 40% during ECLS.

The decision to wean a child from ECLS was based on his or her cardiac and pulmonary status. Generally, patients were treated with dopamine, milrinone, and low-dose epinephrine infusions. Clear lung field on chest x-ray and pulsatile wave on arterial blood pressure were considered mandatory for a trial of weaning from ECLS. The patients were sedated and their muscles were relaxed to minimize oxygen consumption. Decannulation was performed in the ICU, and the sternotomy wound was usually kept open for an additional 2–3 days. Usually the patients required adjustment of inotropic agents after weaning from ECLS.

Data Analysis

The primary outcome evaluated was survival at the time of hospital discharge. Age, gender, cardiac physiology, indication for ECLS, duration of ECLS support, presence of acute renal failure during ECLS (defined as urine output < 0.5 $ml \cdot kg^{-1} \cdot h^{-1}$), and re-exploration for mediastinal bleeding were compared between survivors and nonsurvivors.

We collected data regarding arterial blood gas and serum biochemistry in the first week after the initiation of ECLS support. To compare biochemistry before ECLS, serum levels of bilirubin, aspirate aminotransferase (AST), blood urea nitrogen (BUN), creatinine, and lactate were compared between survivors and nonsurvivors. After ECLS, the highest value of bilirubin, AST, BUN, creatinine, creatine kinase (CK), creatine-kinase MB (CK-MB), and cardiac troponin I (cTnI) in the first 4 days was chosen to compare the severity of organ damage between survivors and non-survivors. The lactate level was routinely checked in each blood gas analysis, and the highest and lowest lactate level within the second to fourth days after initiation of ECLS were chosen for comparison.

Statistical Analysis

The demographic and outcome data were analyzed with a standard statistical package (SPSS 8.0 for Windows; SPSS Inc., Chicago, IL). Data are presented as medians with 25th and 75th quartiles. Patients who survived to hospital discharge were compared with those who died in this cohort. Categoric data were compared with the Fisher exact test, whereas continuous variables were compared with the Mann-Whitney test. A significant difference was defined as a p value of less than 0.05.

Results

Patient Characteristics

During the study period, 2,107 children had cardiac surgery in our institute. Sixty-eight patients (3.2%) were treated with ECLS within 7 days after an initial cardiac surgery for either repair or palliation of a congenital heart lesion (n = 65), or after cardiac transplantation (n = 3). Children who received ECLS before cardiac surgery were excluded from the study population. The initial surgical procedures and cardiac physiology after repair are presented in **Table 1**.

Risk Factors for Hospital Mortality

The overall survival rate of this cohort was 32.4% (22 of 68 patients). The demographic and clinical characteristics of survivors and nonsurvivors are presented in **Table 2**. Age, body weight, and sex did not correlate with outcome. The patients with biventricular physiology had significantly better outcomes than those without biventricular physiology. The patients with acute renal failure during ECLS had an increased risk of mortality (odds ratio, 3.92; 95% CI, 1.95-7.89). The requirement of re-exploration for bleeding did not influence the clinical outcome.

Indication for ECLS

In this cohort, 67.6% (46/68) of the patients received ECLS in the operating room. ECLS was initiated in the ICU in 22 patients, and the time elapsed before initiation of ECLS ranged from 1 to 96 hours after surgery. Most patients (21 of 22) required ECLS within 24 hours after cardiac surgery, with a median of 8 hours. Only one patient received ECLS 4 days after surgery with coronary artery bypass grafting for Kawasaki disease, because of progressive low-cardiac output syndrome. The survival rate for patients who received ECLS in the operating room was 37% (17 of 46 patients) and 36% (4 of 11 patients) for those with postoperative low cardiac output syndrome. Only 1 of the 11 patients (9%) who received ECLS during cardiac massage (so-called ECPR) survived. Although the difference was not statistically significant, patients with cardiac arrest had the worst outcome (survival: 9% in the CPR group *vs.* 37% in non-CPR group).

