Extracorporeal membrane oxygenation support after the Fontan operation

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Objective: Extracorporeal membrane oxygenation has been used to support children with cardiac failure after the Fontan operation. Mortality is high, and causes of mortality remain unclear. We evaluated the in-hospital mortality and factors associated with mortality in these patients.

Methods: Extracorporeal Life Support Organization registry data on patients requiring extracorporeal membrane oxygenation after the Fontan operation from 1987 to 2009 were retrospectively analyzed. Demographics and extracorporeal membrane oxygenation data were compared for survivors and nonsurvivors. A multivariable logistic regression model was used to identify factors associated with mortality.

Results: Of 230 patients, 81 (35%) survived to hospital discharge. Cardiopulmonary resuscitation was more frequent (34% vs 17%, $P = .04$), and median fraction of inspired oxygen concentration was higher (1 [confidence interval, 0.9–1.0] vs 0.9 [confidence interval, 0.8–1.0], $P = .03$) before extracorporeal membrane oxygenation in nonsurvivors compared with survivors. Extracorporeal membrane oxygenation duration and incidence of complications, including surgical bleeding, neurologic injury, renal failure, inotrope use on extracorporeal membrane oxygenation, and bloodstream infection, were higher in nonsurvivors compared with survivors ($P < .05$ for all). In a multivariable model, neurologic injury (odds ratio, 5.18; 95% confidence interval, 1.97–13.61), surgical bleeding (odds ratio, 2.36; 95% confidence interval, 1.22–4.56), and renal failure (odds ratio, 2.81; 95% confidence interval, 1.41–5.59) increased mortality. Extracorporeal membrane oxygenation duration of more than 65 hours to 119 hours (odds ratio, 0.33; 95% confidence interval, 0.14–0.76) was associated with decreased mortality.

Conclusions: Cardiac failure requiring extracorporeal membrane oxygenation after the Fontan operation is associated with high mortality. Complications during extracorporeal membrane oxygenation support increase mortality odds. Prompt correction of surgical bleeding when possible may improve survival. (J Thorac Cardiovasc Surg 2011;142:504-10)

Extracorporeal membrane oxygenation (ECMO) has been used to provide mechanical circulatory support for patients with congenital or acquired cardiac disease in cardiac failure when conventional medical management has failed. ECMO has been used with increasing frequency to support the postoperative patient with cardiac failure after repair or palliation of congenital heart disease.[1-9] Indications for ECMO support in the postoperative period include severe cardiac dysfunction from postcardiotomy cardiac failure, hemodynamically unstable and refractory arrhythmias, and circulatory support during and after cardiac arrest (extracorporeal cardiopulmonary resuscitation [ECPR]) as a bridge to recovery or transplantation.[8-12] Morbidity and mortality associated with ECMO use are high; survival in children with heart disease requiring ECMO support is reported to be 33% to 60%.[1-5,8,10-12] Factors associated with mortality in children supported with ECMO after cardiac surgery for congenital heart disease remain variable.[1-8,11]

The Fontan procedure is an established surgical palliation procedure for single ventricle cardiac anomalies in which completion of a total cavopulmonary connection is achieved by anastomosis of the inferior vena cava to the pulmonary arteries, thus allowing passive return of all systemic venous blood into the pulmonary circulation.[13] The use of ECMO to support severe cardiac dysfunction in children with the Fontan circulation has been reported.[14] However, current knowledge of outcomes after ECMO support in this population is limited to case reports and small single-center series. It is therefore difficult to draw inferences regarding the applicability of ECMO for support of severe cardiac dysfunction in this population.[4-7,10,11,15-18]

The purpose of this study was to use a large multi-institutional data set to better evaluate in-hospital mortality

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Abbreviations and Acronyms

CI = confidence interval
CNS = central nervous system
CPR = cardiopulmonary resuscitation
CPT = Common Procedural Technology
ECMO = extracorporeal membrane oxygenation
ECPR = extracorporeal cardiopulmonary resuscitation
ELSO = Extracorporeal Life Support Organization
HLHS = hypoplastic left heart syndrome
IQR = interquartile range
IRB = institutional review board
OR = odds ratio

for children with severe cardiac failure requiring ECMO support after the Fontan operation. We aimed to identify factors associated with mortality to potentially direct management decisions and to help improve patient outcomes.

