SIGNA VITAE 2008; 3(2): 18 - 23

ORIGINAL

Pediatric surgical extracorporeal membrane oxygenation - a case series

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ABSTRACT

Objective. To review demographic and procedural factors and their association with weaning rate and survival from extracorporeal membrane oxygenation (ECMO) in pediatric patients undergoing repair of cardiac malformations.

Methods. The hospital records of children requiring ECMO during cardiac operation due to failure to wean from cardiopulmonary by pass (CPB) were retrospectively reviewed, and an analysis of variables affecting survival was performed.

Results. Thirty-five pediatric patients between January 1, 2000 and December 31, 2006 required ECMO for cardiopulmonary support during cardiac operations. ECMO survival was 54.3% and was comparable across all age groups. The lowest pH during ECMO treatment was the only predictor of mortality (P = 0.006). No other patient, surgical or anesthetic, factor was associated with either weaning from ECMO or hospital survival.

Conclusions. No clear risk factor could be identified for survival from ECMO in our pediatric patients who underwent cardiac surgery and failed weaning from cardiopulmonary bypass.

Keywords: congenital, cardiopulmonary bypass, infants, neonates, failure to wean for cardiopulmonary bypass, survival

Introduction

Extensive repairs of complex cardiac anomalies utilizing cardiopulmonary bypass (CPB) may result in severe myocardial dysfunction leading to inability to wean pediatric patient from CPB. (1) Occasionally this complication may be refractory even to the most intensive pharmacologic therapy and the use of extracorporeal membrane oxygenator (ECMO) may be the only alternative. A significant body of literature exists regarding the use of ECMO in postoperative course after cardiac surgery in children, (2-5) and more limited information exists regarding the use of intraoperative ECMO. In present study we report outcome in 35 pediatric patients who received ECMO intraoperatively after failing weaning from CPB following repair of complex heart malformations. Incidence and survival analysis of this patient population was recently described. (6) In present report we expand the analysis to examine association between demographic, co-morbid, and procedural factors in these patients and failure to wean from surgical ECMO or hospital survival.

Methods

Study Design, Patients and Setting. After Mayo Clinic Institutional Review Board (Rochester, MN, USA) approval, we ascertained all patients 0-17 years of age who were treated with ECMO during cardiac operations requiring CPB at Mayo Clinic, Rochester, MN, between January 1, 2000 and December 31, 2006. All identified charts were authorized for review by the Institutional Review Board. Cases were identified from the Mayo Clinic ECMO registry. We reviewed only medical records of children who were treated with ECMO during their index cardiac surgery. Successful weaning from ECMO was considered if the child survived at least 48 hours after separation.

Data collection and analysis. The medical records of all index patients were abstracted. The primary objective was to examine the potential risk factors for failure to wean from ECMO in pediatric patients undergoing repair of cardiac malformations. We analyzed patient demographics (age, gender, American Society of Anesthesiologists Physical Status [ASA PS] score), patient-related factors: surgical urgency status, and dominant cardiac anatomy, univen-

tricular physiology (encompasses a wide variety of heart defects that functionally and physiologically constitute a single ventricular chamber) (7,8) or biventricular heart physiology. Finally, we analyzed the following procedural factors: use of circulatory arrest, use of intraoperative ultrafiltration, continuous veno-venous hemofiltration (CVVHF), requirement for other means of mechanical circulatory support (intraaortic balloon pump [IAB], left ventricular assist device [LVAD]), duration of anesthesia before ECMO, duration of CPB, and completeness of surgical repair (complete vs. incomplete repair). The variables assessed while on-ECMO included: duration of ECMO therapy, and highest creatinine, and lowest pH during ECMO treatment.

Statistical Analysis. The bivariate association between each of the candidate risk factors and weaning success and hospital survival was first evaluated using the rank sum test for continuous variables and Fisher's exact test for categorical variables. Duration of anesthesia before ECMO, duration of CPB, duration of ECMO therapy, highest creatinine level while on ECMO and lowest pH value while on ECMO were analyzed as continuous variables, while all other variables were analyzed as categorical variables. In all cases, two-tailed P-values ≤ 0.05 were considered statistically significant. Analyses were performed using SAS statistical software (Version 8.2; SAS Institute, Inc., Cary, NC, USA).

