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Preoperative extracorporeal membrane oxygenation as a bridge to cardiac surgery in children with congenital heart disease

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Abstract

Background—The efficacy of extracorporeal membrane oxygenation (ECMO) in bridging children with unrepaired heart defects to a definitive or palliative surgical procedure has been rarely reported. The goal of this study is to report our institutional experience with ECMO used to provide preoperative stabilization after acute cardiac or respiratory failure in patients with congenital heart disease before cardiac surgery.

Methods—A retrospective review of the ECMO database at Children's Hospital Boston was undertaken. Children with unrepaired congenital heart disease supported with ECMO for acute cardiac or respiratory failure as bridge to a definitive or palliative cardiac surgical procedure were identified. Data collection included patient demographics, indication for ECMO, details regarding ECMO course and complications, and survival to hospital discharge.

Results—Twenty-six patients (18 male, 8 female) with congenital heart disease were bridged to surgical palliation or anatomic repair with ECMO. Median age and weight at ECMO cannulation were, respectively, 0.12 months (range, 0 to 193) and 4 kg (range, 1.8 to 67 kg). Sixteen patients (62%) survived to hospital discharge. Variables associated with mortality included inability to decannulate from ECMO after surgery ($p = 0.02$) and longer total duration of ECMO ($p = 0.02$). No difference in outcomes was found between patients with single and biventricular anatomy.

Conclusions—Extracorporeal membrane oxygenation, used as a bridge to surgery, represents a useful modality to rescue patients with failing circulation and unrepaired complex heart defects.

Extracorporeal membrane oxygenation (ECMO) provides excellent cardiopulmonary support for children with refractory postoperative cardiopulmonary (1, 2, 3, 4) after repair of congenital heart defects, and it has also been shown to successfully bridge some of these children to heart transplantation (5, 6, 7). Support of failing cardiorespiratory function in patients with unrepaired congenital heart disease (CHD) remains a challenging clinical scenario. Reports of ECMO support as a preoperative bridge to a surgical procedure in children with CHD are lacking and restricted to small series of patients or case reports (8, 9).

The goal of this study is to report on survival to hospital discharge of children with CHD who require preoperative ECMO support from a single institution and to evaluate

preoperative, procedural, and ECMO support-related factors associated with mortality. We hypothesized that some children with CHD requiring preoperative ECMO for refractory cardiopulmonary failure can be successfully supported, stabilized, and bridged to reparative or palliative cardiac surgery.

Patients and Methods

Retrospective data collection for purposes of this study was approved by the Institutional Review Board at Children's Hospital Boston, and the need for informed consent was waived. We included patients placed on ECMO for preoperative stabilization and who remained on ECMO until their palliative or definitive cardiac surgical procedure. Patients supported with ECMO after an index cardiac surgical procedure and who had a subsequent surgical operation during ECMO support and those who used ECMO as a bridge to cardiac transplantation were excluded. Data collected included patient demographics, indications for ECMO, details of ECMO cannulation and ECMO course, ECMO complications, details of the surgical procedure, and survival to hospital discharge. These data are summarized for survivors and nonsurvivors and compared using the Mann-Whitney *U* test for continuous data and Fisher's exact test for categorical data. A *p* value of less than 0.05 was considered statistically significant.

Results

Study Population

From January 1996 to December 2008, we identified 26 CHD patients with refractory cardiopulmonary failure requiring ECMO support as a bridge to a cardiac surgical procedure. These 26 patients represent 6.5% of our total ECMO experience (442 ECMO uses in 399 patients) during the same period. Males constituted 69% of the cohort (*n* = 18). Median age at cannulation was 0.12 months (range, 0 to 193). At the time of cannulation 17 patients were neonates (less than 1 month of age) and 6 patients were less than 1 year of age. Median weight was 4.00 kg (range, 1.8 to 67 kg). Indications for ECMO included severe hypoxemia in 17 patients, cardiogenic shock in 4, and cardiopulmonary resuscitation in 5. Our institution has an in-house ECMO team 24 hour a day, 7 days a week that was responsible for all ECMO runs in this study. Other demographic characteristics of these patients are shown in Table 1.