MATERIALS AND METHODS

Data Source

Data for this study were obtained from the Extracorporeal Life Support Organization's (ELSO) data registry. The ELSO registry collects data on ECMO used for purposes of supporting critically ill patients with cardiorespiratory failure from all indications. Data are reported to the registry from 116 reporting centers, including 14 international centers. Data are collected using a standardized data-collection form containing patient demographic information, diagnosis, and procedures at the time of ECMO onset and at death or discharge, information regarding the indication and conduct of ECMO including details of equipment used, ECMO complications and survival to hospital discharge, and discharge disposition. Data reported to the registry are approved at each member institution by their local internal scientific institutional review board (IRB). Waiver of patient consent for data reporting to ELSO is institution dependent and governed by their local IRB. The registry's data user agreement allows individual member centers to obtain de-identified data for purposes of research and scientific publication without the need for additional IRB approval.

For purposes of this study we extracted data for all patients receiving ECMO who had a primary procedure diagnosis code for the Fontan operation (Common Procedural Technology [CPT] code 33615 [simple Fontan] or 33617 [Fontan operation]). The primary procedure code details patient procedures during the index hospital admission before onset of ECMO. Patient demographic information, primary and secondary diagnosis and procedures, indication for ECMO, pre-ECMO support, pre-ECMO blood gases and ventilator settings, details of ECMO course and duration of ECMO, ECMO complications, survival to hospital discharge, and discharge disposition data were extracted.

Data Categorization

International Classification for Diseases 9th Revision code for hypoplastic left heart syndrome (HLHS; 746.7) was used to categorize patients into those with HLHS and non-HLHS using their reported primary and secondary diagnosis codes. Arterial and venous cannulation sites reported for conduct of ECMO were used to categorize access into thoracic or peripheral vessel cannulation. Patients with a cannulation site reported as either "aorta" or "right atrium" were considered to be cannulated via the thoracic route. Secondary procedural codes and discharge procedure CPT codes for heart transplantation (CPT code 33945) were used to identify patients who underwent cardiac transplantation before hospital discharge.

ECMO complications were categorized using codes created by the ELSO registry for the explicit purpose of reporting complications. We categorized complications as follows: 1. Mechanical complications: defined as mechanical failure of an ECMO circuit component, report of circuit air embolus, or mechanical problems related to the cannula; 2. Circuit thrombus: included the report of thrombus in any area of the ECMO circuit; 3. Surgical bleeding: defined as bleeding from the surgical site or cannulation requiring an intervention with transfusion or surgical intervention; 4. Neurologic injury (central nervous system [CNS] injury): defined as the presence of a clinical diagnosis of brain death, clinical or electroencephalographic evidence of seizures, or radiologic evidence (head ultrasound or computed tomography) of cerebral infarction or bleeding; 5. Renal failure: defined as serum creatinine greater than 1.5 mg/dL regardless of age or need for renal replacement therapy; 6. ECMO-related complications: included continued need for inotropic support while on ECMO, need for cardiopulmonary resuscitation (CPR) while on ECMO, and continued metabolic acidosis defined as pH less than 7.2 despite ECMO support; 7. Cardiac complications: included cardiac arrhythmia during ECMO support requiring treatment and cardiac tamponade requiring intervention; 8. Respiratory complications: defined as pulmonary hemorrhage or pneumothorax requiring drainage during ECMO support; 9. Infectious complications: included culture-proven bloodstream infection; 10. Metabolic complications: included hypoglycemia defined as a blood glucose level less than 40 mg/dL for all ages, and hyperglycemia defined as blood glucose level greater than 240 mg/dL for all ages; and 11. Gastrointestinal complications: defined as gastrointestinal hemorrhage requiring intervention or hyperbilirubinemia defined as total serum bilirubin total greater than 15 mg/dL, indirect bilirubin greater than 13 mg/dL, or direct bilirubin greater than 2 mg /dL. For purposes of purposes of this study, we defined mortality as death before hospital discharge from the institution providing ECMO support. The ELSO registry does not collect information regarding timing of ECMO use after the index operation, pre-Fontan operation hemodynamic data, type of Fontan operation (lateral tunnel or extracardiac conduit), information regarding the use of a fenestration in the Fontan pathway, functional neurologic outcomes at discharge, quality of life information for survivors, and longer-term survival data; thus, these data were not available for analysis.