Results

Between January 1, 2000 and December 31, 2006 35 pediatric patients failed weaning from CPB and received ECMO intraoperatively. Table 1 shows demographics, primary diagnosis, surgical details and outcome of our ECMO patients. Table 2 shows association between demographic, patient and procedural characteristics (all categorical variables) and ability to be weaned from ECMO (n=24) as well as hospital survival (P values in table 2 compare those who were "able to wean" vs. "unable to wean", and "survived vs. died"). None of the tested characteristics were significantly associated with weaning success or survival. The frequency of successful weaning from ECMO was 68.6% (24/35), however subsequently 5 patients died from other postoperative complications (cardiac arrest, malignant dysrhythmias, etc), and the overall survival rate was 54.3%. All 5 deaths occurred greater than 48 hours after separation from ECMO.

From exploratory analyses, no patient or procedural characteristics were found to differ significantly between patients who were successfully weaned from ECMO vs. not. Furthermore, none of the tested characteristics were different between the survivors and non-survivors. However, there was a trend toward better survival for patients who received either ultrafiltration or hemofiltration during surgery ($P = 0.063$). Table 3 shows association between patient and procedural (continuous) variables and weaning success and hospital survival. None of the tested variables was associated with weaning success, and only one, the lowest pH while on ECMO, was associated with worse hospital survival ($P=0.006$). While the duration of ECMO in those who were successfully weaned tended to be shorter (61 vs. 106 hours) this difference did not reach statistical significance (tested using the rank sum to account for outliers). Among our ECMO patients, 9 required surgical reexploration for bleeding, 4 had intracranial hemorrhage, 1 intracranial thromboembolic event, while 3 received orthotropic heart allotransplant (1 as a primary procedure, and 2 following failed index surgery).

Discussion

Inability to regain cardiopulmonary function to sustain life, regardless of maximal pharmacologic support, is one of the most significant complications of surgery for congenital heart malformations. A mechanical cardiopulmonary support via ECMO has been increasingly used in our institution for pediatric patients with post-CPB refractory heart failure. At Mayo Clinic the decision to institute the ECMO is always made by cardiovascular surgeon and typically when inotropic support of epinephrine exceeds 0.15 mcg/kg/min, when one or more following conditions exist: systemic ventricular dysfunction with elevated filling pressures (right atrial pressure (RAP) >20 mmHg, left atrial pressure (LAP) >15 mmHg), difficulty with oxygenation and/or ventilation, pulmonary hypertension with right ventricular dysfunction.

We recently reported survival of 35 children who received ECMO for pharmacologically refractory heart failure during repair of congenital heart malformations. (6) Over half of our children (54.3%) requiring ECMO were neonates followed by infants (22.3%). The weaning rate from ECMO was 68.7%, and the hospital survival was 54.3% which is the range reported by others. (5,9,10) The small number of children in present study does not allow for comprehensive analysis of risk factors. Therefore, we conducted only an exploratory analysis which did not identify any demographic or procedural characteristics associated with outcome including age, gender, ASA PS, primary cardiac physiology (univentricular vs. biventricular), type of repair (complete vs. incomplete), use of circulatory arrest, intraoperative use of ultrafiltration or need for preoperative ventricular assist (left ventricular assist device or intra-aortic balloon pump), and shorter anesthetic course before initiation of ECMO. Only one factor, the lowest pH during ECMO treatment, was associated with worse hospital survival.

In other ECMO studies several predictors of mortality have been identified, albeit majority of predictors were associated with complications that occurred in later postoperative course. For example, Morris et al. (11) identified kidney or hepatic failure, and Montgomery et al. (12) the presence of multiple organ dysfunction and infections during ECMO treatment as predictors of survival. However, these are not consistent findings, as another study failed to establish association between the degree of renal dysfunction or infection and survival. (13) The only predictor of

Table 1. Patients who failed separation from cardiopulmonary bypass (CPB) received intraoperative extracorporeal membrane oxygenation (ECMO) and survived to leave the operating room.

