Clinical outcomes of pediatric patients treated with extracorporeal membrane oxygenation

Desfechos clínicos de pacientes pediátricos tratados com oxigenação por membrana extracorpórea

Eduesley Santana-Santos[1]
Jéssica Ribeiro Silva[1]
Ana Carolina Alcântara Ribeiro Mascarenhas Oliveira[1]
Rafael Nascimento Nogueira de França Santos[1,2]
Larissa Bertacchini de Oliveira[1,2]

Keywords
Extracorporeal membrane oxygenation/ adverse effects; Mortality; Advanced practice nursing; Nursing practical; Child

Descritores
Oxigenação por membrana extracorpórea/efeitos adversos; Mortalidade; Prática avançada de enfermagem; Enfermagem prática; Criança

Submitted
March 14, 2016
Accepted
September 5, 2016

Corresponding author
Eduesley Santana-Santos
Dr. Enéas de Carvalho Aguiar Avenue, 44, 05403-000, São Paulo, SP, Brazil.
eduesley.santos@gmail.com

DOI
http://dx.doi.org/10.1590/1982-0194201600056

Abstract

Objective: To identify factors related to mortality, and evaluate the survival of pediatric patients treated with extracorporeal membrane oxygenation.

Methods: A retrospective cohort study that included pediatric patients using the device in the last five years. The groups were divided into those who survived after therapy, and those who did not. Multivariate logistic regression was used for assessing the predictive factors of death, and the Kaplan-Meier and log-rank for assessing survival.

Results: Left ventricular ejection fraction was higher in the group of survivors (74% + 14.6% vs 56.2% + 22%, p = 0.038), and the number of patients who required dialysis was higher in the group of non-survivors (52.4% vs. 12.5%, p = 0.039), showing significantly lower survival in this group (log-rank = 0.020).

Conclusion: Previous ventricular dysfunction, evidenced by a left ventricular ejection fraction <55%, and requirement of concomitant renal replacement therapy, increased the risk of death.

Resumo

Objetivo: Identificar os fatores relacionados à mortalidade e avaliar a sobrevida de pacientes pediátricos tratados com oxigenação por membrana extracorpórea.

Métodos: Estudo de coorte retrospectivo, que incluiu pacientes pediátricos que utilizaram o dispositivo nos últimos cinco anos. Os grupos foram divididos com base naqueles que sobreviveram ou não após a terapia. Para avaliar os fatores preditivos de morte, foi utilizada análise multivariada com regressão logística e, para a sobrevida, o método de *Kaplan-Meier* e *Log-Rank*.

Resultados: A fração de ejeção do ventrículo esquerdo era maior no grupo de sobreviventes (74%+14,6% vs 56,2% + 22%, p=0,038) e o número de pacientes que necessitaram de diálise foi maior no grupo de não sobreviventes (52,4% vs. 12,5%, p=0,039), sendo a sobrevida significativamente menor neste grupo (*log-rank*=0,020).

Conclusão: Disfunção ventricular prévia, evidenciada pela fração de ejeção do ventrículo esquerdo <55%, e necessidade de terapia de substituição renal concomitante aumentaram o risco de morte.

[1]Instituto do Coração, Hospital das Clínicas, Faculdade de Medicina, Universidade de São Paulo, São Paulo, SP, Brazil.
[2]Escola de Enfermagem, Universidade de São Paulo, São Paulo, SP, Brazil.

Conflicts of interest: there are no conflicts of interest to declare.

Introduction

Extracorporeal membrane oxygenation (ECMO) - is a mechanical circulatory support (MCS) mode, widely used in pediatric patients with heart failure, either acquired or secondary to congenital heart disease, which is refractory to conventional treatment.[1] Although indications have increased exponentially over the years and present promising results, especially as a bridge to heart transplantation, the use of this therapy involves many risks and complications.[2-4] A 12-year cohort study by the *Extracorporeal Life Support Organization* (ELSO) [5] which assessed the survival of pediatric patients with an indication for ECMO due heart failure, showed that only 23% survived to hospital discharge.