Statistical Analysis

Demographic, pre-ECMO, ECMO support data, and ECMO complications were compared for survivors and nonsurvivors. The Mann–Whitney *U* test was used to compare continuous variables, and the chi-square test was used to compare categoric data between the two groups. The Fisher exact test was used for comparison of categoric data when the expected value in more than 25% of cells was less than 5. A multivariable logistic regression model was used to evaluate factors associated with mortality for patients receiving ECMO support after the Fontan operation. Candidate demographic, pre-ECMO, ECMO, and ECMO complications variables were selected if their univariate *P* value comparing survivors and nonsurvivors was less than .1. Candidate variables were entered in the logistic regression model using the forward selection procedure. Variables were retained in the model if their adjusted *P* value was less than .05. Continuous variables retained in the multivariable model were tested for the presence of linearity in their association with mortality by categorizing the variable based on the quartile values of their distribution and re-entering the categorized variable into the model. Demonstration of a linear increase or decrease in odds ratio (OR) across categories was considered essential to satisfy criteria for linearity. Continuous variables not meeting the linearity criteria were retained in their categoric form. For patients with multiple ECMO runs (n = 2), only information from the first ECMO run was included in the analysis. Data are

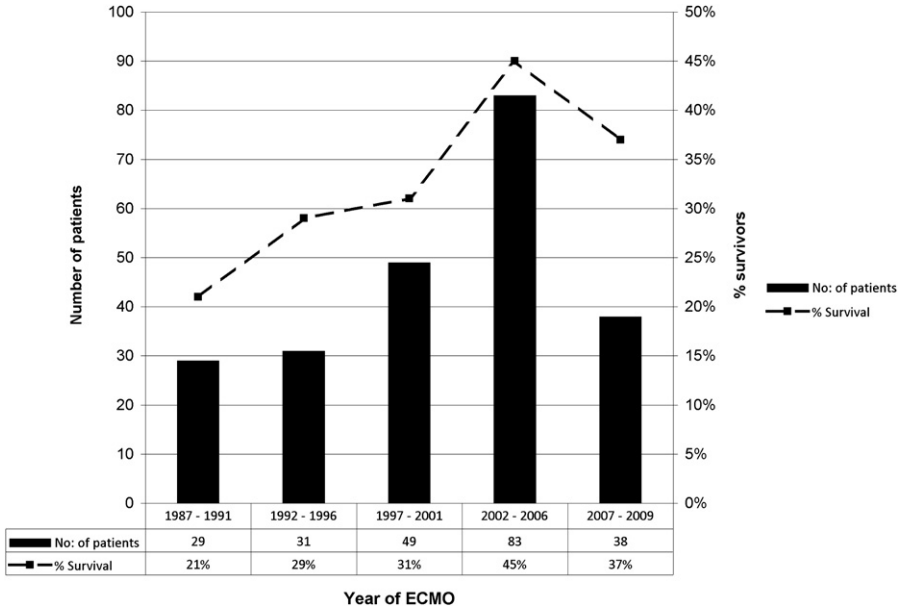

FIGURE 1. Trends in use and survival for patients supported with ECMO after the Fontan operation. Linear trend *P* value for survival = .03 indicating improved survival over time. *ECMO,* Extracorporeal membrane oxygenation.

shown as median (interquartile range [IQR]: 25th, 75th percentiles] and number (%). All authors had access to the data and agree with data analysis and interpretation as presented.

