Venoarterial extracorporeal membrane oxygenation in heart surgery post-operative pediatric patients: A retrospective study at Christus Muguerza Hospital, Monterrey, Mexico

Gerardo Vargas-Camacho¹, Verónica Contreras-Cepeda¹, Rene Gómez-Gutierrez¹, Guillermo Quezada-Valenzuela¹, Adriana Nieto-Sanjuanero¹, Jesús Santos-Guzmán² and Francisco González-Salazar³,⁴

Abstract
Objectives: Extracorporeal membrane oxygenation is a life support procedure developed to offer cardiorespiratory support when conventional therapies have failed. The purpose of this study is to describe the findings during the first years using venoarterial extracorporeal membrane oxygenation in pediatric patients after cardiovascular surgery at Christus Muguerza High Specialty Hospital in Monterrey, Mexico.

Methods: This is a retrospective, observational, and descriptive study. The files of congenital heart surgery post-operative pediatric patients, who were treated with venoarterial extracorporeal membrane oxygenation from January 2013 to December 2015, were reviewed.

Results: A total of 11 patients were reviewed, of which 7 (63.8%) were neonates and 4 (36.7%) were in pediatric age. The most common diagnoses were transposition of great vessels, pulmonary stenosis, and tetralogy of Fallot. Survival rate was 54.5% and average life span was 6.3 days; the main complications were sepsis (36.3%), acute renal failure (36.3%), and severe cerebral hemorrhage (9.1%). The main causes of death were multi-organ dysfunction syndrome (27.3%) and cerebral hemorrhage (18.2%).

Conclusion: The mortality rates found are very similar to those found in a meta-analysis report published in 2013 and the main complication and causes of death are also very similar to the majority of extracorporeal membrane oxygenation reports for these kinds of patients. Although the results are encouraging, early sepsis detection, prevention of cerebral hemorrhage, and renal function monitoring must be improved.

Keywords
Extracorporeal membrane oxygenation, extracorporeal life support, cardiovascular surgical procedures, newborns, congenital heart defects

Date received: 31 May 2019; accepted: 4 February 2020

¹Pediatric Intensive Care Unit, Christus Muguerza High Specialty Hospital, Monterrey, Mexico
²School of Medicine, Tecnologico de Monterrey, Monterrey, Mexico
³Northeastern Biomedical Investigation Center, Mexican Social Security Institute, Monterrey, Mexico
⁴Department of Basic Sciences, University of Monterrey, San Pedro Garza García, Mexico

Corresponding author:
Francisco González-Salazar, Department of Basic Sciences, University of Monterrey, Av. Ignacio Morones Prieto 4500 Pte. Col. Jesús M Garza, San Pedro Garza García, Nuevo León 66238, México.
Email: fgonz75@hotmail.com
Introduction

Extracorporeal membrane oxygenation (ECMO) is a life support procedure that has been used around the world since the 1970s. During this life support procedure, the cardiorespiratory function is substituted by a machine placed next to the patient’s bed. Its use is indicated when there is severe respiratory or cardiorespiratory failure that does not respond to conventional treatments.

Since the 1970s, ECMO has been used as a therapeutic alternative at most tertiary-care hospitals in the United States and Europe; however, in Mexico its use was not established until 2013. In Latin American countries, some investigation has been conducted in which the use of this procedure is reported, but with a high mortality rate. After 2013, the pediatric ECMO program was initiated at the Pediatric Intensive Care Unit of Christus Muguerza High Specialty Hospital in Monterrey, Nuevo Leon, Mexico.

The main purpose of this procedure is to offer life support to patients with cardiorespiratory failure when conventional treatments have failed. To achieve this goal, the blood is drained into a machine placed at the patient’s bed side, oxygenated, heated, and finally returned to the patient.

