Venovenous extracorporeal membrane oxygenation for patients with single-ventricle anatomy: A registry report

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ABSTRACT

Objective: Support with extracorporeal membrane oxygenation for cardiopulmonary failure is done so with venoarterial cannulation in the majority of children with single-ventricle anatomy. However, there is a growing experience for patients with pure oxygenation/ventilation impairment supported with venovenous extracorporeal membrane oxygenation. We describe that experience.

Methods: Data were collected from the Extracorporeal Life Support Organization registry for patients with single-ventricle anatomy supported with venovenous extracorporeal membrane oxygenation from 1990 to 2012. Descriptive statistics and multivariate analyses for associations with mortality were conducted.

Results: A total of 89 patients with single-ventricle anatomy had venovenous extracorporeal membrane oxygenation performed at a median age of 66 days (8-221). Survival to discharge was 48%. Fifty-four patients (61%) had shunt physiology, 22 patients (25%) had cavopulmonary connections, and 13 patients (14%) had single-ventricle anatomy but with no previous cardiac surgery. Indication for extracorporeal membrane oxygenation was respiratory failure in 59 patients (63%) and cardiac failure in 30 patients (32%). Double-lumen cannulas were used in 62 patients (70%). Bivariate analysis demonstrated that the duration of intubation before extracorporeal membrane oxygenation, mean airway pressure before cannulation, partial pressure carbon dioxide before cannulation, peak inspiratory pressure before cannulation, pump flow at 24 hours, extracorporeal membrane oxygenation run duration, and presence of renal injury were associated with mortality. Multivariate logistic analysis demonstrated that the duration of intubation (adjusted odds ratio, 1.01; 95% confidence interval, 1.003-1.016; $P = .003$), partial pressure carbon dioxide (adjusted odds ratio, 1.04; 95% confidence interval, 1.01-1.068; $P = .007$), mean airway pressure (adjusted odds ratio, 1.16; 95% confidence interval, 1.0-1.342; $P = .05$), and renal injury (adjusted odds ratio, 6.6; 95% confidence interval, 1.879-23.2; $P = .003$) were associated with mortality.

Conclusions: Patients with single-ventricle anatomy in respiratory failure may be treated successfully with venovenous extracorporeal membrane oxygenation, with survival comparable to those treated with venoarterial extracorporeal membrane oxygenation for cardiac failure. Future research on indications for venovenous extracorporeal membrane oxygenation may aid clinicians in deciding the optimal approach for this challenging cohort. (*J Thorac Cardiovasc Surg* 2016;151:1730-6)

Cannulation strategy used for patients with single-ventricle anatomy supported with VV ECMO.

Central Message

Patients with single-ventricle anatomy with respiratory failure may be treated with VV ECMO; however, more data are needed to refine the indications.

Perspective

Patients with single-ventricle anatomy supported with VV ECMO had a survival of 48%. Mean airway pressures and renal injury were associated with mortality. Timely support with ECMO and attention to limiting ventilator-induced injury may improve survival. Although this is technically possible, further delineation of patient selection and cannulation strategies will aid clinicians in the decision-making process.

See Editorial Commentary page 1737.

See Editorials page 1444 and 1446.

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Abbreviations and Acronyms

CPB	= cardiopulmonary bypass
ECMO	= extracorporeal membrane oxygenation
ELSO	= Extracorporeal Life Support Organization
Paco ₂	= partial pressure of carbon dioxide
VA	= venoarterial
VV	= venovenous

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Extracorporeal membrane oxygenation (ECMO) has been used for patients with congenital or acquired heart disease in cardiac or respiratory failure when conventional therapies and interventions have failed. The use of ECMO in the postoperative period for patients with complex congenital heart disease has increased in frequency.¹⁻³ Reports using the Extracorporeal Life Support Organization (ELSO) Registry data examining the outcomes of children undergoing various stages of palliation for single-ventricle physiology (stage 1 palliation, superior cavopulmonary anastomosis, and Fontan operation) demonstrate poor survival compared with overall cardiac ECMO survival.⁴⁻⁶

Venoarterial (VA) ECMO traditionally has been the mode of support for patients with single-ventricle physiology and anatomy in cardiac or respiratory failure. The use of venovenous (VV) ECMO in neonatal and pediatric respiratory failure has been established^{7,8} but has not been applied to patients with single-ventricle anatomy because of physiologic or technical concerns. VV ECMO generally portends a more favorable risk profile than VA ECMO,⁹ and with recent improvements and advancements in cannula and pump technology, the use of VV ECMO may become more feasible.