RESULTS

Study Population

A total of 232 ECMO runs (230 patients) were identified in the ELSO registry from 1987 to 2009 in patients with a primary procedure code for the Fontan operation. Median age was 3 years (IQR: 2, 5) and weight was 13 kg (IQR: 11, 16). Indications for ECMO included cardiac failure in the majority of patients (n = 196; 85%), respiratory failure (n = 12; 5%), and ECMO to support CPR (E-CPR; n = 22; 10%). Time from endotracheal intubation to onset of ECMO flow was 25 hours (IQR: 12, 54). The majority of patients (n = 225; 98%) were supported with venoarterial ECMO. A combination mode (venoarterial followed by veno-venous) was used in 1 patient, and 4 patients were cannulated with ''other'' mode. Cannulation sites for ECMO included open chest thoracic cannulation in 100 patients (43%) and peripheral vessel cannulation in 56 patients (24%). Documentation of cannulation site was not available in the remaining patients.

In-hospital mortality for this cohort was 65% (n = 149). ECMO was successfully weaned in 128 patients (56%), but only 81 patients (35%) survived to hospital discharge. ECMO was used primarily as a bridge to transplantation in 16 patients; 5 patients had successful transplants, and 4 patients survived to hospital discharge. The number of patients supported with ECMO after the Fontan operation increased over time. A statistically significant improvement in survival for patients supported with ECMO after the Fontan operation during the study period (chi-square *P* value for linear trend: .03; Figure 1) was observed.

Extracorporeal Membrane Oxygenation Survivors and Nonsurvivors

Demographic data. Table 1 shows the differences in demographic features of survivors and nonsurvivors in the study population. Patient age, weight, gender, race, and year of ECMO use did not vary significantly between survivors and nonsurvivors. Indications for ECMO, including respiratory, cardiac, and ECPR, did not differ significantly between survivors and nonsurvivors.

TABLE 1. Demographic features of study population

Variable	Survivors n = 81	Nonsurvivors n = 149	*P* value
Age (y)	3 (2–4)	3 (2–5)	.69
Weight (kg)	13 (11–16)	13 (11–16)	.55
Gender (male)	50 (62%)	93 (62%)	.75
Race			.11*
White	43 (53)	50 (34)	
Black	9 (11)	14 (9)	
Other	13 (16)	34 (23)	
Missing	16 (20)	51 (34)	
HLHS diagnosis	26 (32)	39 (26)	.34
Year of ECMO			.14
1987–1991	6 (7)	23 (15)	
1992–1996	9 (11)	22 (15)	
1997–2001	15 (19)	34 (23)	
2002–2006	37 (46)	46 (31)	
2007–2009	14 (17)	24 (16)	

HLHS, Hypoplastic left heart syndrome. **P* values exclude comparison of missing patients.

TABLE 2. Pre-extracorporeal membrane oxygenation and extracorporeal membrane oxygenation features of patients supported with extracorporeal membrane oxygenation after the Fontan operation

