# Predictors of neurological complications of pediatric post-cardiotomy extracorporeal life support

## Recommended Citation

# Predictors of Neurological Complications of Pediatric Post-Cardiotomy Extracorporeal Life Support

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## Abstract

*Background*: Post-cardiotomy extracorporeal membrane oxygenation (ECMO) was associated with significant neurological complications affecting the overall outcome. The aim of the work is to determine the incidence and the predictors of neurological events during pediatric extracorporeal life support after cardiac surgery.

*Patients & Methods*: This is a retrospective study that encompassed all neonates, infants, and children (<18 years of age) who need extracorporeal life support following cardiac surgery between January 2015 and December 2018 at San Donato Hospital, Italy. Data as regards surgical procedure of congenital heart disease, in-hospital mortality, length of ECMO, hospital stay durations, short-term neurological ECMO complications and outcome were analyzed.

*Results*: The sixty-three patients who received post-cardiotomy ECMO, Neurological complications were evident in 31.7% in the form of ischemic stroke in 17.5% and hemorrhagic stroke in 11.1%. By multivariable analysis, the older age of cyanotic cases, the need for a venting cannula, and the rapid $CO_2$ drop in the first 24 h were the most independent risk factors for neurological complications. Prolonged ECMO support and hospital stay duration were associated with neurological sequelae.

*Conclusion*: Neurological complications either ischemic or hemorrhagic strokes were common during pediatric post-cardiotomy ECMO and were significantly related to prolonged ECMO support and hospital stay. Predictors of these neurological sequelae are the older cyanotic cases, the need for a venting cannula, the oxygenator thrombosis, and the rapid $CO_2$ drop in the first 24 h of ECMO.

*Keywords*: ECMO, Pediatrics, Postoperative −cardiac, Neurological complications

## 1. Introduction

Post-cardiotomy ECMO has a potential survival benefit in pediatric cardiac surgery in a group of patients whom would have otherwise not survived without its use. However, institution of ECMO was associated with significant rate of severe complications [1]. Some studies have demonstrated that neurologic complications are rather common among patients receiving ECMO. Intracranial hemorrhage (ICH), acute ischemic stroke, and seizures affect approximately 11% of patients on ECMO. ICH is an independent predictor of mortality, while stroke is associated with a higher rate of discharge to a long-term facility [2]. In the context of post-cardiotomy ECMO, there are additional risk factors that could lead to higher rate of neurological injury, for example, the need for CPB in performing the original operation increases the risk of embolic and other neurological complications [3].

## 2. Methods

Data were collected retrospectively for all neonates, infants, and children (<18 years of age) who need extracorporeal life support following cardiac surgery between January 2015 and December 2018 at San Donato Hospital - Milan−Italy. The

study design was approved by the Scientific Research Committee of Pediatrics Department, Faculty of Medicine and Ethics Committee of Faculty of Medicine, Cairo University.

Cases with known neurological disability prior to surgery were excluded. Neurological complications were classified to ischemic stroke, hemorrhagic stroke or epileptogenic focus based on the imaging modalities by brain CT, brain MRI, and EEG. Also the incidence and the clinical presentations of each type were studied. The following data; type of congenital heart diseases, timing and indications of ECMO support, ECMO related complications, and laboratory results before and during ECMO were analyzed as well as its relation to the risk of neurological complications. The overall outcome of neurological sequelae were evaluated in light of mortality rate, duration of ECMO support and hospital stay, and the grades of neurological disability during discharge in survived cases.

## 2.1. Statistical analysis

Data were fed to the computer and analyzed using IBM SPSS software package version 20.0. (Armonk, NY: IBM Corp). Qualitative data were described using number and percent. Quantitative data were described using range (minimum and maximum), mean, standard deviation, median and interquartile range (IQR). Categorical data were compared using Chi-square or Fisher's exact test, while numerical data were compared using student t test. Logistic regression analysis was used to identify predictors of neurological complications. ROC curve was used to choose the optimal cut-off value. Multivariable logistic regression was used to explore the association of neurological complications during ECMO support with different variable.