Currently, only isolated case reports exist regarding the use of VV ECMO in patients with single-ventricle anatomy.¹⁰ We examined the ELSO registry to describe this cohort of patients with respiratory disease supported with VV ECMO.

MATERIALS AND METHODS

Design

Data for this study were retrospectively obtained from the ELSO Registry from January 1, 1999, to December 31, 2012. The study was approved by the Institutional Review Board of the Albert Einstein College of Medicine with a waiver of parental or patient consent. Data were reported to the registry from 251 centers, including international centers. We extracted data for all patients receiving VV ECMO support who had a primary International Classification of Diseases, 9th Revision code for any variant of single ventricle anatomy, 745.31 (single ventricle, right ventricle dominant), 745.32 (single ventricle,

left ventricle dominant), 745.33 (single ventricle, indeterminate), 745.64 (common atrioventricular canal, right ventricle dominant), 745.65 (common atrioventricular canal, left ventricle dominant), 746.11 (tricuspid atresia), 746.31 (aortic atresia), 746.51 (mitral atresia), and 746.7 (hypoplastic left heart syndrome). In addition, Common Procedural Technology codes if available before cannulation of ECMO support were recorded for all patients. Patient demographic information, diagnosis, procedures, indications for ECMO, pre-ECMO support, pre-ECMO clinical status, cannulation type and site, ECMO complications, duration of ECMO, survival to hospital discharge, and discharge disposition were extracted.

Statistical Analysis

Data were analyzed using SAS software (version 9.2; SAS Institute Inc, Cary, NC). Descriptive statistics were performed. Continuous variables were expressed as medians with interquartile ranges for parametric and nonparametric variables. The Mann-Whitney *U* test was performed for non-normally distributed continuous variables, and chi-square test or Fisher exact analysis was performed on all categorical variables. Bivariate analysis was performed to determine the association of variables and mortality. Variables that were associated ($P < .1$) with mortality in the bivariate analyses were cast into a model and examined using multivariate stepwise logistic regression analysis. Variables entered into a multivariate analysis for mortality were age, weight, ECMO run duration, duration of intubation before cannulation, ECMO flow at 24 hours postcannulation, peak inspiratory pressure before cannulation, mean airway pressure before cannulation, partial pressure of carbon dioxide (Paco₂) before cannulation, and the presence of renal injury. Odds ratios and associated confidence intervals were calculated for each variable. Furthermore, a comparison between VA and VV ECMO was undertaken, examining the neurologic complications and mortality within the respective palliated groups of patients with single-ventricle anatomy.

RESULTS

The study population included 89 patients with single-ventricle anatomy who had VV ECMO performed. The study cohort had a median age of 66 days (interquartile range, 8-221) and a median weight of 4 kg (interquartile range, 3.2-6.8). Fifty-four patients (61%) had single ventricles with shunt physiology, 22 patients (25%) had cavopulmonary connections (classic Glenn shunt, bidirectional Glenn shunt, or Fontan), and 13 patients (14%) had single-ventricle anatomy but no recorded previous cardiac surgery or procedure. A total of 23 patients (25%) had a diagnosis of hypoplastic left heart syndrome. The primary indication for ECMO support was respiratory in 59 patients (63%) and cardiac in 30 patients (32%). Acute respiratory failure and respiratory syncytial virus were the most common respiratory diagnoses documented. Survival to hospital discharge was 48%. Survival for respiratory indications was 51% and 53% for cardiac indications. No patient was bridged with VV ECMO to transplantation. Patient characteristics for survivors and nonsurvivors are demonstrated in [Table 1](#). There was no significant difference in demographic, era, or indication data between survivors and nonsurvivors.