The benefits from the use of ECMO should be analyzed according to its risks. A study that evaluated a cohort of 303 infants who used ECMO for heart failure showed that 98% of the 46% of patients who progressed to death had any kind of complications, including: stroke, gastrointestinal, pulmonary and surgical site bleeding, disseminated intravascular coagulation, acute kidney injury (AKI), and infection. Furthermore, low birth weight, incidence of cardiorespiratory arrest, and the need for dialysis were the factors that were independently associated with mortality.[2] Another multicenter study, [6] which evaluated 998 pediatric patients who received ECMO, also due to heart failure, showed that longer use of this therapy was associated with increased mortality, ventilatory weaning time, Intensive Care unit (ICU) length of stay, and hospital costs.

The interest in conducting this study emerged from work as nurses in an ICU of a specialized cardiology center, who routinely attend pediatric patients on ECMO; because of the high complexity of these patients and the care they require; as well as the fact that the studies[2-7] still demonstrate high mortality rates, unfavorable clinical outcomes and complications related to this therapy, and the observed results with these patients in our service. Thus, our purpose is to identify the factors data related with mortality, and to evaluate the survival of pediatric patients treated with ECMO.

Methods

This was a retrospective cohort single center study, performed in a teaching hospital specializing in high complexity cardiopneumology, in the city of São Paulo, Brazil, and a member of the Extracorporeal Life Support Organization (ELSO).

During data collection, the records of all patients who used any type of MCS between January of 2010 and March of 2015 were evaluated. All were surgical patients, up to 18 years of age, who used the therapy and the ECMO as support. We excluded patients for whom we could not recover the physical records, and those whose data records were incomplete or missing. For data analysis, patients were separated into two groups (survivors and non-survivors), based on those that survived and those who did not survive the use of this therapy until discharge from the hospitalization episode that used the device. The final sample consisted of 29 patients, as presented in figure 1.

The data collection was performed by two researchers, in an independent manner, between the months of May and October, 2015. The instrument used consisted of: sociodemographic data (gender, age and skin color); clinical characteristics (left ventricular ejection fraction, heart attack or previous stroke, diabetes, heart failure, hypertension, and baseline creatinine); data procedure (indication, type of cannulation, duration of the procedure, and complications); clinical evaluation of the six hours after the procedure, the first seven days, and device removal (vital signs, laboratory tests, use of vasoactive drugs, and clinical outcomes) and scores to assess the degree of acute lung injury (Murray Score),[8] risk assessment of pediatric mortality (PRISM Score),[9] and the degree of organ dysfunction in ICU (SOFA Score).[10]

The PRISM score was calculated for each patient based on the data found in the health record on the day the therapy was initiated. The