ECMO Circuit and Cannulation

Indications for ECMO were severe hypoxemia, cardiogenic shock, or cardiopulmonary resuscitation. Twenty-four patients had venoarterial ECMO cannulation, and 2 patients had venovenous cannulation. One patient was switched to venoarterial cannulation before surgery because of persistent hypoxemia. Although we preferred the use of venoarterial ECMO in children with cardiac disease, we have rarely used venovenous ECMO to support children with heart disease and respiratory failure in the presence of good cardiac function. The circuit was primed with plasmalyte solution in 13, and whole blood was used to prime the other patients in the series (*n* = 13). The right internal jugular vein and the right common carotid artery were the most common sites used for ECMO cannulation (*n* = 20), usually

with an 8F to 10F arterial cannula in the right common carotid artery and a 10F to 12F venous cannula in the right internal jugular vein. Four patients had thoracic cannulation, and the femoral vessels were used in 2 patients. Thoracic cannulation was only used in patients with previous cardiac surgery and known peripheral vascular occlusions. Femoral vessel cannulation was used in older children. Anticoagulation for conduct of ECMO is initiated with a bolus dose of heparin (50 U/kg) administered at the time of ECMO cannulation and followed by a heparin infusion, maintaining activated clotting times in the range of 180 s to 240 s. Blood product replacement during ECMO is based on our institutional guidelines for management of ECMO patients. Neurologic monitoring during ECMO included daily bedside evaluation by a pediatric neurologist and neurologic imaging using ultrasonography or computed tomography scanning.

Surgical Management

The most common procedure in our series was an arterial switch operation for D-transposition of the great arteries in 8 patients, followed by staged palliation of single-ventricle lesions including hypoplastic left heart syndrome (HLHS) and other anatomic variants: Norwood operation (n = 3); bidirectional Glenn (n = 3); aortopulmonary shunt (n = 1); and bilateral pulmonary artery bands (n = 1). Bilateral pulmonary artery bands were performed on a newborn with HLHS (aortic atresia/mitral stenosis variant), left ventricular-coronary fistulas, and extensive cystic adenoid malformation of the lung. Details of other cardiac surgical procedures in this study population are listed in Table 2. All patients in the D-transposition of the great arteries group had a balloon atrial septostomy before operation. Adequacy of the balloon atrial septostomy (unrestrictive atrial septal defect with left to right shunt) was confirmed by echocardiogram. Sixteen patients (61.5%) did not require ECMO support after surgery, and there were 3 deaths in this group. Decannulation in the operating room was based on patient hemodynamics, oxygenation, and inotropic support required soon after weaning off cardiopulmonary bypass. Of 10 patients who could not be decannulated immediately after surgery, 7 died. Weaning and decannulation from ECMO were undertaken after recovery of hemodynamics and respiratory function. Median time on ECMO before repair was 3 days (range, 0 to 13), and total median duration of ECMO support was 6 days (range, 0 to 27). Specific pre-ECMO and on-ECMO surgical procedures as well as anatomic diagnoses and outcomes are also shown in Table 2.

ECMO Complications

Twenty-one patients in our series (81%) had one or more complications on ECMO. The most frequent complication on ECMO was central nervous system injury (n = 10; 38%). This was defined broadly as any change in an ultrasonography scan or computed tomography scan of the head consistent with hemorrhagic or ischemic injury. Reexploration for bleeding occurred in 7 patients (27%). Other serious complications included blood stream infection (n = 6), renal injury (defined as creatinine greater than 1.5 mg/dL for all ages; n = 3), and infection (n = 3).

Outcomes

Sixteen patients (62%) survived to hospital discharge. All hospital survivors are alive at a median follow-up of 4 years (range, 2 months to 12 years). Patients who were unable to be

decannulated from ECMO at the end of their operation were more likely to die compared with patients who were (70% versus 19%, $p = 0.02$). A long ECMO run (median 8 days for nonsurvivors versus 4 days for survivors) was also associated with mortality ($p = 0.02$). Mortality among neonates was 47% (8 of 17). Both patients weighing less than 2 kg died. The 3 patients with HLHS who underwent a stage I (Norwood [$n = 2$], bilateral pulmonary artery band [$n = 1$]) died, whereas 1 patient with tricuspid atresia who underwent a Norwood operation survived. The ECMO features and outcomes between survivors and nonsurvivors are compared in Table 3, Table 4.