## 3. Results

The cohort study included 63 cases received post-cardiotomy ECMO, twenty three of them had cyanotic heart lesions. D-TGA was the most common congenital heart disease. D-TGA was the most common congenital heart disease in cases with ischemic stroke (45%), on the other hand, hemorrhagic stroke was common in MAPCAs dependent pulmonary circulation (57%). Concerning RACHS category; 36 cases (57% was category 3, followed by category 4 by 13 cases (20%), categories 5 and 6 represent only 6 cases (6.3%). On the other hand, long cross clamp time and by-pass time were not statistically significant risks for neurological complications. In our series, neurological

**Abbreviations**

| | |
|---|---|
| CPB | Cardiopulmonary bypass |
| CT | Computerized tomography |
| DCL | Disturbed conscious level |
| DIC | Disseminated intravascular coagulation |
| D-TGA | Dextro transposition of great arteries |
| ECMO | Extracorporeal membrane oxygenation |
| EEG | Electroencephalogram |
| ICH | Intracranial hemorrhage |
| MAPCAs | Major aortopulmonary collateral arteries |
| MRI | Magnetic resonance imaging |
| RACHS | Risk adjustment for congenital heart surgery |
| VA | Veno-arterial |

complications were statistically significant complications in cases starting ECMO support postoperatively (P 0.002) (Table 1). Neurological events were evident in twenty patients (31.7%) either in the form of ischemic stroke in 17.5% or hemorrhagic stroke in 11.1%. Seizures were the most common clinical presentation in our series 55% (11/63), followed by disturbance of conscious level (DCL) in 35% (7/63). The most common diagnostic imaging tool for neurological sequelae during ECMO support was brain CT and MRI. The mean value for the first date of imaging and primary clinical presentation was 20 days post-surgical and 18 days from the start of ECMO. In the current study, neurological complications were statistically more common in infant and children with a median age of one and half years. By further analysis, congenital cyanotic heart diseases were highly associated with neurological complications (75%) specially ischemic stroke (91%) (Table 2). Moreover, older age of cyanotic patients was the independent risk factor for neurological complications (P = 0.004). The median weight Z-score for the cases with neurological complications during ECMO support was −1.85, with a statistically significant lower median weight Z−score in cases with hemorrhagic stroke −2.4, (P 0.029). Cardiogenic shock was the most common ECMO indication and highly associated with neurological complications (Table 3), also cardiac arrest was statistically significant an additional indication for cases developed ischemic stroke (P 0.04). The need for using of a venting cannula during ECMO was statistically significant common in cases with neurological complications specially ischemic stroke (70%) (Table 3). Thrombosis in the oxygenator leads to neurological complications in 30% of our cohort study in the form of ischemic stroke (Table 2). In our cohort, the type of anticoagulants used during ECMO support either Heparin or Bivalirudin was not statistically a contributing risk factor for either neurological sequelae or oxygenator thrombosis. In

Table 1. *Demographic data of studied population on post-cardiotomy ECMO support.*