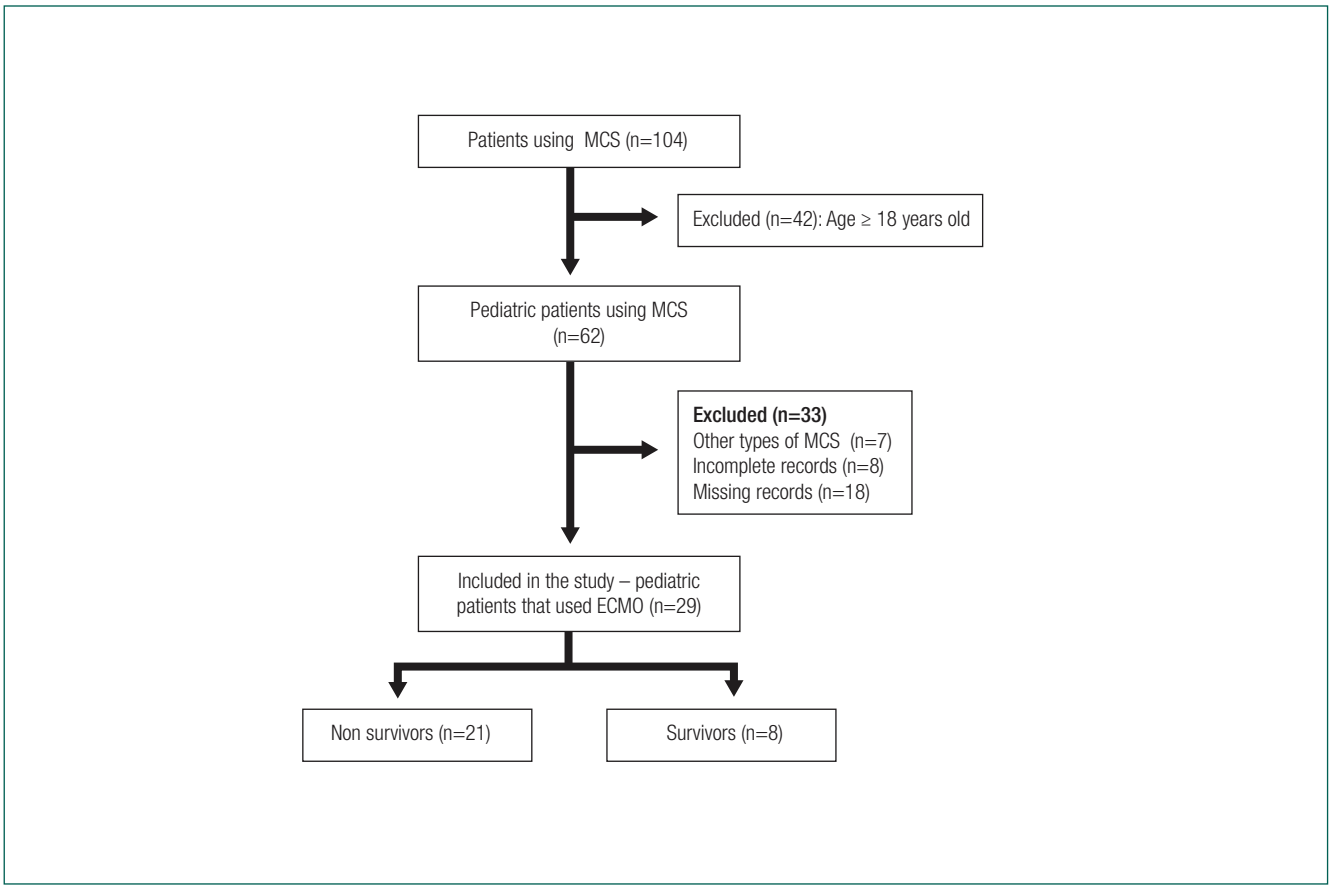

Figure 1. Study flowchart

highest PRISM score reflects a higher severity and increased risk of death. The SOFA was calculated with data collected immediately before initiation of ECMO, to evaluate the degree of organ dysfunction.

For assessment of acute kidney injury (AKI), the RIFLE classification was used, which is an acronym for *Risk* (risk of renal dysfunction); *Injury* (damage / injury to the kidney); *Failure* (failure of kidney function); *Loss* (loss of kidney function) and *End stage renal disease* (kidney disease in the terminal stage) using serum creatinine level criteria (SCr), glomerular filtration rate (GFR), and urine flow.[11] Acute kidney injury was defined by RIFLE criteria using the highest variation in SCr and estimated GFR during the first seven days after the onset of this therapy, as compared to baseline values. The GFR was calculated using the formula of the *Modification of Diet in Renal Disease* (MDRD). The patients were stratified according to the highest RIFLE score, according to the SCr and GFR criteria.

For statistical analysis, the Shapiro-Wilk test was used to verify the normal distribution of the continuous variables. Categorical variables were presented as absolute (n) and relative (%)frequencies; continuous variables were expressed by means and standard deviations, medians and interquartile ranges. The difference between groups was evaluated using the Student t-test, Mann-Whitney, chi-square and Fisher's exact test. A p-value <0.05 was considered significant. Predictive factors of death were evaluated by means of multivariate analysis with logistic regression. Survival curves were constructed using the Kaplan-Meier method and compared using the log-rank method. The Statistical Program for the Social Sciences (SPSS) (version 20.0; IBM, Armonk, USA) was used for data analysis.

The study was registered on *Plataforma Brasil* under *Certificado de Apresentação para Apreciação Ética* (CAAE): 45016115.2.0000.0068.