Comment

Although several reports have addressed the importance of ECMO support for low cardiac output, cardiac arrest, hypoxemia after cardiopulmonary bypass, or as a bridge to cardiac transplantation (5, 10, 11, 12, 13, 14, 15, 16) reports describing outcomes of patients undergoing ECMO cannulation for cardiopulmonary failure as a bridge to a cardiac surgical repair are rare. The present case series of 26 patients is the largest reported to date. Inability to decannulate and a long ECMO run after surgery were significantly associated with poor outcomes, whereas low weight at the time of cannulation and neonatal status depicted a trend toward worse outcomes.

Surgical experience indicates that emergently operating on a moribund patient is likely to yield an unfavorable outcome (17, 18). Stabilization with ECMO allows for a period of cardiopulmonary recovery, as well as recovery of other end-organ functions before proceeding to repair, potentially improving patient outcomes. The only patients who are poor candidates for this approach are neonates with obstructed total anomalous pulmonary venous return, as pulmonary vein pressure often remains unacceptably high despite mechanical support, and therefore a prompt surgical repair should be performed. Regarding indications for ECMO, one could expect that patients going on ECMO under cardiopulmonary resuscitation would have a worse outcome than those with cardiogenic shock or hypoxemia. However, we found no differences between groups in terms of outcomes. That could be due to insufficient statistical power, or because we have an in-house ECMO team on call 24 hours a day, 7 days a week.

Several indications in our series are worth mentioning specifically: the largest subgroup was the 8 patients with D-transposition of the great arteries/intact ventricular septum and intact or highly restrictive interatrial communication. Five had persistent pulmonary hypertension with right-to-left shunting across the ductus, 2 had an absent ductus arteriosus with right ventricular dysfunction, and 1 had severe hypoxemia and metabolic acidosis that worsened during transfer to our institution. All had failed successful balloon atrial septostomy and maximal medical therapy. Two died after an arterial switch operation, 1 of ongoing pulmonary hypertension and pulmonary hemorrhage and 1 of a large cerebral intraventricular hemorrhage. Transposition of the great arteries/intact ventricular septum with persistent pulmonary hypertension has been classically associated with worse surgical outcomes (17, 18). Extracorporeal membrane oxygenation enables stabilization and recovery of end-organ function with the circulation in series before surgery. We did not wean from ECMO before arterial switch operation, preferring to deal with end-organ issues with the

assistance of a repaired circulation in series. This management strategy has been described before, although some have recommended discontinuation of ECMO before surgery (8, 19).

Another group of patients who have generally had favorable outcomes are those in need for ECMO support because of insufficient pulmonary blood flow (occluded aortopulmonary shunts, tetralogy of Fallot spells, and so forth). These patients can often undergo a straightforward repair with discontinuation of ECMO after surgery (9).

The most striking predictor of hospital death was inability to discontinue ECMO support after surgery. Indeed, the mortality was 70% (7 of 10) for this group of patients. Inability to decannulate after surgery likely represents significant residual cardiopulmonary failure and could be a marker for either irreversible organ injury (often the lungs), an imperfect operation, bad timing, or the wrong operation. Inability to decannulate after surgery can therefore be used as a prognostic marker as well, and the association of a long ECMO run with poor outcome is likely a consequence of the underlying anatomic and pathophysiologic derangement leading to the need to remain on ECMO after surgery. Although patients are all given anticoagulation therapy before going to surgery, postoperative bleeding has not been an insurmountable issue, with 27% of patients requiring reexploration.