| | Total (n = 63) | | Neurological complications | | | | Test of Sig. | p |
|---|---|---|---|---|---|---|---|---|
| | | | Without (n = 43) | | With (n = 20) | | | |
| | No. | % | No. | % | No. | % | | |
| **Gender** | | | | | | | | |
| Male | 40 | 63.5 | 28 | 65.1 | 12 | 60.0 | $\chi^2$=0.154 | 0.695 |
| Female | 23 | 36.5 | 15 | 34.9 | 8 | 40.0 | | |
| **Age (years)** | | | | | | | | |
| Neonate | 21 | 33.3 | 20 | 46.5 | 1 | 5.0 | $\chi^2$= 11.368* | 0.003* |
| Infant | 17 | 27.0 | 8 | 18.6 | 9 | 45.0 | | |
| Child | 25 | 39.7 | 15 | 34.9 | 10 | 50.0 | | |
| Min. − Max. | 0.10−13.0 | | 0.10−10.0 | | 0.10−13.0 | | U= 250.0* | 0.007* |
| Median (IQR) | 1.0 (0.10−2.0) | | 0.40 (0.10−2.0) | | 1.50 (0.60−6.50) | | | |
| **Body weight (Kg)** | | | | | | | | |
| Min. − Max. | 2.20−46.0 | | 2.20−33.0 | | 3.60−46.0 | | U = 229.0* | 0.003* |
| Median (IQR) | 5.50 (3.45−10.50) | | 4.0 (3.20−10.0) | | 6.90 (5.55−17.50) | | | |
| **Body weight (z score)** | | | | | | | | |
| Min. − Max. | −6.40−4.20 | | −4.70−4.20 | | −6.40−0.24 | | U = 367.50 | 0.356 |
| Median (IQR) | −1.60 (−2.65−−0.70) | | −1.60 (−2.45−−0.60) | | −1.85 (−3.05−−0.95) | | | |
| **Cyanotic heart lesions** | | | | | | | | |
| Yes | 23 | 36.5 | 18 | 41.9 | 5 | 25.0 | $\chi^2$ = 1.674 | 0.196 |
| No | 40 | 63.5 | 25 | 58.1 | 15 | 75.0 | | |
| **RACHS category** | | | | | | | | |
| 1 | 2 | 3.2 | 1 | 2.3 | 1 | 5.0 | $\chi^2$ = 3.100 | 0.700 |
| 2 | 6 | 9.5 | 4 | 9.3 | 2 | 10.0 | | |
| 3 | 36 | 57.1 | 23 | 53.5 | 13 | 65.0 | | |
| 4 | 13 | 20.6 | 9 | 20.9 | 4 | 20.0 | | |
| 5 | 2 | 3.2 | 2 | 4.7 | 0 | 0.0 | | |
| 6 | 4 | 6.3 | 4 | 9.3 | 0 | 0.0 | | |
| **Intraoperative ECMO** | | | | | | | | |
| No | 20 | 31.7 | 8 | 18.6 | 12 | 60.0 | $\chi^2$ = 10.796* | 0.001* |
| Yes | 43 | 68.3 | 35 | 81.4 | 8 | 40.0 | | |
| **Postoperative ECMO** | | | | | | | | |
| No | 42 | 66.7 | 34 | 79.1 | 8 | 40.0 | $\chi^2$ = 9.377* | 0.002* |
| Yes | 21 | 33.3 | 9 | 20.9 | 12 | 60.0 | | |

ECMO: extracorporal membrane oxygenator, RACHS category: risk adjustment for congenital heart surgery $\chi^2$: Chi square test, U: Mann Whitney test, IQR: Inter quartile range SD: Standard deviation, p: p value for comparing between the studied groups*: Statistically significant at p ≤ 0.05.

Table 2. *The risk factors for ischemic stroke in the studied population.*

| | Ischemic stroke | | | | Sensitivity | Specificity | PPV | NPV |
|---|---|---|---|---|---|---|---|---|
| | No (n = 52) | | Yes (n = 11) | | | | | |
| | No. | % | No. | % | | | | |
| **Cyanotic heart lesions** | | | | | | | | |
| No | 22 | 42.3 | 1 | 9.1 | 90.91 | 42.31 | 25.0 | 95.65 |
| Yes | 30 | 57.7 | 10 | 90.9 | | | | |
| **Thrombosis of oxygenator** | | | | | | | | |
| No | 46 | 88.5 | 6 | 54.5 | 45.5 | 88.6 | 45.45 | 88.46 |
| Yes | 6 | 11.5 | 5 | 45.5 | | | | |

PPV: Positive predictive value, NPV: Negative predictive value.

Table 3. *The risk factors for neurological complications following post-cardiotomy ECMO support.*

| | Neurological complications | | | | Sensitivity | Specificity | PPV | NPV |
|---|---|---|---|---|---|---|---|---|
| | Without (n = 43) | | With (n = 20) | | | | | |
| | No. | % | No. | % | | | | |
| **Cardiogenic shock** | | | | | | | | |
| No | 30 | 69.8 | 6 | 30.0 | 70.0 | 69.77 | 51.85 | 83.33 |
| Yes | 13 | 30.2 | 14 | 70.0 | | | | |
| **Venting cannula** | | | | | | | | |
| No | 28 | 65.1 | 6 | 30.0 | 70.0 | 65.12 | 48.28 | 82.35 |
| Yes | 15 | 34.9 | 14 | 70.0 | | | | |

PPV: Positive predictive value, NPV: Negative predictive value.