Event	Age/	Diagnosis	Type of Operation	ECMO survival	Hospital Survival
(year)	Gender/				
	ASA PS				
2000	5d/F/3	IAA Type A; VSD, ASD	Complete repair, closure of ASD and VSD, and end-to-end aortoplasty between descending aorta and aortic arch.	No	No
2000	17m/M/4	Ebstein's anomaly, PFO, severe TR, atrial flutter	TV replaced, PFO closed, cryoablation right atrial isthmus	Yes	Yes
2000	20m/M/3	TGA, tricuspidal atresia, subaortic stenosis	Relief subaortic stenosis	No	No.
2000	3m/F/4	Anomalous left CA from PA; severe LV dysfunction	Repair of anomalous CA, CABG	No	No
2001	10d/F/3	Complete TGA	ASO	Yes	No
2001	17y/M/4	TV atresia, failing Fontain circulation	Intraatrial conduit, Right Maze procedure, left AV valve anuloplasty; heart transplant (second operation)	No	No
2001	6y/M/3	Pulmonary atresia, VSD, previous Blalock-Taussig shunt	Complete repair	Yes	Yes
2001	6d/M/4	Unbalanced complete AVSD; hypoplastic LV, IAA Type B	Modified Norwood; repair VSD and IAA	Yes	Yes
2001	2m/M/4	Severe congenital AS, PFO	Ross-Konno procedure (aortoventriculoplasty)	Yes	Yes
2002	5m/M/5	TOF, complete ASD, severe regurgitation common AV valve	Complete repair DORV/AV canal (AVSD) defect; residual LVOT-repaired in second operation	No	No
2002	3d/M/4	TGA, IVS	ASO	Yes	Yes
2002	12y/M/4E	Prosthetic MV and AV endocarditis	MV & AV replacement, CABG x1	Yes	Yes
2002	3d/M/3	TGA, PDA, IVS, ASD	ASO		No
2002	48d/F/4E	Hypoplastic left heart	Heart transplant; aortic arch reconstruction	Yes	Yes
2003	14d/F/4	Double outlet R ventricle, VSD, AS	Modified Norwood procedure	Yes	Yes
2003	5d/M/3	IAA Type A, CoA, ASD, VSD,PI	Arch reconstruction, ASD+VSD closure		No
2003	2d/M/4	HLHS, ASD	Norwood procedure, stage I	Yes	Yes
2003	3m/F/3	Complete AVSD; Down syndrome	Complete repair	Yes	No
2003	7d/M/4	Truncus arteriosus, severe truncal valve insufficiency	Complete repair	Yes	Yes
2003	3d/M/4	TGA, VSD, DORV	ASO, VSD repair, PDA ligation	No	No
2003	1d/M/5E	Obstructive TAPVC, PDA	Complete repair, ligation PDA	Yes	Yes
2004	6d/M/4	Obstructive TAPVC (infracardiac). PDA, pulmonary edema	Complete repair TAPVC, ligation of PDA	No	No
2004	40d/M/3	Pulmonary atresia, VSD, PDA	Compete repair, ligation PDA	Yes	Yes
2004	5y/F/4E	Ebstein's anomaly, ASD, severe RV dysfunction	TVR, ASD closure, bidirectional Glenn shunt; Converted to fenestrated Fontain	No	No.
2004	6d/M/4	HLHS, AVSD	Norwood procedure, pulmonary homograft, reconstruction RV, PDA closure	No	No
2005	7y/F/4	Cleft MV, MVR, TVR, CHF	MV, TV repair	Yes	Yes
2005	4d/F/4	CoA, hypoplastic arch, large PDA, PFO	Repair of CoA, ligation PDA	Yes	Yes
2005	7d/M/3	TGA, VSD, ASD, bicuspidal pulmonary valve	ASO, VSD+ASD closure	Yes	Yes
2005	11y/M/3	Congenital AS	AVR	Yes	Yes
2005	4d/M/4	Congenital AS	Ross-Konno aortoventriculoplasty	Yes	No
2006	21d/F/3	Obstructive TAPVC	Compete repair	Yes	Yes
2006	21d/F/3	AVSD, 2 AV valve orifices, large ostium primum defect, VSD, hypoplastic L ventricle	Biventricular repair	Yes	Yes
2006	19d/F/3	Unbalanced AVSD; HLHS and aortic arch; coarctation aorta.	Modified Norwood, stage 1	No	No
2006	25d/M/4	Obstructive TAPVS; PHTN	Complete repair	Yes	Yes
2006	3m/F/4	Interrupted aortic arch; severe subaortic stenosis, severe valvular stenosis, VSD	Complete repair; Heart transplantation (second operation);acute allograft rejection	No	No