Duration of ECLS

The nonsurvivors had a longer duration of ECLS (median: 112.4 hours *vs.* 75.3 hours) (**Figure 1**). Most of the survivors (91%, 20 of 22 patients) were weaned from ECLS within 6 days. Patients who were supported for more than 6 days had a poor prognosis,

Table 1. Surgical Procedures of the ECLS Patients

	No. of Patients (Survivors)	Percentage of Patients
Biventricle (n = 46)		
Arterial switch (simple and complex switch)	17 (7)	25
Rastelli operation for truncus arteriosus	5 (2)	7.4
CABG	2 (0)	2.9
Repair: TAPVR	3 (2)	4.4
Repair: Interrupted aortic arch	3 (3)	4.4
PA-VSD, Rastelli operation	3 (1)	4.4
Heart transplantation	3 (2)	4.4
Other	10 (2)	14.7
Nonbiventricle (n = 22)		
Norwood stage 1 palliation	10 (2)	14.7
PA-IVS, palliative shunt	2 (0)	2.9
Bidirectional Glenn shunt or hemi-Fontan	5 (1)	7.4
TCPC	1 (0)	1.5
Other	4 (0)	7.4
Total	68 (22)	100

CABG, coronary artery bypass grafting; PA, pulmonary atresia; VSD, ventricular septal defect; IVS, intact ventricular septum; TAPVR, total anomalous pulmonary vein return; TCPC, total cavopulmonary connection.

Surgical Procedures of the ECLS Patients

and no patient survived after more than 10 days of ECLS. Two patients survived after 6 days of ECLS. One was supported for right ventricle failure after heart transplantation, and the other had left ventricular failure after an arterial switch operation.

Laboratory Data

Biochemistry data are summarized in **Table 3**. Levels of cardiac enzymes (CK, CK-MB, cTn-I) and peak bilirubin, AST, BUN, and creatinine were not significantly different between survivors and nonsurvivors. Lactate levels before ECLS were not different, but the survivors had a lower trough lactate level within the second to fourth days after initiation of ECLS.

Mortality of ECMO

In this series, 23 patients could not survive without ECMO for more than 24 hours. The causes of death were refractory ventricular failure (n = 8), a residual anatomical problem such as inflow or outflow obstruction (n = 4), prolonged CPR before operation or ECMO initiation (n = 3), sepsis during ECMO (n = 3), pulmonary artery thrombosis after BT shunt clamp (n = 1), airway obstruction (n = 1), primary heart graft failure (n = 1), and sudden death after removal of ECMO (n = 2).

Mortality Rates after Successful Decannulation

In this series, 45 patients (66 %) survived more than 24 hours after ECLS decannulation, but 51% (23/45) of them did not survive to hospital discharge. The survival duration after weaning from ECLS ranged from 2 to 161 days, with a median of 18 days.

The causes of death in these wean-but-die patients were persistent heart failure (n = 9), multiorgan failure (n = 5), *Candida* infection (n = 2), bacterial infection (n = 3), severe neurologic deficit that prompted withdrawal of treatment (n = 2), retroperitoneal bleeding (n = 1), and sudden cardiac arrest 1 month after removal of ECLS (n = 1).

Left Heart Decompression

In the group with biventricular physiology (n = 46), LA drainage was performed in 12 patients (26%). The survival rate was 33.3% in patients receiving LA drainage (4 of 12 patients)

Table 2. Comparison of Clinical Characteristics between Survivors and Nonsurvivors

	Survivors (n = 22)	Nonsurvivors (n = 46)	p
Gender (male/female)	12/10	29/17	0.60
Age, median (range)	1 mo (1 d to 13.1 y)	1 mo (1 d to 14.7 y)	0.60
Weight in kg, median (range)	3.4 (2.3–31)	3.65 (2.4–36.4)	0.26
Cardiac physiology			0.028
Biventricle	19	27	
Nonbiventricle	3	19	
Indication for ECLS			0.14
Failure to separate CPB	17	29	
LCOS in ICU	4	7	
Cardiac arrest in ICU	1	10	
Acute renal failure, n (%)	8 (36.4%)	39 (84.8%)	<0.001
Duration of ECLS in h, median (range)	75.3 (23–234)	112.4 (6–709)	0.015
Re-exploration for bleeding, n (%)	9 (41%)	25 (54.3%)	0.44

CPB, cardiopulmonary bypass; LCOS, low cardiac output syndrome.