This circulation occurs through polyvinyl chloride tubes whose diameter varies depending on the patient’s weight. First, this tube is connected to a double-lumen or venous cannula, depending on the type of ECMO. Then, the old blood travels through this tube and reaches “the bladder,” a type of venous reservoir. The blood then passes to the pump, a system that acts as a heart, and completes the programmed revolutions per minute; after passing through the pump, the blood reaches a membrane oxygenator or artificial lung, where O₂ is added to the blood and CO₂ is removed; finally, the blood passes through a heat exchanger, where it reaches an adequate temperature before returning to the patient, through the double-lumen of a venous cannula, or through an arterial cannula.

In general, two types of ECMO are recognized, according to the blood vessel to which it is connected: venoarterial and venovenous.

Venoarterial extracorporeal membrane oxygenation

In the venoarterial extracorporeal membrane oxygenation (V-A ECMO) system, a cannula is generally placed in the common right femoral vein for the extraction and an arterial cannula is generally placed in the right femoral artery for the infusion. The tip of the venous femoral cannula must be close to the union of the inferior vena cava and the right atrium, while the tip of the femoral artery cannula is maintained in the iliac artery. In adults, access to the femoral artery is preferred because insertion is simpler. A variation of this system occurs when the catheters are placed in central locations which may occur when the first catheter is placed in the right atrium and the second one is placed in the ascending aorta.

The purpose of this study is to describe the findings during the first years using V-A ECMO in pediatric patients after cardiovascular surgery at Christus Muguerza High Specialty Hospital in Monterrey, Mexico.

Materials and methods

This was a retrospective, observational, and descriptive study. The files of pediatric patients with post-operative congenital heart defects after cardiovascular surgery who were treated with V-A ECMO from January 2013 to December 2015 were reviewed.

Population

Monterrey, Mexico, is the largest city in northern Mexico and has the best hospitals. It has a population of 5 million, and four private and three public hospitals with pediatric intensive care units, but only Christus Muguerza has experience with ECMO. This study shows the first experiences treating cardiovascular post-operated pediatric patients with V-A ECMO in the Pediatric Intensive Care Unit of Christus Muguerza High Specialty Hospital from January 2013 to December 2015.

Selection criteria. All files of complex congenital heart surgery post-operative patients who were treated with V-A ECMO were included, regardless of their age, gender, or reason for the heart surgery.

Exclusion criteria. All files of patients with chromosomic alterations or congenital coagulation disorders were excluded from the study.

Elimination criteria. All files with incomplete or illegible data were eliminated.

Procedures

This protocol was first registered with the research and ethics committees. Once registration was obtained, an authorization was requested from the person in charge of the hospital’s clinical files, who assigned a person to assist in locating the files with the diagnoses.

Only 11 files that met the selection criteria were located, and therefore we decided to include all the files. The data were collected directly from the files. The files were located according to the patient’s diagnosis and previous registration at the intensive care unit. These data were collated with the records of the intensive care unit to confirm their consistency.

The data were obtained from the files through direct observation and with the assistance of two medical school students. All data were registered in an Excel database.

Sample and sampling

Considering that only 11 newborn records met the selection criteria, we decided not to perform a sampling and no
sample size calculation was performed. Then, we decided to conduct a census study including files of all patients. The data were collected directly from the files. The files were located according to the patient’s diagnosis and previous registration at the intensive care unit. These data were collated with the records of the intensive care unit to confirm their consistency.

Data analysis
All data were recorded on an Excel spreadsheet designed especially for this project and statistical analysis was performed with the assistance of SPSS v18. Descriptive statistics were used exclusively, where the qualitative variables were expressed as frequencies and the quantitative variables were reported as mean and standard deviation.

Study variables
Given that this is a descriptive study, all variables were considered independently; there was no cross-referencing between variables since this is a study limited in its sample size and it is not the objective of this research. The operationalization of variables is shown in Table 1.

Ethical considerations
This project was registered with the bioethics and research committee of the Christus Muguerza High Specialty Hospital in Monterrey, Mexico, and the University of Monterrey (ref.: 02052019-CI). Waiver for not requesting informed consent was also obtained (ref.: 16082019-a-C-CI). All patient data were handled confidentially.