Results

Among the 29 patients included in the study, 21 (72.4%) died, and eight (27.6%) survived up to the time of hospital discharge for the hospitalization that used ECMO. Table 1 shows the sociodemographic information, the procedure data, and clinical and laboratory evaluation of pediatric survivors and non-survivors treated with ECMO between 2010 and 2015. There was no statistically significant difference between the groups in relation to males (47.6% vs. 75%, p=0.176), age (60 ± 62 months vs. 37 ± 60 months, p=0.381) and body mass index - BMI (15.3 ± 2.5 kg/m^2 vs. 17.6 ± 9.3 kg/m^2, p=0.554). In relation to the indications for ECMO, cardiogenic shock was the most common indication (95.2% vs. 87.5%, p=0.263) among non-survivors and survivors, respectively. Patients who survived had higher left ventricular ejection fraction (LVEF) when compared to non-survivors (74% ± 14.6% vs 56.2% ± 22%, p=0.038).

Regarding the use of vasoactive drugs, the group of non-survivors used higher doses when compared with the group of survivors: dobutamine (13.5 ± 10.3 mcg/kg/min vs. 5 ± 3.5 mcg/kg/min, p=0.018) and norepinephrine (0.6 ± 0.24 mcg/kg/min vs. 0.1 ± 0.05 mcg/kg/min; p=0.017). The presence and extent of lung damage, assessed by Murray Score, were different when comparing the two groups, being higher in the group of non-survivors compared to survivors (2.33 ± 0.48 vs. 2.0 ± 0.01, p=0.005). Differences between groups regarding the PRISM score were demonstrated as higher in the group of non-survivors (22 [17-27] vs 11 [10.5 to 14], p=0.009). There was no difference between the groups in relation to hemodynamic parameters and laboratory data (Table 1).

Clinical outcomes of pediatric survivors treated with ECMO, between 2010 and 2015, are listed in table 2. A significant difference was identified between the patients of the non-survivor group compared to the survivor group on the dialysis outcome (52.4% vs. 12.5%, p = 0.039) and duration of using ECMO (14.6 ± 9.8 days vs. 9.2 ± 4.3 days, p=0.047).

Table 1. Socio-demographic characterization, procedure data, clinical and laboratory evaluation of pediatric patient survivors and non-survivors treated with ECMO

Variables	Non-survivals (n=21)	Survivals (n=8)	p-value
Male sex	10(47.6)	6(75)	0.176
Age, months	60+62	37+60	0.381
BMI, kg/m^2	15.3+2.5	17.6+9.3	0.554
LVEF, %	56.2+22	74+14.6	0.038
Skin color	19(90.5)	7(87.5)	0.817
RV dysfunction	11(52.4)	3(37.5)	0.471
Pulmonary hypertension	2(9.5)	2(25)	0.303
ECMO indications			
Cardiogenic shock	20(95.2)	7(87.5)	0.263
Bridge for heart transplant	0	1(12.5)	
Postcardiotomy syndrome	1(4.8)	0	
Duration of the procedure, minutes	176+176	248+202	0.391
ScvO2, %	58.4+22	87.7+15.5	0.166
Arterial pH	7.37+0.12	7.4+0.10	0.710
SaO_2, %	89.4+15.7	88+6.5	0.816
Lactate, mg/dL	62.5+63.9	40.3+45.8	0.468
Delta CO_2, mmHg	8.4+4.6	8.5+5.1	0.981
Hb, g/dL	11.6+2.6	10.4+0.5	0.443
PaO_2/FiO_2, mmHg	203.8+127	118+35.7	0.064
MAP, mmHg	64+17	60+20	0.697
CVP, mmHg	15.5+5.4	16+8.5	0.948
Diuresis, mL/kg/h	2.4+2	2.4+2.4	0.971
Dobutamine, mcg/kg/min	13.5+10.3	5+3.5	0.018
Norepinephrine , mcg/kg/min	0.6+0.24	0.1+0.05	0.017
Epinephrine, mcg/kg/min	0.4+0.41	0.25+0.21	0.493
Milrinone, mcg/kg/min	0.77+0.45	1.37+1.42	0.543
SOFA score (onset of da ECMO)	8.9+4.5	8.0+3.5	0.725
PRISM score	22[17-27]	11[10.5-14]	0.009
Murray score	2.33+0.48	2.0+0.01	0.005