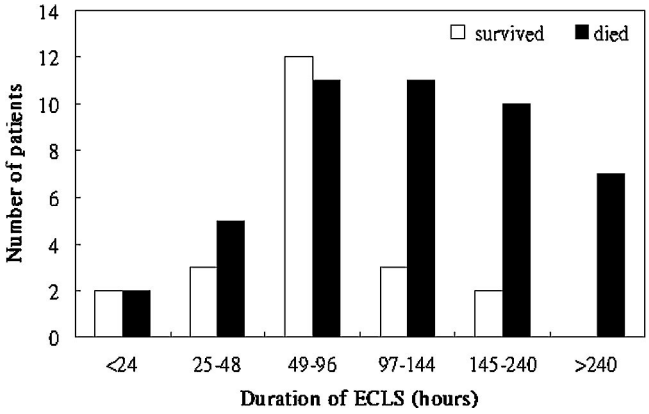

Figure 1. Duration of ECLS of survivors and nonsurvivors

and 44% in those without LA drainage (15 of 34 patients); this difference was not statistically significant ($p = 0.735$).

Survival Rate by Cohort

The survival rates for each 2-year period were 27% (6 of 22 patients, 1999 and 2000), 24% (6 of 25 patients, 2001 and 2002), and 47.6% (10 of 21 patients, 2003 and 2004).

Discussion

In this study, the survival rate was 32.5% overall and 47.6% in the most recent 2-year period. The survival rate was consistent with the global registry provided by the Extracorporeal Life Support Organization.[4]

Biventricle versus Single-Ventricle Physiology

The cardiac physiology with separate biventricle circulation was associated with a better outcome in this study. The result is consistent with the reports by Kolovos *et al.*[2] and the Extracorporeal Life Support Organization.[4] ECLS for patients with Fontan or hemi-Fontan repair was generally associated with a lower survival rate.[2,8]

We had poor outcomes in patients with single-ventricle physiology, particularly after Norwood stage 1 palliation. This may be related to the limited experience in management of such patients, as discussed in the early report by Kulik *et al.*[9] The relatively small sample size limited finer comparison of survival by specific surgical diagnosis.

Timing for Postcardiotomy ECLS

For the timing of initiation of ECLS, the worst result was achieved in patients who received cardiac massage during initiation of ECLS. The poor outcome favored early initiation of ECLS to avoid multiorgan failure.[7] A recent report by Chaturvedi *et al.*[10] confirmed that a better result could be achieved by initiating ECLS in the operating room to avoid prolonged hypoperfusion and catastrophic cardiac arrest. The Michigan group also advocates the initiation of ECLS sooner in the postoperative period.[2]

Postoperative low cardiac output syndrome typically occurs between 6 and 18 hours.[11] In our series, ECLS was usually initiated in the ICU within the same period, with a median of 8 hours after operation. ECLS helped patients overcome postoperative low cardiac output syndrome, and recovery usually occurred within 1 week.

Organ Dysfunction and Mortality

The presence of organ dysfunction defined by biochemistry data (GOT, creatinine) was considered a risk factor for hospital mortality,[6] but we could not demonstrate statistically significant differences in our patient populations. However, acute renal failure during ECLS support is a strong predictor of mortality ($p <$

Table 3. Biochemistry Data of the Survivors and Nonsurvivors

	Survivors	Nonsurvivors	p
Laboratory value (median, 25th–75th quartiles)			
Pre-ECLS			
Bil (mg/dl)	1.5 (0.8–3.4)	1.75(1–2.94)	0.72
GOT (U/l)	50 (32.8–92.3)	45.5 (29.8–171)	0.76
BUN (mg/dl)	10.9 (7–18.9)	15 (10.2–21.2)	0.08
Cre (mg/dl)	0.5 (0.4–0.7)	0.6 (0.48–1)	0.12
Lactate (mmol/l)	11.5 (6.1–11.7)	10.4 (3.2–17.2)	0.9
Post-ECLS			
Peak Bil (mg/dl)*	3.5 (2.8–8.3)	5.6 (2.8–8.3)	0.18
Peak GOT (U/l)*	345 (148–998)	439 (142–2,211)	0.56
Peak BUN (mg/dl)*	34.2 (19.7–38.0)	27.2 (19.3–52.0)	0.94
Peak Cre (mg/dl)*	1.1 (0.75–2.2)	1.2 (0.9–1.85)	0.93
Peak CK (U/l)*	1,047 (819–2,833)	1,292 (621–4,325)	0.92
Peak CK-MB (U/l)*	125 (72–206)	193 (98–295)	0.22
Peak cTnI (ng/ml)*	50 (42–100)	50 (32–100)	0.83
Highest lactate (mmol/l)†	3.7 (2.8–7.2)	6.6 (3.9–11.6)	0.06
Lowest lactate (mmol/l)‡	2.4 (1.3–3.7)	3.3 (2.1–5.5)	0.04