Pre- and Initial Extracorporeal Membrane Oxygenation Support and Cannulation

Pre-ECMO support for survivors and nonsurvivors is demonstrated in [Table 2](#). Nonsurvivors had a significantly

TABLE 1. Patient characteristics: Survivors versus nonsurvivors

	Survivors (N = 46)	Nonsurvivors (N = 43)	P*
Age (d), median (IQR)	68.5 (8-221)	46 (8-226)	.62†
Male	24 (52%)	23 (52%)	.89‡
Weight (kg), median (IQR)	4.8 (3.4-6.8)	4.0 (3-7.9)	.18†
Race§			.81
White	25 (54%)	22 (51%)	
Black	4 (9%)	5 (12%)	
Other	12 (26%)	9 (21%)	
Diagnosis of HLHS	9 (20%)	14 (33%)	.16‡
Year on ECMO			.50‡
1990-2001	13 (27%)	15 (35%)	
2002-2012	33 (72%)	28 (65%)	
Duration of ventilation before ECMO	24 (8, 55)	76 (29, 295)	.004†
ECMO indication			.82‡
Cardiac	16 (35%)	14 (33%)	
Respiratory	30 (65%)	29 (67%)	

IQR, Interquartile range; HLHS, hypoplastic left heart syndrome; ECMO, extracorporeal membrane oxygenation. *All comparisons were made between survivors and nonsurvivors. †Mann-Whitney U test. ‡Chi-square test. §Data were incomplete. ||Fisher exact test.

longer duration of ECMO support compared with survivors, as well as longer durations of mechanical ventilation before ECMO. Nonsurvivors appeared to have significantly higher mean airway pressures on the ventilator compared with survivors, as well as a trend toward higher $Paco_2$ on their pre-ECMO arterial blood gas. In addition, nonsurvivors had a significantly higher initial ECMO pump flow at 24 hours after cannulation compared with survivors.

Double-lumen venous cannulas were used in 62 patients (70%). Cannulation sites included the internal jugular vein in 57 patients (64%), right atrium in 24 patients (27%), and femoral veins in 10 patients (11%). Figure 1 demonstrates cannulation sites and cannula type between survivors and nonsurvivors. The most common cannulation approach for patients who were unrepaired or palliated with a central or Sano shunt was a double-lumen venous cannula in the right internal jugular vein. There was no difference between survivors and nonsurvivors. Patients with a classic or bidirectional Glenn shunt commonly underwent multisite cannulation in the right atrium or femoral vein. Location of cannulation had no effect on survival in either group. There was no difference between survivors and nonsurvivors. The patients palliated with a Fontan had multisite cannulation in the right internal jugular vein with the femoral veins.

Extracorporeal Membrane Oxygenation Complications

Air and thrombus in the circuit, surgical bleeding, renal injury, and cardiac support with inotropes were the most common complications. Only the presence of renal injury was significantly more common in nonsurvivors compared

TABLE 2. Pre- and initial extracorporeal membrane oxygenation support

	Survivors (N = 46)	Nonsurvivors (N = 43)	P*
Inotropes	33 (72%)	33 (77%)	.59‡
iNO	26 (57%)	24 (56%)	1.0‡
Neuromuscular blocker	26 (57%)	24 (56%)	1.0‡
HFOV	5 (11%)	11 (26%)	.12‡
Sodium bicarbonate	8 (17%)	7 (16%)	.88‡
Pacemaker	2 (4%)	2 (5%)	1.0§
Narcotics	32 (70%)	26 (60%)	.36‡
Pre-ECMO arrest	3 (7%)	4 (9%)	.7§
Pre-ECMO ventilator setting			
Rate (beats/min)	30 (20-40)	30 (24-40)	.80†
F_{IO_2} (%)	100 (100-100)	100 (100-100)	.34†
PIP (cm H_2O)	29 (23-35)	34 (27-45)	.08†
PEEP (cm H_2O)	5 (4-6)	6 (4-8)	.15†
MAP (cm H_2O)	13 (11-20)	18 (14-22)	.04†
Pre-ECMO ABG			
pH	7.30 (7.21-7.39)	7.28 (7.17-7.37)	.46†
$Paco_2$ (mm Hg)	45.5 (39-57)	57 (37-74)	.05†
PAO_2 (mm Hg)	30 (23-38)	31 (22-40)	.68†
HCO_3 (mmol/L)	23 (21-26)	31.5 (23-40)	.16†
SpO_2 (%)	52 (41-65)	57 (50-69)	.63†
24-h ECMO ventilator setting			
Rate (beats/min)	16 (10-20)	15 (10-18)	.39†
F_{IO_2} (%)	39 (30-50)	40 (30-40)	.92†
PIP (cm H_2O)	24 (20-28)	24 (20-30)	.32†
PEEP (cm H_2O)	8 (5-10)	8 (5-10)	.76†
MAP (cm H_2O)	10 (8-13)	10 (9-15)	.37†
Vital signs			
Systolic BP (mm Hg)	78 (65-95)	66 (53-79)	.15†
Diastolic BP (mm Hg)	41 (35-50)	38 (35-43)	.49†
Mean arterial pressure (mm Hg)	52 (44-66)	48 (44-64)	.64†
Hours on ECMO	88.5 (57-116)	183 (71-288)	.001†
24-h pump flow	81 (68-100)	99.4 (78-110)	.06†

