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ORIGINAL ARTICLE

Use of venovenous ECMO for neonatal and pediatric ECMO: a decade of experience at a tertiary children's hospital

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Abstract

Background Advances in extracorporeal membrane oxygenation (ECMO) have led to increased use of venovenous (VV) ECMO in the pediatric population. We present the evolution and experience of pediatric VV ECMO at a tertiary care institution.

Methods A retrospective cohort study from 01/2005 to 07/2016 was performed, comparing by cannulation mode. Survival to discharge, complications, and decannulation analyses were performed.

Results In total, 160 patients (105 NICU, 55 PICU) required 13 ± 11 days of ECMO. VV cannulation was used primarily in 83 patients with 64% survival, while venoarterial (VA) ECMO was used in 77 patients with 54% survival. Overall, 74% of patients ($n = 118$) were successfully decannulated; 57% survived to discharge. VA ECMO had a higher rate of intra-cranial hemorrhage than VV (22 vs 9%, $p = 0.003$). Sixteen VA patients (21%) had radiographic evidence of a cerebral ischemic insult. No cardiac complications occurred with the use of dual-lumen VV cannulas. There were no differences in complications ($p = 0.40$) or re-operations ($p = 0.85$) between the VV and VA groups.

Conclusion Dual-lumen VV ECMO can be safely performed with appropriate image guidance, is associated with a lower rate of intra-cranial hemorrhage, and may be the preferred first-line mode of ECMO support in appropriately selected NICU and PICU patients.

Level of evidence II.

Keywords ECMO · Venovenous · Venoarterial · Cannulation · Critical care

Introduction

Extracorporeal membrane oxygenation (ECMO) is an effective therapy for use in children with profound cardiorespiratory failure. In 1970, Baffes and colleagues reported one of the first successful uses of extracorporeal membrane oxygenation as support in infants with congenital heart defects who were undergoing cardiac surgery [1]. Following Baffes, in 1975, Bartlett and colleagues were the first to successfully use ECMO in neonates with severe respiratory distress [2]. ECMO has now become an important tool in the armamentarium of clinicians for cardiopulmonary support in children whom have exhausted all conventional medical therapies.

Historically, ECMO was performed through venoarterial (VA) access utilizing most commonly the internal jugular vein for venous return and the common carotid artery for infusion of oxygenated blood. The resultant common carotid artery ligation and associated high rate of neurologic complications, including hemorrhage and seizures, have prompted a shift towards the use of venovenous (VV) ECMO [3–6]. With the advent of newer cannula technologies, the use of VV ECMO has steadily increased and the literature would suggest that VV ECMO has been favorably

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compared to VA ECMO in both the neonatal and pediatric populations [7–11].

Several studies have demonstrated the effectiveness and safety of VV ECMO, including the use of newer double-lumen single-site catheters [12–16]. However, the current body of literature is still based on small institutional studies or database data, such as the ELSO database. The objective of this paper was to present the evolution of VV ECMO, including management trends and outcomes, over a 10-year time period in a tertiary neonatal and pediatric ECMO program. The hypothesis of the paper is that VV ECMO is a safe and effective form of ECMO with comparable mortality and decreased neurologic complications when compared to VA ECMO patients.

Materials and methods

Study design

Approval for this retrospective cohort study was obtained through the Baylor College of Medicine Institutional Review Board (H-30201). A retrospective cohort study was performed of all patients cannulated for ECMO by pediatric general surgeons at a tertiary children's hospital from 2005 to 2016. Comparison groups included patients that were cannulated by VA ECMO versus VV ECMO. The formatting and design of this paper has been edited to be compliant in the applicable categories with the STROBE checklist for cohort studies.

Participants

Patients were identified through the Texas Children's Hospital surgical database using ICD-9 code 39.65 (extracorporeal membrane oxygenation). Selection criteria included all ECMO cannulations in both the neonatal intensive care unit (NICU) and pediatric intensive care unit (PICU) during the recruitment period. Patients that were cannulated for primary congenital heart disease were excluded from the study. Follow-up for discharged patients occurred at outpatient facilities within 30 days of discharge.