### Table 1. System of variables used in this study.

| Variable               | Definition                                                                 | Operative definition                                      | Scale                  |
|------------------------|-----------------------------------------------------------------------------|-----------------------------------------------------------|------------------------|
| Age                    | Time the person has lived since birth                                        | Months of life the person has left according to their file | Discreet quantitative (months) |
| Gender                 | Physical traits that differentiate a male from a female                      | According to the file data                                 | Binomial: masculine or feminine |
| Diagnosis              | Name of the disease affecting a person                                       | Disease for which person underwent surgery                 | Nominal: name of the disease |
| Surgical risk scale    | Risk of mortality in surgical patients                                       | According to the RACHS-1 scale                             | Discreet quantitative from 1 to 6 |
| ECMO time span         | Length of time a person receives ECMO life support                          | According to the time registered in the file               | Continuous quantitative (minutes) |
| Time of aortic impingement | Time that the aorta remained impinged                                       | Time of impingement registered in the file                 | Continuous quantitative (minutes) |
| Complications          | Presence of a disease secondary to another disease or procedure              | Complications registered in the file                       | Nominal                 |
| Mortality              | Death                                                                       | Registered deaths                                          | Binomial: yes/no        |
| Cause of death         | Reason the person died                                                       | Cause of death registered in the file                      | Nominal                 |

RACHS-1: The Risk Adjustment for Congenital Heart Surgery; ECMO: extracorporeal membrane oxygenation.

### Table 2. Distribution of patients according to their sociodemographic data, diagnoses, and surgical risk.

| Gender | Diagnosis                      | Age (days) | Weight (kg) | RACHS-1 |
|--------|--------------------------------|------------|-------------|---------|
| F      | Severe pulmonary stenosis      | 2          | 2.6         | 3       |
| F      | Multiple IVC                   | 270        | 5.1         | 2       |
| F      | APVR                           | 330        | 9.2         | 3       |
| M      | TGV + EP                       | 5          | 2.7         | 4       |
| M      | TGV                            | 4          | 3.5         | 4       |
| M      | TGV                            | 2          | 3.1         | 4       |
| F      | Tetralogy of Fallot            | 7          | 3           | 4       |
| M      | LHHS                           | 5          | 2.7         | 6       |
| M      | Tetralogy of Fallot            | 575        | 8           | 3       |
| M      | TGV + IVC + EP                 | 15         | 4.5         | 4       |
| M      | Pulmonary atresia              | 425        | 8.5         | 4       |

RACHS-1: The Risk Adjustment for Congenital Heart Surgery; IVC: interventricular communication; APVR: anomalous pulmonary venous return; TGV: transposition of the great vessels; EP: Pulmonary stenosis; LHHS: Left heart hypoplastic syndrome.

Outcomes
Eleven patients were reviewed, of which seven (63.7%) were neonates and four (36.3%) were of pediatric age. Of those 11 patients, 7 (63.7%) were male and the rest were female. The diagnoses were very diverse but the most common were transposition of great vessels, pulmonary stenosis (EP), and tetralogy of Fallot. Average surgical risk was 3.7 on the RACHS-1 (The Risk Adjustment for Congenital Heart Surgery) scale. The main diagnoses for which the patients were surgically intervened are shown in Table 2.