The type of circulation (single ventricle versus two ventricles) established after surgery did not affect outcomes in this small series of patients bridged with ECMO to their cardiac surgical procedure. This finding is possibly due to the relatively large number of single-ventricle patients who had low-complexity and low-risk surgical procedures during ECMO support, including aortopulmonary and cavopulmonary shunts ($n = 6$). When ECMO was used as a bridge to the more complex Norwood procedure in 3 patients, only 1 patient survived (with tricuspid atresia). The 2 other patients who underwent the Norwood operation had HLHS with intact atrial septum, and died of pulmonary complications despite evidence of a good repair. Patients with HLHS and intact atrial septum have been shown to have poor outcomes compared with other variants of HLHS in other studies (20). The relatively encouraging survival with the single-ventricle population bridged using preoperative ECMO may also reflect the increasing experience and expertise with ECMO management of single-ventricle patients as a whole (21, 22). Indeed, Hintz and colleagues (21), using data from the registry of the Extracorporeal Life Support Organization, reported the outcome of extracorporeal life support used in neonates for cardiac indications from 1996 to 2000, with no significant difference in survival between HLHS patients and those with other defects. Further evidence for that is that the present series includes 9 patients with single-vessel anatomy (as opposed to single-vessel physiology)—HLHS or anatomic variants ($n = 5$), pulmonary atresia/intact ventricular septum ($n = 2$), and tricuspid atresia ($n = 2$)—with 3 deaths only in this group.

The small number of patients, retrospective nature of the study, the single-institution experience, and the long timespan involved limit drawing definitive conclusions based on this study. However, this study represents the largest series of patients with CHD supported with ECMO as a bridge to a cardiac repair.

In conclusion, ECMO may be a useful modality for bridging patients with CHD and cardiopulmonary collapse to a definitive or palliative cardiac repair. Inability to discontinue ECMO in the operating room after surgical repair is associated with significantly higher mortality.

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Table 1**Demographics of Patients Receiving Presurgical Extracorporeal Membrane Oxygenation (ECMO)**

Variable	Value
Total number of patients	26
Age, months, median (range)	0.12 (0–193)
Weight, kg, median (range)	4.00 (1.8–67)
Male	18 (69%)
Diagnosis, n	
D-transposition of the great arteries	8
Hypoplastic left heart syndrome	5
Tetralogy of Fallot, PA-IVS	5
Ventricular septal defects	3
Tricuspid atresia	2
Endocarditis	2
Total anomalous pulmonary venous return	1
Indication for ECMO	
Hypoxemia	17
Cardiogenic shock	4
Cardiopulmonary resuscitation	5
Procedures on ECMO	
Arterial switch operation	8
Stage 1 palliation	4
Bidirectional Glenn	3
Blalock-Taussig shunt	3
Septal defect closure	2
Aortic or mitral valve replacement	2
Tetralogy of Fallot repair	2
Pulmonary artery band	1
Total anomalous pulmonary venous return	1
Duration of ECMO before procedure, days, median (range)	3 (0–19)
Total duration of ECMO, days, median (range)	6 (0–27)
Total number of survivors	16 (62%)

PA-IVS = pulmonary atresia–intact ventricular septum.

Table 2

Procedures by Diagnosis and Outcomes

Pt. No.	Diagnosis	Prior Procedures	Indication for ECMO	Surgery	Survival
1	D-TGA/IVS	BAS	Hypoxemia	ASO	No
2	D-TGA/IVS	BAS	Hypoxemia	ASO	No
3	D-TGA/IVS	BAS	Hypoxemia	ASO	Yes
4	D-TGA/IVS	BAS	Hypoxemia	ASO	Yes
5	D-TGA/IVS	BAS	Hypoxemia	ASO	Yes
6	D-TGA/IVS	BAS	Hypoxemia	ASO	Yes
7	D-TGA/IVS	BAS	Hypoxemia	ASO	Yes
8	D-TGA/IVS	BAS	Hypoxemia	ASO, LVOT muscle resection	Yes
9	HLHS/CAM	Lung resection	CPR	Bilateral Pa bands	No
10	HLHS/IAS	BAS/LA suture	CPR	Stage I Norwood	No
11	HLHS/IAS	BAS	Hypoxemia	Stage I Norwood	No
12	Unbalanced CAVC	Stage I Norwood	CPR	BDG, aortoplasty	Yes
13	HLHS	Stage I Norwood	Hypoxemia	BDG	Yes
14	TOF/PA	None	Cardiogenic shock	TOF-PA repair	No
15	TOF/PA	RmBTS	Hypoxemia	Central shunt	Yes
16	TOF/PA	None	Hypoxemia	Unifocalization, RV-Pa conduit	Yes
17	PA-IVS	None	Hypoxemia	RVOT patch, RmBTS	Yes
18	PA-IVS	RmBTS	Hypoxemia	BDG	Yes
19	CAVC+multiple VSDs	PC VSD closure	CPR	CAVC repair	No
20	VSD/left CDH/PPHN	CDH repair	Hypoxemia	Fenestrated VSD closure	No
21	CAVC/TOF	CAVC/TOF repair	CPR	MV replacement	Yes
22	Tricuspid atresia, IB	RmBTS	Hypoxemia	RmBTS, RPA plasty	Yes
23	Tricuspid atresia, IIB	None	Cardiogenic shock	Stage I Norwood	Yes
24	Endocarditis	None	Cardiogenic shock	Ao valve replacement	No
25	Endocarditis	Ao & MV repair	Cardiogenic shock	Ao & MV replacement	Yes
26	TAPVR (supra)	None	Hypoxemia	TAPVR repair	No