iNO, Inhaled nitric oxide; HFOV, high-frequency oscillatory ventilator; ECMO, extracorporeal membrane oxygenation; F_{IO_2} , fraction inhaled oxygen; PIP, peak inspiratory pressure; PEEP, positive end-expiratory pressure; MAP, mean airway pressure; ABG, arterial blood gas; $Paco_2$, partial pressure of carbon dioxide; PAO_2 , partial pressure of oxygen; HCO_3 , standardized bicarbonate; SpO_2 , peripheral oxygen saturation; BP, blood pressure. *All comparisons were made between survivors and nonsurvivors. †Mann Whitney U test. ‡Chi-square test. §Fisher exact test.

with survivors. Overall complications related to ECMO support compared between survivors and nonsurvivors are shown in Table 3. A comparison of neurologic complications and mortality as it relates to patients supported by VA or VV ECMO is demonstrated in Table 4.

Mortality

Variables entered into the multivariate stepwise logistic analysis for mortality were the duration of mechanical ventilation before ECMO cannulation, duration on ECMO support, ventilator mean airway pressure before ECMO

FIGURE 1. Cannulation strategy for patients with single-ventricle anatomy supported with VV ECMO. VVDL-V, Venovenous double lumen cannula with additional single-lumen venous cannula; VV, venovenous; VVDL, venovenous double lumen.

cannulation, peak inspiratory pressure before ECMO cannulation, partial pressure of CO₂ before ECMO cannulation, ECMO pump flow at 24 hours, and presence of renal injury during ECMO run. The multivariate analysis with categorical and continuous variables is presented in Table 5. Multivariate analysis demonstrated that longer duration of intubation before ECMO, higher Paco₂, higher mean airway pressures, and the presence of renal injury were associated with increased odds of mortality in our analysis.

DISCUSSION

In this analysis of ELSO registry data of patients with single-ventricle anatomy who underwent VV ECMO for respiratory support, the survival was 48%. Variables significantly associated with in-hospital mortality (ECMO run duration, Paco₂, mean airway pressure, and the presence of renal injury) suggest that impairment of pulmonary mechanics contributes to a lower survival. Poor pulmonary compliance from an intrinsic process exacerbated with renal compromise and fluid overload during the ECMO run potentially further impair adequate recovery of lung mechanics. Of note, pump flow at 24 hours trended toward significance in the multivariate analysis (*P* = .06). The higher pump flow may have been a surrogate variable for

TABLE 3. Extracorporeal membrane oxygenation complications

	Survivors (N = 46)	Nonsurvivors (N = 43)	P*
Mechanical complications			
Circuit	2 (4%)	6 (14%)	.15†
Air	8 (17%)	9 (21%)	.67‡
Thrombus	8 (17%)	8 (19%)	.88‡
Hemorrhagic complications			
Surgical bleeding	13 (28%)	9 (21%)	.42‡
DIC	0	0	
Hemolysis	1 (2%)	4 (9%)	.19†
Neurologic complications			
Brain death	1 (2%)	1 (2%)	1.0†
Seizures	3 (7%)	2 (5%)	1.0†
CNS hemorrhage	2 (4%)	3 (7%)	.67†
CNS infarct	1 (2%)	2 (5%)	.61†
Renal complications			
Renal injury and RRT	12 (26%)	25 (58%)	.002‡
Cardiac complications			
CPR on ECMO	1 (2%)	3 (7%)	.35†
Inotropes	21 (46%)	21 (49%)	.76‡
pH <7.2	2 (4%)	2 (5%)	1.0†
Arrhythmia	3 (7%)	2 (5%)	1.0†
Tamponade	0	0	
Pulmonary complications			
Pulmonary hemorrhage and pneumothorax	3 (7%)	7 (16%)	.19†
Infectious complications			
Positive blood culture	3 (7%)	6 (14%)	.30†

DIC, Disseminated intravascular coagulation; CNS, central nervous system; RRT, renal replacement therapy; CPR, cardiopulmonary resuscitation; ECMO, extracorporeal membrane oxygenation. *All comparisons made between survivors and nonsurvivors. †Fisher exact test. ‡Chi-square test.

patients with greater pulmonary vein desaturation or sepsis, which specifically in the neonatal period may elicit constriction of the pulmonary vasculature leading to pulmonary hypertension, hypoxemia, and right heart failure,^{8,11,12} necessitating greater pump flows to maintain adequate oxygenation and carbon dioxide removal.