our series, fifty percent of cases with neurological complications during ECMO support were statistical significantly associated with acute kidney injury and/or acute liver injury during ECMO support (P 0.01). In cases with neurological sequelae, sepsis and need for vasopressors were reported in 60% of cases, DIC was found in only 10% of cases. Hemorrhage and hemolysis were found in 30% and 25% of cases respectively. However, all these risk factors were not predictors for serious neurological events. On the other hand, the best predictor of neurological sequelae was low PH below 7.33 in pre-ECMO laboratory findings. Moreover, the most statistically significant laboratory predictors during ECMO support were high lactate above

5.1 mmol/L, high ALT above 23 IU/L, high serum creatinine above 0.75 mg/dl, and rapid drop of $CO_2$ within the first 24 h of ECMO support by > 20% (Fig. 1, Table 4). In addition, rapid drop of $CO_2$ > 20% within the first 24 h of ECMO support was the most statistically significant laboratory predictor for hemorrhagic stroke (Table 4). By multivariable analysis, the older age of cyanotic cases, the need for a venting cannula, and the rapid $CO_2$ drop in first 24 h were the most independent risk factors for neurological complications. The oxygenator thrombosis was the most independent risk factor for ischemic stroke, while the rapid $CO_2$ drop in first 24 h was the most independent risk factor for hemorrhagic stroke (Table 5). In our series,
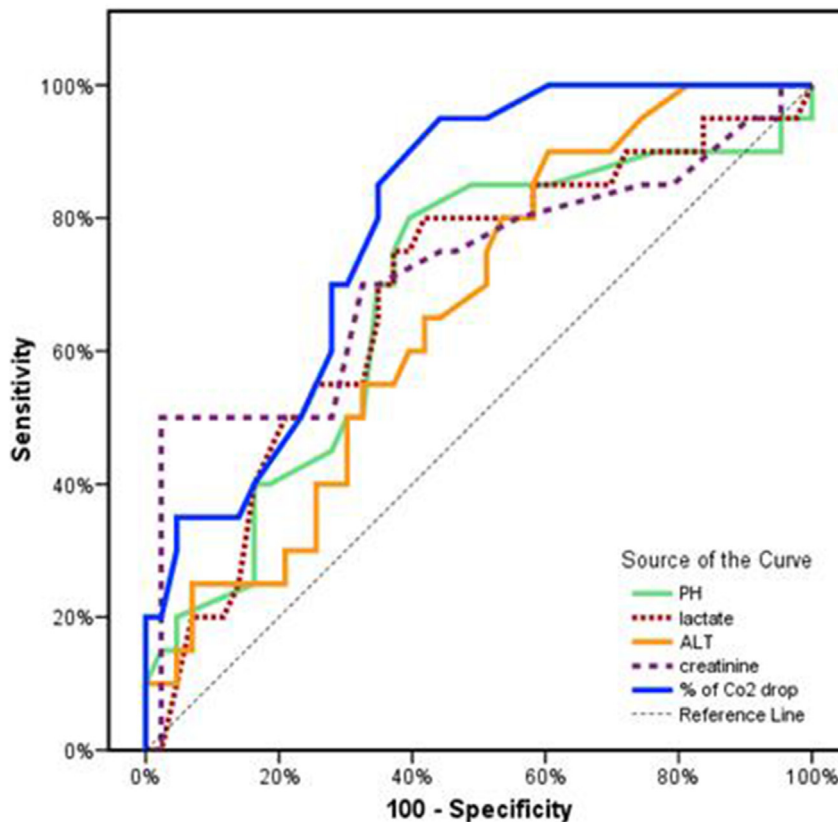


Fig. 1. Laboratory predictors of neurological complications during ECMO support.

Table 4. Laboratory predictors of neurological complications during ECMO support.

| Laboratory variables | | AUC | p | 95% C.I | Cut off | Sensitivity | Specificity | PPV | NPV |
|---|---|---|---|---|---|---|---|---|---|
| Pre-ECMO | Blood PH | 0.682 | 0.021* | 0.536−0.828 | ≤7.33 | 80.0 | 60.47 | 48.5 | 86.7 |
| During ECMO | Serum lactate | 0.685 | 0.019* | 0.542−0.828 | >5.1 | 75.0 | 62.79 | 48.4 | 84.4 |
| | ALT | 0.659 | 0.044* | 0.522−0.796 | >23 | 75.0 | 48.84 | 40.5 | 80.8 |
| | Serum creatinine | 0.717 | 0.006* | 0.567−0.868 | >0.75 | 70.0 | 67.44 | 50.0 | 82.9 |
| | Percentage of drop of $Co_2$ | 0.796 | <0.001* | 0.688−0.904 | >20 | 95.0 | 55.81 | 50.0 | 96.0 |

ALT: alanine aminotransferase, AUC: area under curve, p value: probability value, CI: confidence intervals, NPV: negative predictive value, PPV: positive predictive value.