Ao = aortic; ASO = arterial switch operation; BAS = balloon atrial septostomy; BDG = bidirectional Glenn; CAM = cystic adenoid malformation; CAVC = complete atrioventricular canal; CDH = congenital diaphragmatic hernia; CPR = cardiopulmonary resuscitation; D-TGA = D-transposition of the great arteries; ECMO = extracorporeal membrane oxygenation; HLHS = hypoplastic left heart syndrome; IAS = intact atrial septum; IVS = intact ventricular septum; LA = left atrium; LVOT = left ventricular outflow tract; MV = mitral valve; PA = pulmonary atresia; PC = pulmonary artery; PC =

percutaneous; PPHN = persistent pulmonary hypertension of the neonate; Pt. = patient; RmBTS = right modified Blalock-Taussig shunt; RPA = right pulmonary artery; RVOT = right ventricular outflow tract; RV = right ventricle; TAPVR (supra) = total anomalous pulmonary venous return (supracardiac); TOF = tetralogy of Fallot; VSD = ventricular septal defect.

Table 3

Comparison of Survivor and Nonsurvivor Clinical Variables

Variable	Survivors (n= 16)	Nonsurvivors (n = 10)	p Value
Age, months (range)	0.6 (0–33)	0.1 (0–193)	0.12
Sex			1.0
Male	11	7	
Female	5	3	
Weight, kg (range)	4.0 (2.9–12.5)	3.2 (1.8–67)	0.12
History of prior cardiac surgery	6	1	0.19
Prematurity and other comorbidities	3	1	0.30
Indication for ECMO			0.41
Hypoxemia	12	5	
Cardiogenic shock	2	2	
Emergency CPR	2	3	
CPR before ECMO	5	6	0.23
Post-ECMO circulation			1.0
Two ventricle	10	7	
One ventricle	6	3	
Post-ECMO procedure type			0.71
Definitive repair	8	4	
Palliative repair	8	6	
Use of ECMO postoperatively	3	7	0.02

CPR = cardiopulmonary resuscitation; ECMO = extracorporeal membrane oxygenation.

Table 4

Comparison of Survivor and Nonsurvivor Extracorporeal Membrane Oxygenation (ECMO) Features

Variable	Survivors	Nonsurvivors	<i>p</i> Value
Duration of ECMO before surgery, days, median (range)	3 (0–7)	6 (0–19)	0.22
Mode of ECMO			0.33
Venoarterial	15	9	
Venovenous and combination	1	1	
Prime solution			0.67
Plasmalyte	7	6	
Blood	9	4	
Cannulation site			0.63
Thoracic cannulation	2	2	
Peripheral cannulation	14	8	
Total ECMO duration, days, median (range)	4 (0–14)	8 (2–27)	0.02
ECMO complications			0.121
At least one complication	11	10	
No Complications	5	0	
Central nervous system injury	4	6	0.11
Renal injury	1	2	0.54
Nosocomial infection	4	3	1.0
Bleeding requiring transfusion	3	4	0.40