Variable	Survivors n = 81	Nonsurvivors n = 149	*P* value
Pre-ECMO support			
Inotrope use	54 (67%)	90 (60)	.35
Cardiac pacing	6 (7)	17 (11)	.33
Inhaled nitric oxide	24 (30)	32 (22)	.17
HFOV	2 (3)	6 (4)	.72*
Bicarbonate replacement	21 (26)	36 (24)	.77
NMB use	41 (51%)	59 (40)	.11
Pre-ECMO cardiac arrest	17 (21)	51 (34)	.04
ECMO indication			.51
Respiratory	3 (4)	9 (6)	
Cardiac	72 (89)	124 (83)	
ECPR	6 (7)	16 (11)	
Bridge to cardiac transplant	6 (7)	10 (7)	.84
Pre-ECMO arterial blood gas			
pH	7.3 (7.23–7.37)	7.33 (7.21–7.41)	.32
Paco2 (mm Hg)	44 (33–53)	42 (34–53)	.75
Pao2 (mm Hg)	55 (39–74)	48 (39–74)	.31
Standardized bicarbonate (mmol/L)	21 (19–24)	22 (19–25)	.56
Pre-ECMO ventilator settings			
F_{IO_2}	0.98 (0.80–1.0)	1.0 (0.9–1.0)	.03
PIP (cm of H_2O)	29 (23–35)	30 (26–36)	.14
PEEP (cm of H_2O)	4 (3–6)	5 (3–6)	.33
MAP (cm of H_2O)	10 (9–16)	12 (10–15)	.32
Hemodynamics before ECMO			
Systolic blood pressure (mm Hg)	60 (54–69)	61 (50–75)	.38
Diastolic blood pressure (mm Hg)	36 (30–47)	39 (32–49)	.28
Mean blood pressure (mm Hg)	45 (38–51)	46 (39–59)	.41
Time to ECMO from intubation (h)	27 (12–52)	24 (12–56)	.66
Mode of ECMO			
VA ECMO	80 (99)	145 (97)	.67*
Other mode	1 (1)	4 (3)	
Arterial cannulation site			.73*
Aorta	35 (57)	63 (66)	
Carotid artery	19 (31)	23 (24)	
Femoral artery	6 (10)	8 (9)	
Other	1 (2)	1 (1)	
Venous cannulation site			.40*
Right atrium	29 (48)	45 (48)	
Internal jugular vein	15 (25)	26 (28)	
Femoral vein	12 (20)	10 (11)	
Other	5 (8)	12 (13)	
Thoracic cannulation	36 (59)	64 (67)	.29
ECMO flow at onset (mL/kg/min)	93 (75–104)	93 (76–109)	.74
Duration of ECMO (h)	99 (65–146)	145 (64–256)	.003

ECMO, Extracorporeal membrane oxygenation; *HFOV,* high-frequency oscillatory ventilation; *NMB,* neuromuscular blockade; *ECPR,* extracorporeal cardiopulmonary resuscitation; P_{ACO_2}, partial pressure of carbon dioxide; P_{AO_2}, partial pressure of oxygen; F_{IO_2}, fraction of inspired oxygen concentration; *PIP,* peak inflation pressure; *PEEP,* positive end-expiratory pressure; *MAP,* mean airway pressure. Missing observations (pH: 30; P_{CO_2}: 31; P_{O_2}: 31; standarized bicarbonate: 51; F_{IO_2}: 45; PIP: 44; PEEP: 90; mean arterial pressure: 148: systolic blood pressure: 63; diastolic blood pressure: 66; mean arterial pressure: 86; intubation to ECMO: 18; arterial cannulation site: 74; venous cannulation site: 74; left atrial vent: 74; ECMO flow at onset: 96). *Fisher exact test.

Pre-extracorporeal membrane oxygenation and extracorporeal membrane oxygenation support data. Table 2 shows differences in pre-ECMO and initial ECMO parameters between survivors and nonsurvivors. The incidence of cardiac arrest before ECMO cannulation (not ECPR) was significantly higher in nonsurvivors compared with survivors. The need for inotrope support, temporary cardiac pacing, intravenous bicarbonate administration, use of advanced respiratory support therapies (eg, inhaled nitric oxide and high-frequency oscillatory ventilation) before ECMO deployment, and duration of ventilation before ECMO were not significantly different between survivors and nonsurvivors. Although ventilator settings before ECMO were similar between the 2 groups, nonsurvivors required a significantly higher fraction of inspired oxygen concentration (F_{IO_2}) compared with survivors. Hemodynamics and pre-ECMO arterial blood gas were not significantly different between survivors and nonsurvivors. Mortality was not associated with the use of open-chest thoracic cannulation technique or specific arterial and venous cannulation sites. Duration of ECMO support in survivors was significantly shorter in survivors than nonsurvivors.

Extracorporeal membrane oxygenation complications. Table 3 shows differences in the incidence of ECMO complications between survivors and nonsurvivors. Surgical bleeding, CNS injury, renal failure, need for support with intravenous inotropes while on ECMO, and presence of bloodstream infections during ECMO occurred more frequently in nonsurvivors compared with survivors. There was a trend toward a higher incidence of hyperglycemia and gastrointestinal complications in nonsurvivors compared with survivors. Mechanical problems, such as circuit-related complications and circuit thrombus, were not different for survivors compared with nonsurvivors.