Table 5. *Univariate and multivariate analyses for the risks and the predictors of neurological complications in the studied population.*

| Variables | Univariate | | #Multivariate | |
|---|---|---|---|---|
| | p | OR (95%C.I) | p | OR (95%C.I) |
| **Age** | 0.020* | 1.265 (1.038—1.542) | 0.061 | 1.250 (0.990—1.580) |
| **Age of cyanotic cases** | 0.004* | 3.250 (1.448—4.760) | 0.009* | 3.120 (1.220—4.320) |
| **Body weight Z score** | 0.273 | 0.829 (0.592—1.160) | | |
| **Cyanotic heart lesions** | 0.201 | 2.160 (0.664—7.027) | | |
| **Indication for ECMO:** | | | | |
| **Cardiogenic shock** | 0.004* | 5.385 (1.693—17.122) | 0.999 | — |
| **Respiratory failure** | 1.000 | 3.321 (0.942—11.710) | | |
| **Cardiac arrest** | 0.062 | | | |
| **Venting cannula** | 0.012* | 4.356 (1.388—13.669) | 0.040* | 4.703 (1.074—20.592) |
| **Oxygenator thrombosis** | 0.083 | 3.257 (0.857—12.385) | | |
| **Number of vasopressor** | 0.379 | 0.727 (0.357—1.479) | | |
| **Sepsis** | 0.133 | 2.294 (0.776—6.779) | | |
| **Acute kidney injury** | 0.013* | 4.375 (1.364—14.032) | 0.550 | 2.049 (0.195—21.481) |
| **Acute liver injury** | 0.023* | 3.778 (1.204—11.856) | 0.488 | 1.779 (0.350—9.053) |
| **PH** *(Pre-ECMO)* | 0.024* | 0.018 (0.001—0.589) | 0.596 | 4.640 (0.016—1359.625) |
| **Lactate** *(Pre-ECMO)* | 0.018* | 1.153 (1.025—1.297) | | |
| **Platelets***(Pre-ECMO)* | 0.629 | 0.998 (0.990—1.006) | | |
| **INR** *(Pre-ECMO)* | 0.736 | 1.085 (0.674—1.748) | | |
| **D-Dimer** *(Pre-ECMO)* | 0.656 | 1.030 (0.905—1.172) | | |
| **Peak serum lactate** *(During ECMO)* | 0.029* | 1.136 (1.013—1.275) | 0.713 | 0.967 (0.806—1.159) |
| **Peak ALT** *(During ECMO)* | 0.122 | 1.001 (1.0—1.002) | — | — |
| **Peak serum creatinine** *(During ECMO)* | 0.005* | 3.758 (1.478—9.551) | 0.387 | 2.014 (0.413—9.829) |
| **Peak bilirubin** *(During ECMO)* | 0.270 | 0.914 (0.779—1.072) | | |
| **Peak D-Dimer** *(During ECMO)* | 0.230 | 1.073 (0.956—1.204) | | |
| **Lowest platelets value** *(During ECMO)* | 0.679 | 0.997 (0.985—1.010) | | |
| **Peak INR** *(During ECMO)* | 0.086 | 1.270 (0.966—1.670) | | |
| **Lowest INR** *(During ECMO)* | 0.574 | 0.642 (0.137—3.010) | | |
| **% of Co2 drop** *(in first 24 h)* | 0.002* | 2.054 (1.019—3.089) | 0.009* | 2.061 (1.015—3.108) |

ECMO: extracorporeal membrane oxygenator, INR: international normalized ratio, CO2: cardon dioxide OR: odd's ratio, C.I: confidence interval.

neurological events in post-cardiotomy ECMO support were not contributing to the mortality rate as only 15% (3 cases) died during ECMO support and 10% (2 cases) died in hospital after weaning of ECMO support. However, cases with neurological complications were highly associated with prolonged ECMO support duration, and prolonged hospital stay (Table 6). Variable degree of neurological disability was evident on the discharged patients ranging from mild degree in 35%, to moderate and severe degree in 20%

for each. Poor neurological outcome with severe disability during discharge or in hospital mortality during or after weaning of ECMO support were statistically significant in cases with hemorrhagic stroke (85%), p = 0.047. By multivariate analysis, neurological complications were the most independent risk factor for prolonged ECMO support duration (adjusted odd's ratio 0.432, CI 0.226—0.826), and prolonged hospital stay (adjusted odd's ratio 0.344, CI 0.188—0.630).