There have been several published reports analyzing patients with single-ventricle physiology, including neonates, who have undergone support with VA ECMO. Booth and colleagues¹³ reported a survival of 40% for patients receiving the Fontan and bidirectional Glenn. All patients except 1 in this series were supported with VA ECMO as a result of an inability to wean from cardiopulmonary bypass (CPB), low cardiac output syndrome, or cardiac arrest. Sherwin and colleagues⁵ described a large cohort of patients with single-ventricle anatomy supported with VA ECMO after stage 1 palliation, demonstrating 31% survival. This cohort comprised a large portion of patients who were unable to wean successfully from CPB and had low cardiac output syndrome, requiring VA ECMO support within a short period after surgery. Rood and associates⁴ analyzed a cohort of patients with single-ventricle

TABLE 4. Comparison of outcomes: Venoarterial versus venovenous extracorporeal membrane oxygenation§

	VA ECMO	VV ECMO	P
Stage I Norwood†			
Neurologic complication	165 (22%)	4 (7%)	.009¶
In-hospital mortality	512 (69%)	21 (39%)	<.001‡
Superior cavopulmonary anastomosis			
Neurologic complication	24 (23%)	4 (22%)	1.0¶
In-hospital mortality	61 (59%)	7 (39%)	.1‡
Fontan*			
Neurologic complication	46 (20%)	0	
In-hospital mortality	149 (65%)	1 (100%)	1¶

VA, Venoarterial; ECMO, extracorporeal membrane oxygenation; VV, venovenous.

*VA ECMO group n = 230, VV ECMO group n = 1. †VA ECMO group n = 738, VV ECMO group n = 54. ‡Chi-square test. §Data regarding VA ECMO neurologic complication and mortality were obtained from previous studies.^{4,6} ||VA ECMO group n = 103, VV ECMO group n = 18. ¶Fisher exact test.

physiology who were supported with VA ECMO after Fontan completion surgery, with a survival of 35%. The analysis demonstrated that the majority of patients were supported with VA ECMO primarily as a result of cardiac failure. Finally, Jolley and collaborators⁶ published a discussion of a cohort of patients with single-ventricle anatomy supported predominantly with VA ECMO after undergoing a superior cavopulmonary anastomosis, with survival to discharge of 41%. Consistent with other studies mentioned previously, the cohort included mostly patients who were unable to be weaned from CPB and those with low cardiac output syndrome. The majority of the patients in these studies required mechanical support resulting from inability to wean from CBP and low cardiac output syndrome, which is in contrast to the majority of our cohort who were supported with VV ECMO with preserved cardiac function and isolated oxygenation or ventilation impairments, and might be expected to have slightly better outcomes. We acknowledge that one third of our cohort were determined to require VV ECMO because of a cardiac indication. It is certainly plausible that a primary respiratory event/arrest may have precipitated a cardiac event in high-risk cohorts (eg, single ventricle, cyanotic, and ductal-dependent pulmonary blood flow) necessitating ECMO support. We can only hypothesize that this may have been the scenario, although this is a significant potential limitation. Of interest to this point, there was no difference in the use of inotropic support during the VV ECMO run, whether a pulmonary or cardiac indication (46% vs 49%) as indicated by the provider.