Multivariable logistic regression model of factors associated with mortality. Table 4 shows the results of a multivariable logistic regression model developed to evaluate factors associated with in-hospital mortality. Candidate variables for inclusion in the multivariable model included pre-ECMO Fio2, surgical bleeding, CNS injury, renal failure, need for intravenous inotropes while on ECMO, cardiac tamponade, bloodstream infection, hyperglycemia, gastrointestinal complications while supported with ECMO, and

TABLE 3. Complications in patients supported with extracorporeal membrane oxygenation after the Fontan operation

Complications	Survivors n = 81	Nonsurvivors n = 149	*P* value
Mechanical complications	16 (20)	41 (28)	.19
Circuit related	10 (12)	27 (18)	
Air in circuit	2 (3)	5 (3)	
Cannula related	4 (5)	18 (12)	
Circuit thrombus	13 (16)	24 (16)	.99
Surgical bleeding	23 (28)	69 (43)	.01
Neurologic injury	6 (7)	40 (27)	<.001
Brain death	0 (0)	17 (11)	
Seizures	4 (5)	15 (10)	
Cerebral infarction	2 (3)	5 (3)	
Intracranial bleed	1 (1)	9 (6)	
Renal failure	18 (22)	71 (48)	<.001
Serum creatinine > 1.5 mg/dL	11 (14)	49 (33)	
Renal replacement therapy	14 (17)	44 (30)	
ECMO related			
Need for inotropes on ECMO	49 (61)	109 (73)	.05
CPR on ECMO	1 (1)	5 (3)	.67
pH < 7.2 on ECMO	2 (3)	6 (4)	.72
Cardiac complications			
Arrhythmia	17 (21)	31 (21)	.98
Tamponade during ECMO	1 (1)	9 (6)	.10
Respiratory complications	5 (6)	10 (7)	.87
Pulmonary hemorrhage	3 (4)	7 (5)	
Pneumothorax	2 (3)	5 (3)	
Bloodstream infection	4 (5)	20 (13)	.04
Metabolic complications			
Hypoglycemia (blood glucose < 40 mg/dL)	0 (0)	4 (3)	.14
Hyperglycemia (blood glucose > 240 mg/dL)	7 (9)	26 (17)	.07
Gastrointestinal complications	2 (3)	12 (8)	.09
Gastrointestinal hemorrhage	1 (1)	5 (3)	
Hyperbilirubinemia	1 (1)	7 (5)	

ECMO, Extracorporeal membrane oxygenation; *CPR,* cardiopulmonary resuscitation.

TABLE 4. Factors associated with mortality in patients supported with extracorporeal membrane oxygenation after the Fontan operation

Variable	OR	95% CI	*df, P* value
Surgical bleeding	2.36	1.22–4.56	1, .01
Neurologic complication	5.18	1.97–13.61	1, .001
Renal failure	2.81	1.41–5.59	1, .003
Duration of ECMO (h)			3, .003
≤65	Reference		
>65–119	0.33	0.14–0.76	.01
>119–211	0.71	0.30–1.69	.44
>211	1.72	0.67–4.43	.27

OR, Odds ratio; *CI,* confidence interval; *ECMO,* extracorporeal membrane oxygenation. n = 230; model area under curve: 0.77.

duration of ECMO. Neurologic complications (OR, 5.18; 95% confidence interval [CI], 1.97–13.61; $P = .001$), surgical bleeding (OR, 2.36; 95% CI, 1.22–4.56; $P = .01$), and renal failure (OR, 2.81; CI, 1.41–5.59; $P = .003$) were independently associated with increased odds of mortality. ECMO duration was evaluated after categorizing the variable into quartiles. The second quartile of ECMO duration (>65 to ≤119 hours) was independently associated with decreased odds of mortality compared with ECMO duration values in the first quartile. The curvilinear association of adjusted mortality for the study population and ECMO support duration using generalized additive modeling technique is illustrated in Figure 2.