Variables

Patient variables included birth weight (kg), gestational age (weeks), age at time of surgery (days), indication for ECMO (primary diagnosis), mode of ECMO cannulation, and acid/base status (PaO_2, $PaCO_2$, and pH) recorded at time of cannulation. The primary outcome was survival to discharge. Secondary outcomes included decannulation rate and ECMO-associated complications. Complications due to ECMO were grouped according to the ELSO registry into the following categories: (1) metabolic (2) cardiovascular (3) infectious (4) renal (5) hemorrhagic (6) neurologic (7) pulmonary and (8) mechanical. Data collection was performed using individual chart review of the electronic medical record (EMR) system. Reoperation was defined as any re-cannulation, repositioning, or revision of cannulas, circuit change, chest tube placement, conversion from VA to VV ECMO, thoracotomy, or exploratory laparotomy. Review of outpatient medical records during participant follow-up was performed using the integrated EMR system.

Statistics

Patient baseline demographics and characteristics were computed using descriptive statistic techniques. Bivariate analysis was performed using the χ^2 test and Student's t test for categorical variables and continuous variables, respectively, for outcomes including survival to discharge, re-operation, complications, and decannulation rate. Kaplan–Meier survival analysis with Breslow tests were performed to compare patient survival based on indication for therapy and cannulation mode. Analyses were performed using IBM SPSS statistics version 2.0 (IBM Corporation, Armonk, NY) and Microsoft Excel (Microsoft Corporation, Redmond, WA). Descriptive results are listed as medians and ranges, unless otherwise specified. A p value of ≤ 0.05 was considered significant for all analysis.

Results

Participants and descriptive data

A total of 160 patients were examined for and confirmed eligible for the study during the study time period; 105 NICU and 55 PICU patients. Indications for ECMO are listed in Table 1. The most common diagnoses requiring ECMO were congenital diaphragmatic hernia ($n=64$) and pneumonia ($n=37$). Thirteen patients (8%) had cardiac arrest

Table 1 Indications for ECMO

Indication	VV $n=83$ (%)	VA $n=77$ (%)	p value
Congenital diaphragm hernia	13/83 (16)	51/77 (66)	**<0.001**
Pneumonia	27/83 (33)	3/77 (4)	**<0.001**
Persistent pulmonary hypertension	13/83 (16)	2/77 (3)	**0.005**
Meconium aspiration	8/83 (10)	3/77 (4)	0.214
Cardiac	0/83 (0)	3/77 (4)	0.109
Sepsis	3/83 (4)	10/77 (13)	**0.042**
Other	20/83 (24)	5/77 (6)	**0.002**

Bold values indicate the significance at $p < 0.05$

requiring CPR prior to ECMO cannulation. Demographics are listed in Table 2. Patient age ranged from 0 days to 19 years with a median weight at time of cannulation of 3.2 kg (IQR 2.8–5.4 kg). VV ECMO patients were further broken down into four age categories: < 30 days ($n=40$, 48%); 31–365 days ($n=11$, 13%); 366 days–3 years ($n=9$, 11%); >3 years ($n=23$, 28%). VA ECMO patients had a lower median weight at time of surgery (2.95 kg, range 1.5–50) compared to VV ECMO patients (4.14 kg, range 2.2–89.4) ($p<0.001$). There was no significant difference in the median time on ECMO between the VA ECMO (11 days, range 1–45 days) and VV ECMO (8 days, range 1–77 days) groups ($p=0.882$). The median length of stay for all patients was 42 days (IQR 23–80 days). Patients who required VA ECMO had a significantly longer median hospital length of stay (49 days, range 2–308 days) than VV ECMO patients (34 days, range 4–290 days) ($p=0.009$).

ECMO cannulation mode

VV ECMO was the primary cannulation mode in 83 patients (52%) and VA ECMO cannulation in 77 patients (48%). Nine VV ECMO patients (11%) required conversion to VA ECMO; five of which were < 30 days of age at the time of cannulation. VV cannulas were placed percutaneously in 45% of patients ($n=37$) with 16 placed over an existing central line. There were no cardiac or vascular injuries with the insertion or use of dual-lumen VV cannulas during the ECMO course. Over the 10-year study period, the frequency of VA cannulations steadily declined and the frequency of VV ECMO has increased in both the NICU and PICU populations (Fig. 1). At the start of the pediatric ECMO program 100% of patients received VA ECMO. VV ECMO now accounts for approximately 85% of all ECLS while complication rates and survival to discharge remain unchanged.