All patients were treated with a V-A ECMO Marquet© circuit with Bioline cover, and Quadrox© oxygenating pediatric membrane with centrifugal Rotaflow system.
An ultrasound was performed on all neonates prior to the procedure to rule out cerebral hemorrhage prior to ECMO. The cannulation sites were central in all patients, leaving the chest exposed and covered with sterile plastic. During the procedure, \( \text{SvO}_2 \), hematocrit, and post-membrane saturation were monitored continuously. All patients were treated in the same way during the procedure with commencement of anticoagulation with heparin until activated coagulation time (ACT) was <300 s and partial thromboplastin time (PTT) <80 s. ACT was determined every 3 h, prothrombin time (PT) PTT and platelets every 6 h, and XA anti-factor and antithrombin III every 24 h; homeostasis was maintained according to ELSO (Extracorporeal Life Support Organization) guidelines. Blood flows were maintained between 100 and 150 mL/kg/h with pulmonary flow at rest and volume-controlled ventilation (CMV). All patients’ vital signs were monitored, including hydric balance, diuresis, and near-infrared tissue spectroscopy (NIRS) to monitor tissue oxygenation. All patients were treated with analgesia and sedation. Hemofiltration or hemodiafiltration was performed on 54.5%, as applicable. A pediatric cardiologist performed an echocardiogram every 24 h to measure ejection fraction, ventricular function, and response to flow diminishment. The criteria for weaning were handled in consensus according to clinical data from each patient’s echocardiogram.

The time span for extracorporeal circulation was 266.4 ± 111.3 min and the average time of aortic impairment was 141.0 ± 61.2 min. The main indication for treating a patient with V-A ECMO was failure in the extraction of extracorporeal circulation. The site of placement was 63.7% in the operating room and the rest within the same intensive therapy unit.

Survival rate was 54.5% and average time span was 6.3 ± 4.9 days. The main complications were sepsis (36.3%), multi-organ dysfunction syndrome (MODS; 27.3%), acute renal failure (ARF; 18.8%), and severe cerebral hemorrhage (9.1%). The main causes of death were MODS, 27.3%, ARF, and cerebral hemorrhage, both with 18.8% (Table 3). All patients who died had undergone surgery in the operating room. In addition, all patients who remained on ECMO for more than 4 days died. Surviving patients had an average stay in ECMO of 3.8 ± 0.4 days, while those who finally died had an average stay of 9.4 ± 6.2 days.

**Discussion**

In this investigation, we are presenting our growing experience treating cardiovascular post-operated pediatric patients with V-A ECMO. Even in the context of a city with great economic growth, it is quite difficult to find patients or insurance with economic capacity to cover the costs generated by the ECMO. Hospital costs range from US$42,554 to US$537,554.10,11 For these reasons, we have only obtained a small sample. However, in spite of that, we decided to conduct this study to compare our results with what was reported in the world literature and recognize our areas of opportunity, and thus be able to make specific changes to improve our results. In addition, these results may serve as a reference for other sites with limited experience in ECMO treatment. All data of mortality in this work happens during ECMO more than after ECMO weaning.

The mortality rates found in our patients are very similar to the majority of those found in a meta-analysis report published in 2013.12–14 The main causes of complications and mortality are also very similar to the majority of ECMO reports for these types of patients.15 ECMO is a vital life support tool for patients when all support procedures have failed. However, not all patients are candidates for this therapy. If the pre-existing conditions for ECMO are poor and the

### Table 3. Results according to extracorporeal circulation (ECC) times and time span in ECMO (days).

| ECC time (min) | ECCM setup       | ECMO time span (days) | Complications                        | Result   |
|---------------|------------------|-----------------------|--------------------------------------|----------|
| 128           | Operating room   | 10                    | ARF, S, myocardial dysfunction       | Death    |
| 107           | PICU 72 h        | 4                     | No                                   | Survival |
| 373           | PICU 72 h        | 3                     | No                                   | Survival |
| 392           | Operating room   | 4                     | No                                   | Survival |
| 338           | Operating room   | 3                     | ARF, S, cerebral hemorrhage          | Death    |
| 270           | Operating room   | 3                     | S, MODS                              | Death    |
| 340           | Operating room   | 16                    | MODS                                 | Death    |
| 140           | PICU 3 h         | 4                     | No                                   | Survival |
| 121           | PICU 72 h        | 4                     | No                                   | Survival |
| 357           | Operating room   | 15                    | S, MODS                              | Death    |
| 305           | PICU 48 h        | 4                     | No                                   | Survival |

ECMO: extracorporeal membrane oxygenation; ARF: acute renal failure; MODS: multi-organ dysfunction syndrome; S: sepsis; PICU: pediatric intensive care unit.
possibility of organic recovery in the short term is limited, chances of survival are reduced exponentially. Therefore, proper selection of patients who are candidates for life support with ECMO ensures a greater chance of success and survival.\textsuperscript{16,17}

We find that the average stay in V-A ECMO for patients who survived was almost 4 days, while the average stay of those who died was approximately 9 days. In addition, all patients who remained on ECMO for more than 4 days died.