Table 6. *The outcome of cases with neurological complications during post-cardiotomy ECMO support.*

| | Neurological complications | | | Types of neurological sequelae | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| | | | | Ischemic stroke | | | Hemorrhagic stroke | | |
| | With (N = 20) | Without (N = 43) | P | With (N = 11) | Without (N = 52) | P | With (N = 7) | Without (N = 56) | P |
| ECMO duration (Median hours) | 195 (108—250) | 116 (80—140) | 0.020 | 129 | 126 | 0.351 | 260 | 120 | <0.001 |
| Hospital stay (Median Days) | 45 (30—60) | 23 (7.5—33) | 0.001 | 44 | 23 | 0.079 | 62 | 24 | 0.023 |
| Discharged home | 15 (75%) | 26 (60%) | 0.620 | 9 (80%) | 32 (60%) | 0.376 | 4 (57%) | 37 (66%) | 0.713 |
| Mortality on ECMO | 3 (15%) | 9 (22%) | | 2 (20%) | 10 (20%) | | 1 (15%) | 11 (20%) | |
| In hospital mortality post -ECMO | 2 (10%) | 8 (18%) | | 0 (0%) | 10 (20%) | | 2 (28%) | 8 (14%) | |

ECMO: extracorporeal membrane oxygenator.

## 4. Discussion

The current study has major implications for the care of patients requiring post-cardiotomy ECMO support. Here, we reported that neurological complications in venoarterial-ECMO in children are not uncommon and older cyanotic children and sudden changes of CO2 during the procedure are the predictors of brain insult. Identification of the risk factors of neurological events of postcardiotomy ECMO in pediatrics might help to improve ECMO management and might reduce their occurrence. Extracorporeal membrane oxygenation (ECMO) is an increasingly used technique providing cardiopulmonary support to patients with severe refractory cardiac and respiratory failure [4]. The utility of ECMO in pediatric cardiac surgery has been increased in the past few years due in part to increasing complexity of congenital pathologies encountered [5]. However neonatal and pediatric patients undergoing cardiac surgery who then require ECMO support may be at extremely higher risk for neurological complications [6]. Analysis of neurological complications in pediatric cases on ECMO support after cardiac surgery, showed that the overall incidence of stroke was 12.3% with high rates of hemorrhagic stroke (10%), and low rates of ischemic stroke (2.3%) [7]. The true incidence of neurological complications during ECMO support in children could be underestimated, as many of asymptomatic patients are not routinely examined by neuroimaging. In one study using T2-weighted MRI among children receiving ECMO support, found that nearly all imaging patients had microhemorrhages on MRI [8]. In addition, the difficulty of obtaining reliable imaging in critically ill patients during extracorporeal support [9]. In the current study, we report a higher incidence of neurological complications 31.7% mainly in the form of ischemic strokes. In contrary, previous publications showed higher incidence of hemorrhagic stroke comparing to ischemic stroke in children receiving ECMO support [7,10]. This finding could be interpreted by the type of ECMO cannulation used in our cohort, as all cases had VA ECMO with central cannulation. The direct connection of the ECMO flow to the supra-aortic vessels and bypassing the lungs filter, expose the patient at a higher risk for embolization. In addition, VA ECMO, in absence of pulsatile flow, affects the cerebral auto-regulation and the vascular reactivity. The accurate timing of acute neurological insult is always difficult, as most of patients during ECMO support post operatively are completely sedated which limit proper neurological examination. Also, the routine use of continuous EEG