Table 2 VV ECMO vs VA ECMO patient demographics and outcome parameters

	VV ($n=83$)	VA ($n=77$)	p
Age, days (median and range)	44 (0–7091)	1 (0–4317)	**<0.001**
Male, n (%)	49 (59)	41 (53)	0.527
Weight, kg (range)	4.14 (2.2–89.4)	2.95 (1.5–50.0)	**<0.001**
pH (mean and standard deviation)	7.20 (6.9–7.5)	7.08 (6.7–7.6)	**<0.001**
pO_2 (median and range)	46 (11–295)	51.9 (5.3–550)	0.436
pCO_2 (median and range)	64 (25–148)	84 (29–239)	**0.004**
ECMO duration, days (median and range)	8 (1–77)	11 (1–45)	0.882
Discharged alive, *n* (%)	49 (59)	42 (55)	0.633
Decannulation, *n* (%)	60 (71)	58 (76)	0.475
Death on ECMO, *n* (%)	24 (29)	18 (24)	0.475
Length of stay, days (median and range)	34 (4–290)	49 (2–308)	**0.009**
Re-operation, *n* (%)	20 (24)	17 (22)	0.852

Bold values indicate the significance at $p < 0.05$

VV venovenous, *VA* venoarterial, *ECMO* extracorporeal membrane oxygenation

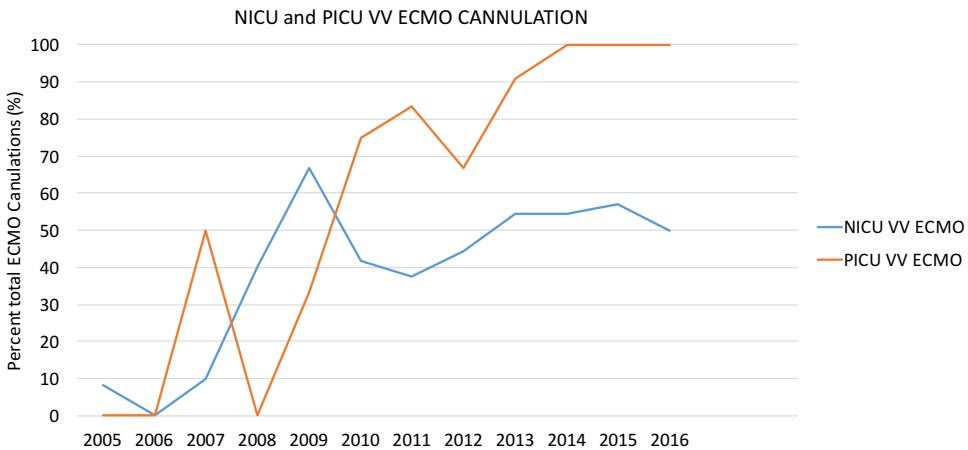

Fig. 1 NICU and PICU VV ECMO cannulation

Survival

Overall, 74% of patients ($n=118$) were successfully decannulated and 57% survived to discharge. There was no difference in the decannulation rate between VV ECMO and VA ECMO groups. Ten VV ECMO patients, all PICU, were extubated to spontaneous respirations while on ECMO; three survived to discharge. The patients who survived to discharge—two males, one female (ages 1, 8, 9 years)—had primary respiratory failure (RSV, influenza). They were extubated on VV ECMO, subsequently decannulated and discharged home after resolution of the underlying pulmonary disease. Two patients who did not survive to discharge developed significant cerebral hemorrhages with herniation. The causes of death for the additional patients were progression of lymphoma, progressive sepsis after lung transplant, progressive right ventricular failure on ECMO, and severe necrotizing pneumonia and cystic fibrosis progression. One patient died from cannula dislodgement.

There were 42 patients who died on ECMO (26%). The mean survival time for VV and VA ECMO was 51 ± 14 days and 30 ± 10 days, respectively; however, this was not statistically different ($p=0.185$) (Fig. 2). There was no difference in survival to discharge between the VV and VA groups ($p=0.663$).