Bil, bilirubin; AST, aspartate aminotransferase; BUN, blood urea nitrogen; Cre, serum creatinine; CK, creatine kinase; CK-MB, creatine kinase, MB form; cTnI, cardiac troponin I, with maximal detection value of 100 ng/ml.

* Peak level indicated the highest value of the first 4 days after ECLS.

† Highest lactate value on the second to fourth days after ECLS start.

‡ Lowest lactate value on the second to fourth days after ECLS start.

Biochemistry Data of the Survivors and Nonsurvivors

0.001). This finding was consistent with many reports dealing with cardiac ECMO.[2,6,7,12] Urine output should be a good indicator of adequate cardiac support for end-organ perfusion. Because we started aggressive renal replacement therapy early, when the patients had poor urine output, the serum creatinine data might not reflect renal function among these patients.

Lactate Level as a Prognostic Factor

Serial lactate measurements in neonatal patients after complex cardiac surgery could be used to predict poor outcome (mortality and need for ECLS),[13] because high lactate levels (9.4 mmol/l) and elevations of lactate of 0.75 mmol/l per hour are associated with poor outcomes. In our patients, lactate was measured routinely in the blood gas analysis. The pre-ECLS lactate level was around 10 mmol/l in both survivors and nonsurvivors, but a lower lactate level (2.4 *vs.* 3.3 mmol/L, $p < 0.05$) achieved within the second to fourth post-ECLS day was noted in the survivors. An early decrease in lactate levels the first day after ECLS initiation is considered a good prognostic sign, but we could not find differences in lactate levels between survivors and nonsurvivors within the first day. We considered that lactate clearance might require more than 24 hours, and we chose the lowest lactate level within the second to fourth post-ECLS day for comparison. Patients with persistent hyperlactemia after ECLS had inadequate tissue perfusion, which might be associated with more severe end-organ injury, and these patients possibly required more advanced mechanical support. We suggest that a decreasing lactate level is a sign of recovery and good prognosis.

ECLS Duration

As previously reported,[2,3,14,15] surviving patients who received ECLS for postcardiotomy cardiogenic shock usually recovered within 3–5 days. The prognosis of patients receiving ECLS longer than 8 or 10 days is quite poor.[15] In this series, most survivors could be weaned off ECLS between 2 and 6 days, and only two patients survived after more than 8 days of ECLS support. Patients who did not recover cardiac function during ECLS may have needed heart transplantation for survival,[12] but none of the survivors had received heart transplantation in this cohort because of limited pediatric donors.

Left Heart Decompression

For patients with biventricular repair, some centers have advocated routine left heart decompression during ECLS.[10] We did not apply the LA drainage in every patient. In small infants, placing the LA drainage may be difficult and thrombus may be formed in the low-flow catheter. We reserve the LA drainage for patients with marked pulmonary edema or a very distended, nonbeating left ventricle.

Study Limitations

Although this study was performed by analyzing a prospectively collected database, there are still some limitations. The patients might have had residual anatomical problems after surgery, and these factors were not thoroughly analyzed in the study. A complete neurologic evaluation was not available in the database, which is an important clinical problem in ECLS patients. The scarcity of pediatric cardiac transplantation in our county might also impact patients with persistent heart failure, who were otherwise suitable for transplantation. Although the study population reflects use of ECLS on "all comers" who remain in cardiogenic shock after cardiac surgery, differences might exist among the surgeons' judgments. The study cohort might represent a learning period, and improvement in perioperative management was not included in the analysis.

Conclusion

In this series, nonbiventricular cardiac physiology, acute renal failure, and a high blood lactate level after ECLS increased the risk of hospital mortality for pediatric patients requiring ECLS for postoperative cardiac support.

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