Data expressed in absolute (n) and relative (%) frequency, mean, standard deviation, median and interquartile range, BMI - body mass index; LVEF - left ventricular ejection fraction; RV: right ventricle; SvO2 - venous oxygen saturation; SaO2 - arterial oxygen saturation; Hb - hemoglobin; PaO2 - arterial oxygen pressure; FiO2 - fraction of inspired oxygen; MAP - mean arterial pressure; CVP - central venous pressure; PRISM - Pediatric Risk of Mortality Score; SOFA - Sequential Organ Failure Assessment

Table 2. Analysis of the clinical outcomes in pediatric patient survivors and non-survivors treated with ECMO

Outcomes	Non-survivors (n=21)	Survivors (n=8)	p-value
Acute kidney injury	14(73.7)	4(57.1)	0.425
Injury (I)	4(21.1)	1(14.3)	0.691
Failure (F)	10(52.6)	3(42.9)	0.658
Dialysis	11(52.4)	1(12.5)	0.039
Infection	6(28.6)	1(12.5)	0.343
Neurologic complications	6(28.6)	1(12.5)	0.343
Hepatic dysfunction	7(33.3)	1(12.5)	0.237
ICU length of stay, days	33.5+27	51+32	0.204
Hospital length of stay, days	37.9+29	72+51	0.109
SOFA score (discharge /death)	10.3+0.6	9.5+2.5	0.393
Duration of ECMO, days	14.6+9.8	9.2+4.3	0.047

Data expressed in mean, standard deviation, absolute (n) and relative (%) frequency, ICU - intensive care unit; SOFA - Sequential Organ Failure Assessment; ECMO - extracorporeal membrane oxygenation; acute kidney injury according to RIFLE

A multivariate analysis showed that LVEF <55%, the presence of AKI and the use of renal replacement therapy were independent risk factors for mortality in pediatric patients treated with ECMO between 2010 and 2015. Patients with reduced LVEF (<55%) had 1.440 times the risk of death when compared to individuals with LVEF above 55% (CI: 1.319 to 1.711, p=0.010). Patients who developed AKI during therapy with ECMO had twice the risk of death (CI: 1.343 to 12.858 p = 0.027). When renal replacement therapy was necessary, which was higher among non-survivors who had kidney failure according to the RIFLE criteria, the risk of death was 7.7 times greater (CI: 1.801 to 74.051, p=0.022) when compared with individuals who did not require dialysis (Table 3).

Table 3. Multivariate analysis of predictive factors for death in pediatric patients treated with ECMO

Variable	OR	CI (95%)	p-value
Age	0.993	0.978-1.0408	0.459
Male sex	0.303	0.049-1.861	0.197
LVEF < 55%	1.440	1.319-1.711	0.010
Acute kidney injury	2.100	1.343-12.858	0.027
Dialysis	7.700	1.801-74.051	0.022

OR - odds ratio; CI - confidence interval; LVEF - Left ventricular ejection fraction

Among the 29 patients included in the study, 21 (72.4%) died during hospitalization and only eight (27.6%) lived through hospital discharge, which shows a high mortality in the population studied. The mortality rate evaluated at six months and one year after discharge showed that, of the eight survivors, two died at six months and three others died one year after discharge.

The Kaplan-Meier analysis demonstrated that the survival, evaluated over the follow-up of patients, was lower for patients who required renal replacement therapy (p=0.020) (Figure 2A). However, when comparing the survival curves, considering the LVEF (Figure 2B) and the presence of AKI (Figure 2C), no difference between the curves was identified.