Complications

Overall 66% ($n=106$) of patients experienced a complication related to ECMO (Table 3). The most frequent complication types were neurologic ($n=43$) and patients requiring re-operation ($n=37$). VA ECMO was associated with a significantly higher rate of overall neurologic complication compared to VV ECMO (36 vs 19% $p=0.033$); specifically, VA ECMO was associated with increased frequency of acute intra-cranial hemorrhage (22 vs 9%, $p=0.003$). Fourteen patients on VA ECMO had radiographic evidence of a cerebral ischemic insult on follow-up imaging with no hemorrhage while on ECMO. There were no significant differences in the metabolic, cardiovascular, infectious, renal, pulmonary, or mechanical complications between the VA ECMO and VV ECMO groups. There was also no difference in the re-operation rate between VA ECMO and VV ECMO groups (22 vs 24%, $p=0.852$).

Table 3 ECMO complications

Complication type, *n* (%)	VV $n=83$	VA $n=77$	*p value*
Hemorrhagic	18 (21)	14 (18)	0.693
Neurologic	16 (19)	27 (36)	**0.033**
CNS hemorrhage	7 (9)	22 (28)	**0.003**
Renal	13 (16)	11 (15)	0.829
Cardiovascular	14 (17)	8 (11)	0.26
Pulmonary	11 (13)	10 (13)	1.000
Infectious	6 (7)	7 (9)	0.775
Metabolic	10 (12)	15 (20)	0.276
Any complication	53 (64)	53 (69)	0.616

Bold values indicate the significance at $p < 0.05$

CNS central nervous system, *VV* venovenous, *VA* venoarterial, *ECMO* extracorporeal membrane oxygenation

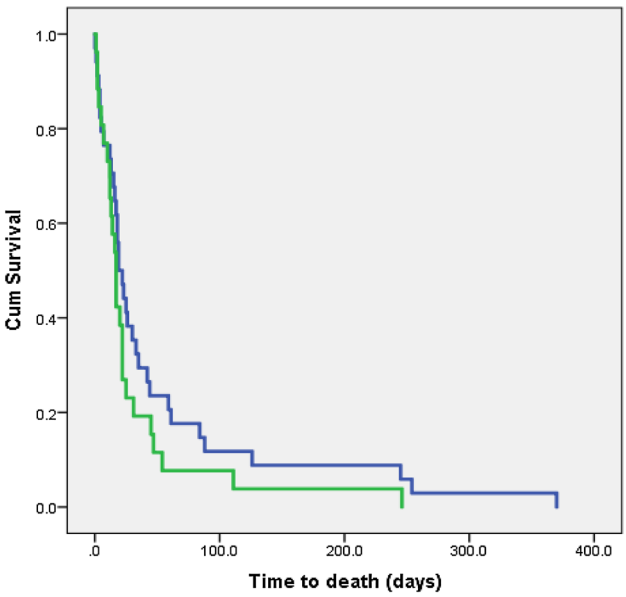

Fig. 2 Survival by ECMO modality. Blue line: *VV* venovenous, green line: *VA* venoarterial ($p = 0.185$)

Discussion

Overview

VV ECMO is an effective alternative to traditional VA ECMO in pediatric and neonatal patients with profound cardiorespiratory failure. VV ECMO is associated with fewer acute neurologic complications than VA ECMO, such as intra-cranial hemorrhage and ischemic insult. In general, patients on ECMO have a significant rate of complications regardless of cannulation modality; however, almost 60% of patients with a likely fatal pre-ECMO diagnosis may survive to discharge.

This paper reports the largest single-institution cohort study regarding the use of VV dual-lumen ECMO in neonates and children. Previous studies investigating comparisons between VA ECMO and VV ECMO have reported on smaller sample sizes or have been database studies. One of the largest pediatric studies by Kugelman et al. reports on the outcomes of 128 neonates with meconium aspiration

syndrome over a 12-year period [17] and they found no difference in survival or time on ECMO between the VV ECMO and VA ECMO cohorts. Our study would suggest that the VV ECMO and VA ECMO population do not have any inherent survival differences; however, it is safe to say that the ECMO modality is not the driver of mortality but it is more the disease state.