These data are congruent with a multi-institutional analysis conducted in the United States and published recently where the direct relationship between ECMO stay and mortality was demonstrated.\textsuperscript{18}

Another interesting outcome of this study is that all patients who died had the ECMO set up in the operating room, while patients who had the ECMO set up in the intensive care unit show greater survival. We did not find other studies with similar outcomes, and several authors reported no difference in survival when ECMO setup locations were compared.\textsuperscript{19}

Complications and mortality are closely related, as previously mentioned, and main causes of complications and mortality are also very similar to the majority of ECMO reports for these types of patients.\textsuperscript{12} Sepsis is, of course, one of the most common complications and preventive measures should be established to reduce this serious condition.\textsuperscript{20}

Another aspect that needs to be closely monitored is renal function to attempt to diminish the occurrence of renal failure.\textsuperscript{21} Early monitoring of biomarkers for sepsis and renal function should reduce mortality rates. Finally, hemorrhagic events, including cerebral hemorrhage, are very common in ECMO-treated patients,\textsuperscript{22} and these events may be related to patient condition, disease factors, factors related to the ECMO treatment, or a combination of all of them.\textsuperscript{23}

The main limitation of this study was sample size, but it was impossible to avoid due to the characteristics of the population and the context of the health care services.

Conclusion

In this novel experience with V-A ECMO in pediatric patients post-operated from cardiovascular congenital diseases, we find a survival similar to what is reported globally. The main complications were sepsis, MODS, acute renal failure, and severe cerebral hemorrhage.

The time spent in ECMO is directly related to mortality, and patients who spend more than 4 days in ECMO have a higher likelihood of dying (100%). Patients who have ECMO set up in the operating room have more probabilities of dying than patients who have ECMO set up in intensive care units.

Acknowledgements

We thank the staff of the intensive care unit of the Christus Muguerza High Specialty Hospital, and the University of Monterrey for making the payment of article processing charge of this article.

Declaration of conflicting interests

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Ethical approval

Ethical approval for this study was obtained from Comité de Investigacion Vicerectoria de Ciencias de la Salud (ref.: 02052019 CI).

Funding

The author(s) disclosed receipt of the following financial support for the research, authorship, and/or publication of this article: The authors received support of the University of Monterrey to make the payment of article processing charge of this article.

Informed consent

Waiver for not requesting informed consent was also obtained (ref.: 16082019-a-C-CI) as only files and non-patients were reviewed.