We compare the survival of the current cohort with the survival of neonatal and pediatric patients supported for pulmonary failure with VV ECMO, reported in the international ELSO registry summary,¹⁴ for the same time period. Neonatal survivals were 73% for VV cannulation and 83% for venovenous double-lumen cannulation. Pediatric survivals were 64% for VV cannulation and 66% for

TABLE 5. Multivariate analysis for mortality

	Adjusted OR	95% CI	P
Duration of intubation before ECMO (per 1 h of intubation)	1.01	1.003-1.016	.003
Paco ₂ before ECMO (per 1-mm Hg increase)	1.04	1.01-1.068	.007
MAP before ECMO (per 1-cm H ₂ O increase)	1.16	1.0-1.342	.05
ECMO pump flow at 24 h (per 1-mL/kg/min increase)	1.03	1.01-1.42	.09
Renal injury	6.6	1.879-23.2	.003

OR, Odds ratio; CI, confidence interval; ECMO, extracorporeal membrane oxygenation; Paco₂, partial pressure of carbon dioxide; MAP, mean airway pressure.

venovenous double-lumen cannulation. Although the survival of 48% in our patients is lower when compared, this may be due to several factors, including the complex nature of single-ventricle physiology and anatomic challenges of cannulation of the venous anatomy in these patients. In addition, the survival in our study was lower when compared with a large analysis performed by Zamora and colleagues¹⁵ in pediatric patients with primary acute respiratory failure. In this study of patients supported with VV ECMO, survival was 64% for VV cannulation and 68% for venovenous double-lumen cannulation. Superior results in the study by Zamora and colleagues may relate to the fact that their review excluded neonates and the majority of their patients had biventricular anatomy.

In contrast, the survival of our patients is comparable to cohorts of patients with congenital diaphragmatic hernia supported with VV ECMO analyzed by Guner and colleagues¹⁶ (46% survival) and Dimmitt and colleagues¹⁷ (48% survival). There may be similarities in pulmonary compliance and vascular resistance in patients with congenital diaphragmatic hernia and those patients in our study with elevated mean airway and peak inspiratory pressures who did not survive their VV ECMO course. These elevated ventilator parameters demonstrated in nonsurvivors in our cohort may be surrogates for abnormal pulmonary compliance. The poor compliance that is likely due to an underlying pulmonary disease process (ie, respiratory syncytial virus or pneumonia) may lead to an elevation in the pulmonary vascular resistance in the nonsurvivors in our cohort. We draw this comparison with patients with congenital diaphragmatic hernia managed with VV ECMO because of similar management challenges of secondary abnormal pulmonary compliance and elevated pulmonary vascular resistance, however, in this case likely due to pulmonary hypoplasia.

Despite the increased use of VV ECMO in most patient populations, its use in children with single-ventricle anatomy has been rare and limited in the literature. Ryan and colleagues⁹ described a 3-month-old patient after a bidirectional Glenn procedure that was successfully supported with VV ECMO secondary to refractory hypoxemia with preserved

ventricle function. Booth and colleagues¹³ reviewed a series of patients with total cavopulmonary or partial cavopulmonary connections undergoing ECMO therapy predominantly for postoperative low cardiac output syndrome and described 1 patient, who did not survive, treated with VV ECMO for postoperative cyanosis with preserved cardiac function. Jolley and collaborators⁶ analyzed a series of patients with a superior cavopulmonary anastomosis supported with ECMO in the postoperative period. This series included 4 patients supported with VV ECMO, all of whom survived with no further discussion of those patients specifically.

Nonetheless, it remains a rather unique setting for patients with single-ventricle anatomy whether palliated or not who have primarily isolated hypoxemia or respiratory failure with preserved cardiac function. We believe our review describes a unique cohort of patients in whom this may be the case. The increased survival of patients treated with VV ECMO versus VA ECMO is likely related to the preservation of cardiac function. We presume that the majority of patients placed on VV ECMO did not have myocardial failure as their primary indication compared with the patients who would be placed on VA ECMO, potentially highlighting the preservation of myocardial performance in this subset of patients in the context of isolated hypoxemia. This assertion may be supported by the fact that the most common primary diagnosis in our study was respiratory syncytial virus or acute respiratory failure. Second, myocardial oxygenation may be improved because coronary artery blood flow that is derived from the systemic ventricle (or single ventricle) may be more fully saturated compared with VA ECMO in which the systemic ventricle (or single ventricle) may eject deoxygenated blood.¹⁸⁻²⁰ Specifically in patients with unrepaired single ventricles or Norwood stage I, perfusion of the vascular bed with oxygenated blood may mitigate the elevation in pulmonary vascular resistance. Furthermore, there is greater preservation of pulsatile blood flow in VV ECMO compared with VA ECMO, which may relieve the myocardium of increased afterload, decrease the resistance in the vascular bed, and thus improve end-organ perfusion. Last, there are typically lower flow rates in VV ECMO compared with VA ECMO,²¹ which may limit the total exposure of blood to exogenous materials in the ECMO circuit potentially prolonging the longevity of the circuit²¹ and possibly curtailing the systemic inflammatory response the patient may mount. This assertion is reinforced when examining median ECMO flow rates during the first 24 hours in the studies⁴⁻⁶ in which VA ECMO was predominant mode of support and our study in which VV ECMO was the only mode of support.