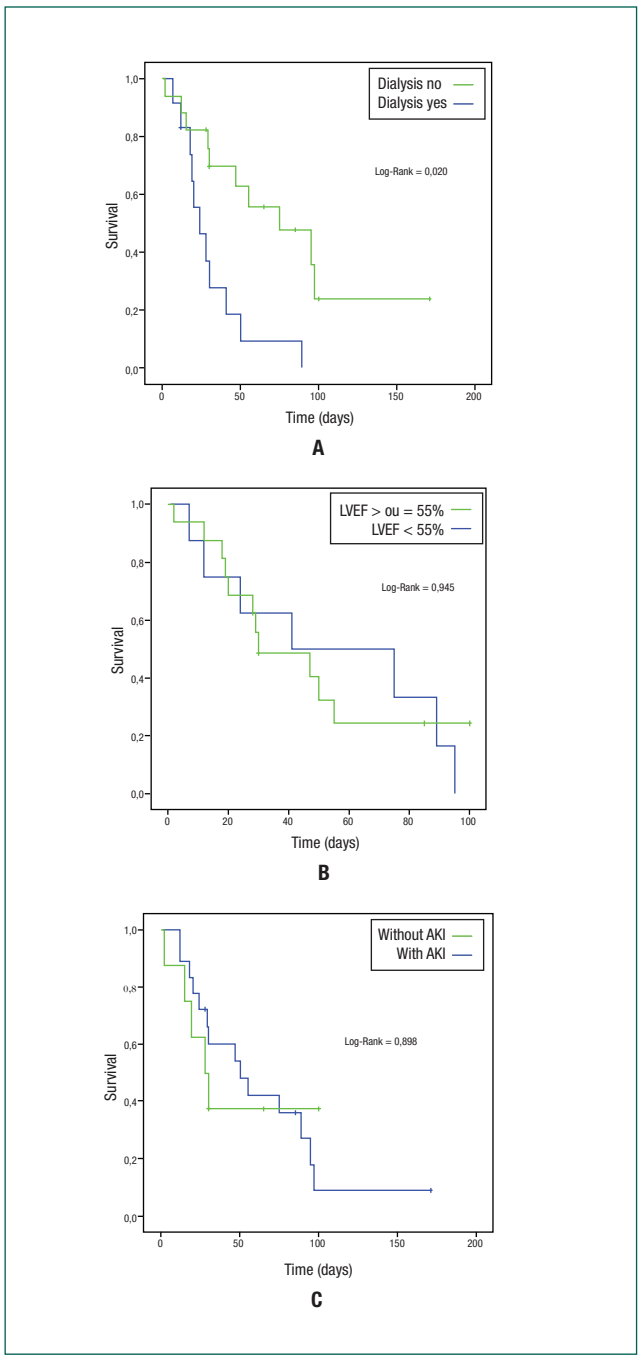

Figure 2. Survival curves of pediatric patients who used ECMO between 2010 and 2015, based on the need for renal replacement therapy - dialysis (Figure 2A), with left ventricular ejection fraction values - LVEF (Figure 2B), and with the presence of acute kidney injury - AKI (Figure 2C)

Discussion

According to the search conducted in the national literature, this study is the first that analyzed the predictors of mortality and survival of pediat-

ric patients with heart failure secondary to complex or acquired congenital heart disease, who used ECMO in a cardiology reference center in Brazil. In addition, the results obtained showed a sociodemographic and clinical characterization of patients using this therapy in the institution, in a cohort of five years.

The clinical and demographic characteristics data demonstrated that the studied sample consisted of seriously ill patients. In the group of non-surviving patients, LVEF was lower, the dose of vasoactive drugs (inotropes and vasopressors) was higher, Murray scores used to characterize the lung injury, as well as the PRISM score used to assess the risk of pediatric mortality, presented high values. These data may explain the high mortality observed in our study.

Even from the multivariate analysis, ventricular dysfunction (LVEF <55%), the development of AKI, and the need for dialysis were independent risk factors for mortality in patients who received ECMO therapy. Lower survival was statistically different for patients who required renal replacement therapy.