ORCID iD

Francisco González-Salazar https://orcid.org/0000-0003-2832-4771

References

1. Lefrak EA, Stevens PM, Noon GP, et al. Current status of prolonged extracorporeal membrane oxygenation for acute respiratory failure. Chest 1973; 63(5): 773–782.
2. Keebler ME, Haddad EV, Choi CW, et al. Venousarterial extracorporeal membrane oxygenation in cardiogenic shock. JACC Heart Fail 2018; 6(6): 503–516.
3. Kattan J, Gonzalez A, Castillo A, et al. Neonatal and pediatric extracorporeal membrane oxygenation in developing Latin American countries. J Pediatr 2017; 93(2): 120–129.
4. Caneo LF and Jatene MB. Pediatric mechanical circulatory support systems in Latin America. Artif Organs 2016; 40(10): 925–928.
5. Prensa Christus Muguerza. En camino a la excelencia, 2015; http://www.christusmuguerza.com.mx/sala-de-prensa/en-camino-a-la-excelencia/ (accessed 13 September 2018).
6. Sosnowski AW, Bonser SJ, Field DJ, et al. Extracorporeal membrane oxygenation. BMJ 1990; 301(6747): 303–304.
7. Gattinoni L, Carlesso E and Langer T. Clinical review: extracorporeal membrane oxygenation. Crit Care 2011; 15(6): 243.
8. Chauhan S and Subin S. Extracorporeal membrane oxygenation, an anesthesiologist’s perspective: physiology and principles. Ann Card Anaesth 2011; 14(3): 218–229.
9. Harvey C. Cannulation for neonatal and pediatric extracorporeal membrane oxygenation for cardiac support. Front Pediatr 2018; 6: 17.
10. Aiello S and Loomba RS. Factors associated with the need for, and the impact of, extracorporeal membrane oxygenation in children with congenital heart disease during admissions for cardiac surgery. Children 2017; 4(11): E101.
11. Harvey MJ, Gaies MG, Prosser LA. U.S and international in-hospital costs of extracorporeal membrane oxygenation: a systematic review. Appl Health Econ Health Policy 2015; 13(4): 341–357.
12. Kattan SJ, González MA and Castillo MA. Oxigenación con membrana extracorpórea neonatal-pediátrica. Rev Chil Pediatr 2013; 84(4): 367–378.

13. Jenks CL, Raman L and Dalton HJ. Pediatric extracorporeal membrane oxygenation. Crit Care Clin 2017; 33: 825–841.

14. Chan T, Thiagarajan RR, Frank D, et al. Survival after extracorporeal cardiopulmonary resuscitation in infants and children with heart disease. J Thorac Cardiovasc Surg 2008; 136(4): 984–992.

15. Brown KL, Ichord R, Marino BS, et al. Outcomes following extracorporeal membrane oxygenation in children with cardiac disease. Pediatr Crit Care Med 2013; 14(5 Suppl. 1): S73–S83.

16. Florez CX, Bermon A, Castillo VR, et al. Setting up an ECMO Program in a South American country: outcomes of the first 104 pediatric patients. World J Pediatr Congenit Heart Surg 2015; 6(3): 374–381.

17. Azizov F, Merkle J, Fatullayev J, et al. Outcomes and factors associated with early mortality in pediatric and neonatal patients requiring extracorporeal membrane oxygenation for heart and lung failure. J Thorac Dis 2019; 11(Suppl. 6): S871–S888.

18. Gupta P, Robertson MJ, Beam B, et al. Relationship of ECMO duration with outcomes after pediatric cardiac surgery: a multi-institutional analysis. Minerva Anestesiol 2015; 81(6): 619–627.

19. Sasson L, Cohen I, Tamir A, et al. Extracorporeal membrane oxygenation in pediatric patients: our experience in the last ten years. Isr Med Assoc J 2013; 15(1): 13–16.

20. Santiago-Lozano MJ, Barquin-Conde ML, Fuentes-Moreno L, et al. Infectious complications in paediatric patients treated with extracorporeal membrane oxygenation. Enferm Infecc Microbiol Clin 2018; 36(9): 563–567.

21. Fleming GM, Sahay R, Zappitelli M, et al. The incidence of acute kidney injury and its effect on neonatal and pediatric extracorporeal membrane oxygenation outcomes: a multicenter report from the Kidney Intervention During Extracorporeal Membrane Oxygenation Study Group. Pediatr Crit Care Med 2016; 17(12): 1157–1169.

22. Carpenter JL, Yu YR, Cass DL, et al. Use of venovenous ECMO for neonatal and pediatric ECMO: a decade of experience at a tertiary children’s hospital. Pediatr Surg Int 2018; 34(3): 263–268.

23. De Mol AC, Liem KD and van Heijst AF. Cerebral aspects of neonatal extracorporeal membrane oxygenation: a review. Neonatology 2013; 104(2): 95–103.