monitoring or brain oxygen saturation monitoring are not common. In addition, the transportation of the postoperative cases during ECMO support for doing CT brain in the radiology department can be challenging. In our series, the mean date of the first image was 20 days from the surgery, and 18 days from starting the ECMO support. Previously, it was published that neonatal age group was independent risk factor for neurological insults [7,10]. However, in our cohort, neurological complications were statistically significant more common in infants and children with a median age of one and half years. This finding could be explained by the type of congenital heart disease and the timing of surgical correction. Around 75% of cases with neurological insults had surgical correction for congenital cyanotic heart lesions. Older infants and children with congenital cyanotic heart lesions are in a higher risk for neurological injury due to long standing uncorrected heart disease, exposing their bodies to chronic hypoxia and making these brains by time highly susceptible for neurological complications [11]. The proper timing of ECMO initiation is a major predictor for morbidity and mortality. Also the availability of ECMO circuit for rapid response in resuscitation at cardiac arrest has a great effect on the outcome . Most of the previously published studies showed that the risk of neurologic injury may be higher in children supported with ECPR [1,12,13]. In the current study, neurological sequelae were statistically significant in cases starting ECMO support postoperatively. Cardiogenic shock was the common ECMO indication highly associated with neurological complications, also cardiac arrest was statistically significant additional indication in cases who developed ischemic stroke. Proper timing and adequate decompression of left ventricle had a high influence on cardiac function recovery, and highly affect morbidity and mortality during ECMO support [14]. In our series, the need for a venting cannula was highly associated with neurological insult, this can reflect the very poor cardiac state in cases who developed neurological complications which were highly associated with cardiogenic shock and cardiac arrest as indications for ECMO support. The timing of venting cannula insertion, the hemodynamic state, and the association of intracardiac thrombus were not evaluated in the current study. Variations in arterial CO2 have a significant impact on the metabolic autoregulatory mechanisms that regulate cerebral blood flow. In many published studies [7,15−17], rapid initial drop of PCO2 > 50% was a significant risk factor for neurological complications. In our series, by multivariable analysis, the rapid CO2 drop >50% in first 24 h was an

independent risk factors for neurological insult specifically the hemorrhagic stroke with a 100% sensitivity, and 96% specificity. Many studies showed that neurological complications during ECMO support were significantly associated with longer ECMO support duration, length of hospital stay, and higher mortality rates. Previously, it was published that neonates and children received ECMO support after cardiac surgeries, the overall in-hospital mortality rate was 53%, with stroke experienced a greater rate of death at cannula removal and in-hospital mortality, also neurological complications were highly associated with prolonged ECMO support duration [7]. Intracranial hemorrhage was independently associated with high risk of mortality [18]. In contrast, we reported that neurological complications during ECMO support were not statistically significant risk for high mortality, however, cases with neurological affection had prolonged ECMO support and prolonged hospital stay.

## 5. Conclusion

Neurological sequelae are common among neonates and children received ECMO support after cardiac surgery with higher incidence of ischemic stroke. The most independent risk factors for these neurological insults were the older age of cyanotic cases, the need for a venting cannula, and the rapid $CO_2$ drop in the first 24 h. Neurological complications were highly associated with prolonged ECMO support and hospital stay durations but not contributing factor for in hospital mortality.

### 5.1. Limitations of the study

The current study has the limitation of being retrospective observational study with small sample size. The following factors were not assessed in our study: preoperative hemodynamic state, quality of the cardiac repair, timing of primary clinical presentation of neurological insult, hemodynamic variables, and ventilator parameters during ECMO support, and long term neurological outcome and cognitive development.

## Ethics approval and consent to participate

Cairo University, Faculty of Medicine Research Ethics Committee approved the study and the code: MD-191-2019.

## Full ethics humans

The study was approved by the research committee of pediatric department in Cairo University.

All methods were carried out in accordance with relevant guidelines and regulations.

The protocol was approved by Scientific Research Committee of Pediatric Department, Cairo University and Ethical committee of Cairo University Faculty of Medicine Research Ethics Committee.

The informed consent was obtained from both the adult participants and the parent(s)/guardian(s) of all under-16s.

## Author contributions

**Hala Mounir Agha:** Conception and design of the study, critical review and manuscript drafting; final approval of the version to be published, **Amr Fathallah:** Data collection and data interpretation, **Giuseppe Isgro:** Data acquisition, clinical evaluation of patients and final approval of the version to be published, **Mauro Cotza.** Perform ECMO, clinical evaluation of patients and final approval of the version to be published.

## Conflict of interest

The authors declare that they have no competing interests in this section.

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