VV ECMO complications and use

Now one of the significant conclusions that can be drawn from this study is that the rate of intra-cranial hemorrhage and CNS insult is significantly less in a VV ECMO population. Guner et al. have reported these findings in a CDH ELSO database study [6] where they found a significantly lower rate of intra-cranial hemorrhage in the VV ECMO population when compared to the VA ECMO population. In the neonatal ECMO population, CNS imaging is performed with head ultrasound for the first 5 days of ECMO support. Additional imaging is performed based on clinical neurologic assessments. In the pediatric population, CNS imaging is performed if there is a change in the patient's baseline clinical neurologic exam. In this study, there was an 18% incidence of intra-cranial hemorrhage with a significantly higher rate of intra-cranial hemorrhage with the use of VA ECMO, 28%.

Possible complications and disadvantages that can be associated with the dual-lumen VV ECMO cannula are mechanical (kinking of the thin polyurethane catheter), limited range of catheter sizes, and instability of catheter after placement [18]. Precise placement of the catheter is required to ensure direction of the infusion jet towards the tricuspid valve and requires radiographic or echocardiographic guidance. One of the described complications of using a dual-lumen VV ECMO cannula is the incidence of cardiac injury or perforation. Zamora et al. [12] described a 5.1% cardiac complication rate with dual-lumen VV cannulas. Based on this number, we should have had about four cardiac complications with the number of VV dual-lumen cannulas to date. Fortunately, we have not seen this complication. Our technique for placement has evolved to rely heavily on fluoroscopy and real-time echocardiography (ECHO). In brief, the use of fluoroscopy or echocardiogram is a standard for accurate placement of the cannulas. In the NICU, our protocol is to use ECHO since the NICU beds are not fluoroscopy compatible and patient size allows for the ability to obtain a good ECHO window into right atrium and supra-hepatic inferior vena cava. In larger patients, such as in the PICU, the patient will be moved onto an operating room table in the patient's room and fluoroscopy will be used to verify wire placement and to follow the cannula into the inferior vena cava. ECHO will then be used to confirm the arterial jet through the tricuspid valve and correct positioning, prior to securing the cannula.

As in this series and reported by Zamora et al., the use of VV ECMO has increased significantly over the past decade. With the advent of newer cannula technology, VV ECMO can now be single site through the internal jugular vein and has allowed for prompt initiation of ECMO using an existing central line or via percutaneous Seldinger technique. Furthermore, dual-lumen cannulas have the benefit of decreasing the recirculation associated with traditional multisite VV approach and allow for greater patient mobility and transfer [19]. In this study, there has been an increase in the use of VV ECMO over the past decade. The increase in use has been an overall awareness of the decreased neurologic complications and the ability to place the cannula using a percutaneous technique.

Limitations

This current study is limited by the retrospective uncontrolled design and the inability to precisely match groups for comparison. Furthermore, we do recognize that there is a selection bias in which patients are selected for VV ECMO versus VA ECMO. The indications for initial selection of venovenous ECMO in our institution, albeit subjective, have been consistent over time and include patient size, indication for ECMO (primary respiratory failure), and degree of vasopressor support. Venovenous ECMO is always considered as the initial ECMO mode if the patient is not on significant cardiovascular support. Historically, this has been defined as two or more vasopressors at the time of ECMO initiation. We also acknowledge that VV ECMO and VA ECMO groups are significantly different at baseline in regard to acid–base status and indication for ECMO. Even with the increased use of VV ECMO in this program, it has been mainly used in the critical care population for primary respiratory failure such as pneumonia or for patients with PPHN and meconium aspiration. VA ECMO continues to be used in the CDH population and for patients that require more cardiovascular support. Finally size also pays a role in cannulation mode since the 13-French cannula may not fit into a small right internal jugular vein. A significant number of our VV cannulations were performed in neonates < 30 days of age (48%) and the neonatal patients had similar rates of conversion to VA ECMO as older children (> 30 days).

Conclusion

In conclusion, this study presents the largest institutional study to date of dual-lumen VV ECMO cannula use and outcomes. VV ECMO use has substantially increased in this institution and is now the most common mode of ECMO

cannulation for the overall ECMO population. Based on this study, VV ECMO may be associated with a lower rate of intra-cranial hemorrhage and may be the preferred first-line mode of ECMO support for primary respiratory failure. Dual-lumen VV cannulation can be safely performed with appropriate image guidance and is an effective mode of ECMO in the appropriately selected NICU and PICU population.

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Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

Ethical approval All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. For this type of study formal consent is not required.

Informed consent Informed consent was obtained from all individual participants included in the study as per the institutional guidelines stated in the IRB. For this type of study formal consent is not required.

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