The cannulation strategy for patients with single-ventricle anatomy supported with VV ECMO whether repaired or at a specific stage of palliation remains a significant challenge. In our cohort, the most frequent approach for patients unrepaired or with shunt physiology was with a double-lumen venous

cannula placed in the atrium via the right internal jugular vein. Patients with the cavopulmonary connections pose an additional technical challenge because at least 1 systemic vein may be separated from the heart. There was no standard cannulation approach in classic or bidirectional Glenn cases; multisite venous cannulation of the right internal jugular and femoral veins was most common. Previous isolated reports have described similar results.^{10,13,22} We could not determine any precedent established in the literature in regard to cannulation strategies for patients with Fontan circulation on VV ECMO. The approach undertaken in the current analysis demonstrated multisite venous cannulation of the right internal jugular and femoral veins.

Study Limitations

There are several limitations to this study. The data obtained from the ELSO registry are retrospective in nature and not complete in all data fields, and can evaluate only short-term clinical outcomes. These data are collected from a heterogeneous group of reporting centers all with their own process of patient selection, clinical expertise, and management of ECMO. In addition, the ELSO registry is not specifically designed to collect data pertinent to patient outcomes because it relates to patients with single-ventricle physiology whether palliated or not. Finally, the data were limited in its ability to give us a detailed picture of cannulation strategies or approaches that are magnified in this analysis of VV ECMO. We can only infer the cannulation approach each center took when placing these patients on VV ECMO.

CONCLUSIONS

Patients with unrepaired single-ventricle physiology or those with shunt physiology who were palliated or not and supported with VV ECMO had a survival to hospital discharge of 48%. Higher mean airway pressures and the presence of renal injury were significantly associated with in-hospital mortality. Potential consideration for more timely support with ECMO and attention to limiting ventilator-induced injury may improve survival. In addition, although technically possible, further delineation of patient selection and cannulation strategies for VV ECMO will aid clinicians in decision-making processes.

Conflict of Interest Statement

Dr Thiagarajan reports consulting fees from Bristol Meyers Squibb, serving as co-chair ECMO registry of ELSO. All other authors have nothing to disclose with regard to commercial support.

References

1. Alsoufi B, Shen I, Karamlou T, Giacomuzzi C, Burch G, Silberbach M, et al. Extracorporeal life support in neonates, infants, and children after repair of congenital heart disease: modern era results in a single institution. *Ann Thorac Surg*. 2005;80:15-21.