AR, aortic regurgitation; ARF, acute renal failure; AS, aortic stenosis; ASA, American Society of Anesthesiologists; ASD, atrial septa defect; ASO, arterial switch operation; AV, atrio-ventricular; AVR, aortic valve replacement; AVSD, atrioventricular septal defect (AV canal); BV, biventricular; CA coronary artery; CABG, coronary artery bypass grafting; CoA, coarctation of the aorta; CHF, congestive heart failure; d, day; DORV, double outlet right ventricle; E, emergency; ECMO, extracorporeal membrane oxygenation; F, female; HLHS, hypoplastic left heart syndrome; IAA, interrupted aortic arch; IVS, intact ventricular septum; LV, left ventricular; LVOT, left venticular outflow tract; m, month; M, male; MS, mitral stenosis; MV, mitral valve; MVR, mitral valve regurgitation; PA, pulmonary artery; PDA, patent ductus arteriosus; PFO, patent foramen ovale; PHTN, pulmonary hypertension; PI, pulmonary insufficiency; RV, right ventricle; S/P, status post; TAPVC, total anomalous pulmonary venous connection; TGA, transposition of great arteries; TOF, tetralogy of Fallot; TR, tricuspidal regurgitation; TV, tricuspidal valve; TVR, tricuspidal valve regurgitation; VSD, ventricular septal defect. RACHS-1 risk for in-hospital death, see classification in Jenkins et al. (16)

Table 2. Bivariate association between patient and procedural characteristics and ability to be weaned from extracorporeal membrane oxygenation (ECMO) or hospital survival.

Variable	N*	Able to Wean N (%)	P-value†	Hospital Survival N (%)	P-value†
Overall	35	24 (68.6)		19 (54.3)	
Gender			0.708		0.503
Male	22	16 (72.7)		13 (59.1)	
Female	13	8 (61.5)		6 (46.2)	
ASA PS			0.733		0.562
3	12	9 (75.0)		5 (41.7)	
4	21	14 (66.7)		13 (61.9)	
5	2	1 (50.0)		1 (50)	
Age groups 0-30 days 31 days-<1 year 1-17 years	 19 8 8	 14 (73.7) 5 (62.5) 5(62.5)	0.701	 10 (52.6) 4 (50.0) 5 (62.5)	0.909
Heart physiology			0.226		1.000
Univentricular	8	4 (50)		4 (50)	
Biventricular	27	20 (74.1)		15 (55.6)	
Surgical repair			0.226		1.000
Incomplete	8	4 (50)		4 (50)	
Complete	27	20 (74.1)		15 (55.6)	
Emergency			0.640		0.187
No	29	19 (65.5)		14 (48.3)	
Yes	6	5 (83.3)		5 (83.3)	
Stable at arrival to OR‡			1.000		0.503
No	13	9 (69.2)		6 (46.2)	
Yes	22	15 (68.2)		13 (59.1)	
Circulatory Arrest			1.000		0.723
No	10	7 (70.0)		6 (60)	
Yes	25	17 (68.0)		13 (52)	
Intraoperative use of UF/HF (any)			0.063		0.379
No	6	2 (33.3)		2 (33.3)	
Yes	29	22 (75.9)		17 (58.6)	
LVAD or IABP on arrival to OR			0.314		0.457
No	34	24 (70.6)		19 (55.9)	
Yes	1	0 (0.0)		0 (0)	

*Overall number in each category used as the denominator when calculating the percentage of patients able to wean from ECMO.

†P-values are from Fisher's exact.

‡Patients were considered unstable if they required either mechanical ventilation or vasopressor support on arrival to the operating room (OR).