A meta-analysis of 12 studies involving 1,763 patients,[7] showed that the main indication for ECMO was respiratory failure, followed by cardiogenic shock. In our center, cardiogenic shock was the main reason for initiating ECMO. In pediatric patients, respiratory failure has been described in the literature as the main indication for ECMO, however, our sample consisted of patients with complex congenital heart disease with cardiac dysfunction after surgical repair, which explains our findings.[11-13]

Mortality is also associated with the duration of ECMO, and the longer the patient depends on the therapy, the greater the risk of complications and, therefore, the higher the mortality.[12] In our study, the mean ECMO time was higher in the group of non-survivors when compared with survivors (14.6 ± 9.8 days vs. 9.2 + 4.3 days, p=0.047). A study evaluating 44 pediatric patients with congenital heart disease[13] undergoing treatment with ECMO, similar to this, showed that the mean time of ECMO support was also higher in the group of non-survivors compared with the survivors.

The AKI is an additional complication in critical patients on ECMO, and is considered a risk factor for mortality in these patients, affecting up to 60% of pediatric patients receiving this therapy.[13-15] Several studies[16-18] showed that AKI is common in critically ill patients using MCS. Oliguria and acute tubular necrosis (ATN) associated with capillary permeability and intravascular volume depletion are frequent during the first 24 to 48 hours of ECMO, due to the acute inflammatory reaction triggered by ECMO.

Among the 29 patients included in this study, the incidence of AKI was 62% (18 patients). Moreover, when the predictive factors for death among patients on ECMO were evaluated, those who developed AKI during therapy had twice the risk of dying. The use of renal replacement therapy was also a predictive factor of mortality in this group, increasing the risk in 7.7. A study evaluating the prognosis of 102 patients who received ECMO[18] showed that 81.4% developed AKI, and 85% of those who required renal replacement therapy combined with the use of ECMO, progressed to death. Despite diagnostic and therapeutic advances, the mortality of patients with AKI remained high in recent decades. Even with the use of new dialysis techniques and resources in the intensive care units, the extension of the life of patients with AKI showed no reduction in mortality.[17]

The institution where the study was conducted was a high complexity hospital, a reference site for cardiopneumology, and has recently become a center of excellence in care for patients with ECMO by the *Extracorporeal Life Support Organization*, however, some limitations of the research can be considered. First, since the data collection was retrospective, some records of patients eligible for the study were not easy to access. As the majority of the patients died, many records were sent to a medical file service in another municipality, which may have led to an underestimation of the mortality of patients who used ECMO. In addition, the collection of ret-

rospective data is subject to interpretation of the records by the researchers, and some medical records contained incomplete data, which was the exclusion criteria. The study was conducted in a single center and the sample size was very small, which may have contributed to the limitation of our findings.

Conclusion

The mortality of 29 pediatric patients included in this study using ECMO, between 2010 and 2015, was high (72.4%). Previous ventricular dysfunction, characterized by low left ventricular ejection fraction (<55%), the development of acute renal failure and the need for concomitant renal replacement therapy with ECMO were independent factors associated with mortality of these patients.

Moreover, the survival of pediatric patients treated with ECMO and renal replacement therapy, concomitantly, was significantly lower than those who were not. Caring for the patient on ECMO is still something new in the Brazilian reality; however, our findings are an incentive for further research in this area. These results can directly influence the nursing care provided, since these patients require highly complex care and an elevated nurse's workload, similar to those found in the literature.

Collaborations

Santos RNNF, Oliveira ACARM e Silva JR declare that they contributed with the article writing, relevant critical review of the intellectual content, and final approval of the version to be published. Santana-Santos E & Oliveira LB collaborated in the study design, analysis, data interpretation, article writing, relevant critical review of the intellectual content, and final approval of the version to be published.