2. Duncan BW, Hraska V, Jonas RA, Wessel DL, Del Nido PC, Lauseen PC, et al. Mechanical circulatory support in children with cardiac disease. *J Thorac Cardiovasc Surg.* 1999;117:529-42.
3. Thiagarajan RR, Laussen PC, Rycus PT, Bartlett RH, Bratton SL. Extracorporeal membrane oxygenation to aid cardiopulmonary resuscitation in infants and children. *Circulation.* 2007;116:1693-700.
4. Rood KL, Teele SA, Barrett CS, Salvin JW, Rycus PT, Fynn-Thompson F, et al. Extracorporeal membrane oxygenation support after the Fontan operation. *J Thorac Cardiovasc Surg.* 2011;142:504-10.
5. Sherwin ED, Gauvreau K, Scheurer MA, Rycus PT, Salvin JW, Almodovar MC, et al. Extracorporeal membrane oxygenation after stage 1 palliation for hypoplastic left heart syndrome. *J Thorac Cardiovasc Surg.* 2012;144:1337-43.
6. Jolley M, Thiagarajan RR, Barrett CS, Salvin JW, Cooper DS, Rycus PT, et al. Extracorporeal membrane oxygenation in patients undergoing superior cavopulmonary anastomosis. *J Thorac Cardiovasc Surg.* 2014;148:1512-8.
7. Cornish JD, Heiss KF, Clark RH, Strieper MJ, Boecler B, Kesser K. Efficacy of venovenous extracorporeal membrane oxygenation for neonates with respiratory and circulatory compromise. *J Pediatr.* 1993;122:105-9.
8. Strieper MJ, Sharma S, Dooley KJ, Cornish JD, Clark RH. Effects of venovenous extracorporeal membrane oxygenation on cardiac performance as determined by echocardiographic measurements. *J Pediatr.* 1993;122:950-5.
9. Maslach-Hubbard A, Bratton SL. Extracorporeal membrane oxygenation for pediatric respiratory failure: history, development and current status. *World J Crit Care Med.* 2013;2:29-39.
10. Ryan LP, Montenegro LM, Bird GL, Gruber PJ. Successful support and separation from veno-venous extracorporeal membrane oxygenation support in a three-month-old patient following bidirectional Glenn procedure. *Interact Cardiovasc Thorac Surg.* 2010;11:496-8.
11. Skinner SC, Iacono JA, Ballard HO, Turner MD, Ward AN, Davenport DL, et al. Improved survival in venovenous vs venoarterial extracorporeal membrane oxygenation for pediatric noncardiac sepsis patients: a study of the Extracorporeal Life Support Organization registry. *J Pediatr Surg.* 2012;47:63-7.
12. Brierley J, Carcillo JA, Choong K, Cornell T, Decaen A, Deymann A, et al. Clinical practice parameters for hemodynamic support of pediatric and neonatal septic shock: 2007 update from the American College of Critical Care Medicine. *Crit Care Med.* 2009;37:666-88.
13. Booth KL, Roth SJ, Thiagarajan RR, Almodovar MC, del Nido PJ, Laussen PC. Extracorporeal membrane oxygenation support of the Fontan and bidirectional Glenn circulations. *Ann Thorac Surg.* 2004;77:1341-8.
14. *ECMO Registry of the Extracorporeal Life Support Organization (ELSO).* Ann Arbor, MI: Extracorporeal Life Support Organization; 2015.
15. Zamora JJ, Shekerdemian L, Fallon SC, Olutoye OO, Cass DL, Rycus PL, et al. Outcomes comparing dual-lumen to multisite venovenous ECMO in the pediatric population: the Extracorporeal Life Support Registry experience. *J Pediatr Surg.* 2014;49:1452-7.
16. Guner YS, Khemani RG, Qureshi FG, Wee CP, Austin MT, Dorey F, et al. Outcome analysis of neonates with congenital diaphragmatic hernia treated with venovenous vs venoarterial extracorporeal membrane oxygenation. *J Pediatr Surg.* 2009;44:1691-701.
17. Dimmitt RA, Moss RL, Rhine WD, Benitz WE, Henry MC, Vanmeurs KP. Venous arterial versus venovenous extracorporeal membrane oxygenation in congenital diaphragmatic hernia: the Extracorporeal Life Support Organization Registry, 1990-1999. *J Pediatr Surg.* 2001;36:1199-204.
18. Kinsella JP, Gerstmann DR, Rosenberg AA. The effect of extracorporeal membrane oxygenation on coronary perfusion and regional blood flow distribution. *Pediatr Res.* 1992;31:80-4.
19. Nowlen TT, Salley SO, Whittlesey GC, Kundu SK, Maniaci NA, Henry RL, et al. Regional blood flow distribution during extracorporeal membrane oxygenation in rabbits. *J Thorac Cardiovasc Surg.* 1989;98:1138-43.
20. Smith HG, Whittlesey GC, Kundu SK, Salley SO, Kuhns LR, Chang CH, et al. Regional blood flow during extracorporeal membrane oxygenation in lambs. *ASAIO Trans.* 1989;35:657-60.
21. Fortenberry JD, Pettignano R, Dykes F. ECMO: extracorporeal cardiopulmonary support in critical care. In: Van Meurs K, Peek G, Zwischenberger JB, eds. *Principles and Practice of Venovenous Extracorporeal Membrane Oxygenation.* 3rd ed. Ann Arbor, MI: Extracorporeal Life Support Organization; 2005:85-105.
22. Imamura M, Schmitz ML, Watkins B, Chipman CW, Faulkner SC, Fiser WP Jr, et al. Venovenous extracorporeal membrane oxygenation for cyanotic congenital heart disease. *Ann Thorac Surg.* 2004;78:1723-7.

Key Words: hypoplastic left heart syndrome, extracorporeal membrane oxygenation, outcomes, single ventricle

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