Abbreviations: UF/HF-ultrafiltration or hemofiltration; American Society of Anesthesiologists Physical Status (ASA PS); LVAD, left ventricular assist device; IABP, intraaortic balloon pump.

mortality in our study was the lowest pH value while on ECMO, which is consistent with a study (13) that showed that the highest lactate level within 48 hours on ECMO predicted death.

Intuitively, the type of heart defect or completeness of surgical repair could affect the survival. For example, Black et al. (14) found better ECMO survival in children who had complete repair than in those with residual heart defect (incomplete repair). However, the completeness of repair was not a significant factor for either ECMO weaning or survival in our patients. Kolovos et al. (13)

Table 3. Bivariate association between procedural characteristics (continuous variables) and ability to be weaned from extracorporeal membrane oxygenation (ECMO) and hospital survival.

Variable	ECMO Unable to Wean N=11	ECMO Able to Wean N=24	P†	Hospital Death N=16	Hospital Survival N=19	P†
Anesthesia time before ECMO (hr)	7.5 (4.3, 9.4)	6.5 (4.0, 10.5)	0.099	7.5 (4.1, 9.4)	6.6 (4.0, 10.5)	0.191
Duration of CPB (min)	256 (87, 433)	189.5 (99, 401)	0.140	233 (87, 433)	191 (105, 401)	0.778
Time of ECMO (hr)	106 (4, 1261)	60.5 (19, 171)	0.126	100.5 (4, 1261)	57 (20, 171)	0.132
Highest creatinine on ECMO	0.8 (0.5, 2.7)	0.75 (0.3, 2.4)	0.421	0.85 (0.3, 2.7)	0.7 (0.4, 2.4)	0.309
Lowest pH on ECMO	7.32 (7.14, 7.36)	7.35 (7.14, 7.49)	0.105	7.32 (7.14, 7.36)	7.36 (7.15, 7.49)	0.006

†P-values are from the rank-sum test.

Values are median (min-max).

reported that children who received ECMO after an adequate two-ventricular repair (biventricular physiology) had lower risk of death compared to those with single ventricle physiology. In contrast, another study reported 61% survival to discharge in infants with univentricular physiology, compared with 43% in those with biventricular physiology. (9) Morris et al. (11) did not confirm the association of univentricular physiology with increased mortality, which agrees with our findings (table 2).

Generally speaking, longer organ ischemia and/or time on bypass, use of circulatory arrest, are all surrogate markers of increased complexity of repair, and therefore could be associated with mortality. However, none of these factors played a significant role in weaning from ECMO or hospital survival in our patients. Another surrogate index of less reversible organ dysfunction is extended time spent on ECMO (14), and its use for more than 72 hours has been related with poor outcome. (9) Others reported no survival after use of ECMO more than 208 (15) or 256 hours. (12) While our non-survivors spent longer time on ECMO (ECMO times were 60.5 vs. 106 hours, for survivors vs. non-survivors, respectively) the difference was not statistically significant. In contrast to some reports (12,14,15), Morris et al. (11) found that ECMO duration over 72 hours is not necessarily the predictor of poor prognosis. Therefore, protracted use of ECMO appears not to be a clear indication for its discontinuation.

Study Limitations. The limitations of this study are the small number of ECMO cases which precludes the performance of meaningful statistical analyses of risk factors associated with weaning and mortality. The retrospective nature of our review carries the inherent limitation of the potentially inconsistent nature of information in the medical record. We cannot exclude that relevant information was omitted from the description of some events.

In conclusion, in pediatric patient who require intraoperative ECMO following CPB hospital survival was 54.3%. We identified association between lowest pH during ECMO treatment and survival and no other demographic or procedural factors were associated with either weaning from ECMO or hospital survival. Therefore, it appears that the complexity of repair and surgical factors related to complex heart anomalies determined the outcome in our patient cohort.

ACKNOWLEDGMENTS

We are grateful to: Shonie L. Buenvenida, R.N., for help in organizing data collection for this study; Mr. Carl Walin (Mayo Clinic Anesthesia Information Services) and Mrs. Judy Lenoch (Data Management Specialists, Division of Cardiovascular Surgery Research, Mayo Clinic) for assistance in data retrieval.

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