References

1. Brown KL, Ichord R, Marino BS, Thiagarajan RR. Outcomes following extracorporeal membrane oxygenation in children with cardiac disease. Pediatr Crit Care Med. 2013; 14(5):S73-83.
2. Bairdain S, Betit P, Craig N, Gauvreau K, Rycus P, Wilson JM, et al. Diverse Morbidity and Mortality Among Infants Treated with Venoarterial Extracorporeal Membrane Oxygenation. Cureus. 2015; 7(4):e263.
3. Nehra D, Goldstein AM, Doody DP, Ryan DP, Chang Y, Masiakos PT. Extracorporeal membrane oxygenation for nonneonatal acute respiratory failure: the Massachusetts General Hospital experience from 1990 to 2008. Arch Surg. 2009; 144(5):427-32.
4. Redaelli S, Zanella A, Milan M, Isgrò S, Lucchini A, Pesenti A, et al. Daily nursing care on patients undergoing venous-venous extracorporeal membrane oxygenation: a challenging procedure! J Artif Organs. 2016. DOI:10.1007/s10047-016-0912-y.
5. Merrill ED, Schoeneberg L, Sandesara P, Molitor-Kirsch E, O'Brien J Jr, Dai H, et al. Outcomes after prolonged extracorporeal membrane oxygenation support in children with cardiac disease--Extracorporeal Life Support Organization registry study. J Thorac Cardiovasc Surg. 2014; 148(2):582-8.
6. Gupta P, Robertson MJ, Beam B, Gossett JM, Schmitz ML, Carroll CL, et al. Relationship of ECMO duration with outcomes after pediatric cardiac surgery: a multi-institutional analysis. Minerva Anestesiol. 2015; 81(6):619-27.
7. Zangrillo A, Landoni G, Biondi-Zoccai G, Greco M, Greco T, Frati G, et al. A meta-analysis of complications and mortality of extracorporeal membrane oxygenation. Crit Care Resusc. 2013; 15(3):172-8.
8. Murray JF, Matthay MA, Luce JM, Flick MR. An expanded definition of the adult respiratory distress syndrome. Am Rev Respir Dis. 1988; 138(3):720-3.
9. Pollack MM, Ruttimann UE, Getson PR. Pediatric risk of mortality (PRISM) score. Crit Care Med. 1988; 16(11):1110-6.
10. Vincent JL, Moreno R, Takala J, Willatts S, De Mendonça A, Bruining H, et al. The SOFA (Sepsis-related Organ Failure Assessment) score to describe organ dysfunction/failure. On behalf of the Working Group on Sepsis-Related Problems of the European Society of Intensive Care Medicine. Intensive Care Med. 1996; 22(7):707-10.
11. Schmidt M, Bailey M, Sheldrake J, Hodgson C, Aubron C, Rycus PT, et al. Predicting survival after extracorporeal membrane oxygenation for severe acute respiratory failure. The Respiratory Extracorporeal Membrane Oxygenation Survival Prediction (RESP) score. Am J Respir Crit Care Med. 2014; 189(11):1374-82.
12. Almond CS, Singh TP, Gauvreau K, Piercey GE, Fynn-Thompson F, Rycus PT, et al. Extracorporeal membrane oxygenation for bridge to heart transplantation among children in the United States: analysis of data from the Organ Procurement and Transplant Network and Extracorporeal Life Support Organization Registry. Circulation. 2011; 123(25):2975-84.
13. Doll N, Kiaii B, Borger M, Bucerius J, Kramer K, Schmitt DV, et al. Five-year results of 219 consecutive patients treated with extracorporeal membrane oxygenation for refractory postoperative cardiogenic shock. Ann Thorac Surg. 2004; 77(1):151-7; discussion 157.
14. Gajarski RJ, Mosca RS, Ohye RG, Bove EL, Crowley DC, Custer JR, et al. Use of extracorporeal life support as a bridge to pediatric cardiac transplantation. J Heart Lung Transplant. 2003; 22(1): 28-34.
15. Mehta U, Laks H, Sadeghi A, Marelli D, Odim J, Alejos J, et al. Extracorporeal membrane oxygenation for cardiac support in pediatric patients. Am Surg. 2000; 66(9):879-86.
16. Villa G, Katz N, Ronco C. Extracorporeal Membrane Oxygenation and the Kidney. Cardiorenal Med. 2015; 6(1):50-60.

17. Chen YC, Tsai FC, Chang CH, Lin CY, Jeng CC, Juan KC, et al. Prognosis of patients on extracorporeal membrane oxygenation: the impact of acute kidney injury on mortality. Ann Thorac Surg. 2011; 91(1):137-42.

18. Lin CL, Pan KY, Hsu PY, Yang HY, Guo HL, Huang CC. Preoperative 24-hour urine amount as an independent predictor of renal outcome in poor cardiac function patients after coronary artery bypass grafting. J Crit Care. 2004; 19:92-8.