DISCUSSION

The use of ECMO to support cardiac failure after the Fontan operation has increased over time. By using ELSO registry data from 1987 to 2009, we found that only 35% of these patients survived to hospital discharge. Variables associated with increased mortality included neurologic complications, surgical bleeding, and renal failure. Patients supported with ECMO for approximately 3 to 5 days had increased odds of survival compared with shorter ECMO duration. In our analysis, morality was higher in patients with complications that developed during the course of ECMO, but not associated with demographic, pre-ECMO support, and ECMO support variables. This suggests that ECMO complications may limit survival outcomes for these patients.

Previously published survivals after ECMO support of patients who have undergone the Fontan operation are variable. In a total of 39 patients supported with ECMO after the Fontan operations, compiled from published case reports and small patient series, 18 (46%) survived to hospital discharge.[1,3-8,10,11,14-21] In a series of Fontan case subjects (n = 14) from a single institution, Booth and colleagues[14] reported a survival of 50%. Our reported survival to hospital discharge rate of 35%, however, is considerably lower. This may be related to the multi-institutional nature of our data reflecting considerable variability in ECMO indications, timing of ECMO deployment, and management of patients on ECMO between institutions. However, we think our estimate of survival for patients supported with ECMO after the Fontan operation may be a more accurate estimate because of the large number of patients available for analysis.

The survival of 35% for patients supported with ECMO after the Fontan operation in the current study is lower than the 47% overall survival reported by the ELSO registry for ECMO used to support pediatric cardiac patients during the same time period.[22] Patients with the Fontan circulation pose unique and difficult challenges for ECMO support that may decrease survival in these patients. The anatomy of the cavopulmonary connection in patients who have undergone the Fontan operation may limit venous drainage and preclude adequate decompression of the heart. The consequent need for multiple venous cannulations complicates

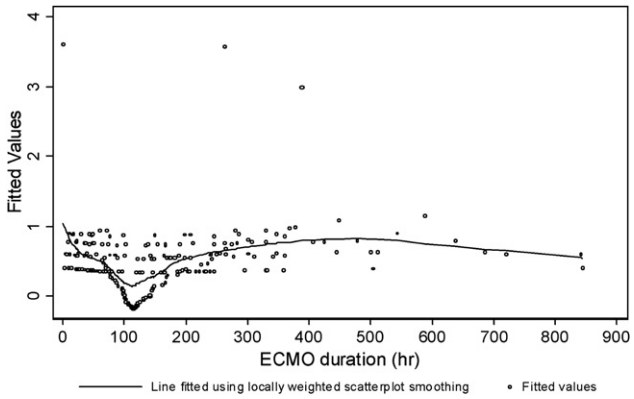

FIGURE 2. Relation of ECMO duration and mortality. Fitted values for ECMO duration were derived from a generalized additive model of factors associated with mortality. The model was adjusted for surgical bleeding, CNS injury, and renal failure. The *solid line* was plotted using locally weighted scatterplot smoothing and shows the curvilinear relationship of ECMO duration and mortality. *ECMO,* Extracorporeal membrane oxygenation.

circuit and patient management. Chronically elevated central venous pressures frequently seen in patients who have undergone the Fontan operation can result in increased susceptibility to end-organ injury before and during ECMO. Furthermore, severe ventricular dysfunction present before ECMO may not recover sufficiently during a short course of cardiac support. These factors either in combination or in isolation may lead to end-organ dysfunction or inhibit ventricular recovery and thus contribute to patient mortality. The trend of improved survival over time may indicate that knowledge of how to support these patients with ECMO may be improving, or that ECMO may be more readily deployed before the onset of severe multiorgan dysfunction in some patients. Unfortunately, these factors cannot be delineated clearly from the available registry data.

In their report of patients supported with ECMO after the Fontan operation, Booth and colleagues[14] report that those patients with an acute and reversible cause for their severe cardiac dysfunction are more likely to benefit from ECMO than those with severe long-standing myocardial dysfunction or patients who require resuscitation or ECPR. The ELSO registry does not collect detailed information on cardiovascular function before ECMO deployment to carefully evaluate these issues. We did not find severity of metabolic acidosis as reflected by arterial blood gas pH to be significantly associated with mortality. Although we were surprised to find that ECPR (ie, ECMO deployed during active CPR) was not associated with patient survival, nonsurvivors had an increased incidence of cardiac arrest during their hospital course before ECMO cannulation. As previously stated, the presence of higher central venous pressure in patients with failing Fontan physiology may increase the risk of CNS and end-organ injury during CPR, thus limiting survival even after ECMO deployment.[9,23] Although not statistically significant, only 17 (25%) of 68 patients who received pre-ECMO CPR in this cohort survived to hospital discharge. Therefore, initiation of ECMO before cardiac arrest may be important in promoting survival in this population.

Complications that occur during the conduct of ECMO have been shown to decrease survival in all patient populations. Similar to prior reports of ECMO use in children with cardiac dysfunction, our analysis demonstrated that renal failure and CNS injury increased odds of mortality. These complications similarly decrease survival in patients supported with ECMO after the Fontan operation. We also found that surgical bleeding requiring intervention decreased odds of survival. Surgical bleeding is common in patients supported with ECMO, particularly those in the postoperative period.[11,13,16] Patients who have undergone the Fontan operation may have a higher propensity to bleed secondary to increased central venous pressure, with consequent liver dysfunction leading to a deficiency of coagulation factors.[24] Careful anticoagulation management, coagulation factor replacement, and attention to surgical hemostasis may decrease the risk of surgical and systemic bleeding (ie, CNS), and decrease the odds of mortality in these patients.

The curvilinear relationship of ECMO duration and survival is interesting and may reflect some of the issues regarding timing of ECMO deployment discussed previously. We found that the odds of mortality were lowest in patients supported with ECMO for more than 65 hours but successfully weaned from ECMO at or before 119 hours. The odds of mortality were not significantly different in patients who were supported with ECMO for more than 119 hours compared with those supported for less than 65 hours. We speculate that many patients supported for less than 65 hours had significant neurologic or other organ dysfunction at the time of ECMO deployment, and were therefore deemed not to be candidates for continuation of ECMO, and subsequently died when ECMO was withdrawn. Patients who required longer duration of ECMO support may have had higher odds of mortality from irreversible cardiac failure or the onset of ECMO complications. It is therefore important to deploy ECMO in a timely fashion before the onset of irreversible end-organ injury and investigate and treat any reversible causes of cardiac dysfunction as quickly as possible so that these patients can be weaned off ECMO expeditiously.

The results presented from this analysis should be interpreted after consideration of the limitations of the data. The ELSO registry data are retrospective and include patients from many reporting centers where experience, indications, patient selection, and management of ECMO may vary considerably. The data-collection instrument is not designed specifically for use with Fontan case subjects; thus, important variables that may be associated with mortality in this population may not have been collected. For example,

time from surgery to onset of ECMO support was not available for analysis. Missing data for some variables precluded their use. Finally, important long-term neurologic and functional data are not collected by the ELSO registry. Despite these limitations, this report contains the largest cohort of Fontan case subjects supported with ECMO to date. It contains useful information about mortality in Fontan case subjects supported with ECMO and may provide guidelines for planning additional studies.

CONCLUSIONS

Patients supported with ECMO after the Fontan operation have a survival to hospital discharge rate of 35%. ECMO complications, including surgical bleeding, renal failure, and CNS injury, decrease survival in these patients. Consideration of early ECMO deployment and correction of surgical bleeding in Fontan case subjects before the onset of end-organ injury may improve survival in these high-risk patients. In addition, the benefits of alternative forms of mechanical support, including short- or long-term ventricular assist devices in patients with cardiac dysfunction after the Fontan operation, should be studied in the future. The trend toward improved mortality over the study period encourages continued investigation and amelioration of factors associated with mortality in these patients.

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