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Use of ECMO and Mortality in Pediatric Cardiac Surgery Patients with Genetic Conditions: A Multicenter Analysis

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Abstract

Objective—Congenital heart disease is commonly a manifestation of Genetic Conditions (GC). Surgery and/or ECMO were withheld in the past from some patients with GC. We hypothesized that surgical care of children with GC has increased over the last decade but their cardiac ECMO use remains lower and mortality greater.

Design—Retrospective Cohort Study

Setting—Patients admitted to the Pediatric Health Information System database 18 years old with cardiac surgery during 2003–14. GC identified by ICD9 codes were grouped as: Trisomy 21 (T21), Trisomy 13 or 18 (T13/18), 22q11 deletion, and all “other” GC and compared to patients without GC

Patients—A total of 95,253 patients met study criteria, no GC (85%), T21 (10%), T13/18 (0.2%), 22q11 deletion (1%), and “others” (5%).

Interventions—None

Measurements and Main Results—Annual surgical cases did not vary over time. Compared to patients without GC, T21 patient ECMO use was just over half (OR 0.54), but mortality with and without ECMO were similar. In T13/18 patients, ECMO use was similar to those without GC, but all 5 treated with ECMO died. 22q11 patients compared to those without GC had similar ECMO use, but greater odds of ECMO mortality (OR 3.44). “Other” GC had significantly greater

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ECMO use (OR 1.22), mortality with ECMO (OR 1.42) and even greater mortality odds without (OR 2.62).

Conclusions—The proportion of children undergoing cardiac surgery who have GC did not increase during the study. Excluding T13/18, all groups of GCs received and benefited from ECMO, although ECMO mortality was greater for those with 22q11 deletion and “other” GC.

Keywords

Extracorporeal Membrane Oxygenation; Congenital Heart Defects; Cardiac Surgical Procedures; Down Syndrome; Trisomy 13 Syndrome; 22q11 Deletion Syndrome

Introduction

Historically, surgical repair and rescue with extracorporeal membrane oxygenation (ECMO) support has been withheld from some patients with congenital heart disease (CHD) and genetic conditions (GC) (1). Over time, GC that excluded patients from cardiac surgical palliation has changed (1). Recognizable syndromes, extracardiac malformations, and chromosomal anomalies associated with GC occur in approximately 20–30% of children with CHD (2–3). Advances in cytogenetic testing and other methods are increasing recognition of GC (4–5). While studies may vary by specific genetic diagnosis, patient age, and anatomic lesion, most report greater morbidity and mortality risk among children with GC (5).

Perioperative ECMO use among children with CHD is 2.7–3% of surgical cases (6–7). Assessment of perioperative risk of mortality or need for ECMO among children with GC and CHD is complex because the number of GC that have associated congenital heart malformation is large but the number of surgical patients with the same GC and cardiac diagnosis are small, with the exception of Trisomy 21 (T21). In the past providers were reluctant to offer ECMO to patients with GC (8). However, recent surveys report changing attitudes, including the use ECMO in children with Trisomy 13 or 18 (T13/18) (1).

Using the Pediatric Health Information System (PHIS database) we identified over 150,000 heart surgeries and 4,300 ECMO runs in the perioperative period. The PHIS database provides a unique opportunity to describe trends in surgical care and ECMO use over the last 10-year time period for patients with known GC.

Our study goals are to describe trends regarding receipt of cardiac surgery by children with known GC and to characterize ECMO use and outcomes for patients with and without GC who had cardiac surgery. We hypothesized an increasing trend in surgical procedures for children with CHD and GC over the past decade and that patients with GC would be less likely to be offered perioperative ECMO support and more likely to die without the use of ECMO.

Materials and Methods

Study Design and Setting

We conducted a retrospective cross sectional analysis using PHIS to identify cardiac surgical admissions discharged between Jan. 1, 2004 and Jun. 30, 2014. The Children's Hospital Association (CHA) both developed and maintains PHIS, which currently contains data from 49 tertiary care children's hospitals located all over the United States. Participating hospitals provide both administrative data, such as patient and hospital demographics, International Classification of Disease (ICD9) codes, length of stay, and discharge disposition. Additional admission characteristics are available such as complex chronic conditions (CCC) according to Feudtner et al (9) and Risk Adjustment for Congenital Heart Surgery (RACHS) scores as described by Jenkins et al (10). Data submitted to PHIS is subject to several reliability and accuracy checks ensuring data integrity. This study obtained data without any patient identifying information compliant with a de-identified data set that the University of Utah Institutional Review Board excludes from need for human study oversight.

Patient Selection Criteria

Using ICD-9 procedure codes we identified cardiac surgical admissions for children 18 years discharged from January 1, 2004–December 31, 2014 defined as being assigned a RACHS score 1 to 6 or having an ICD9 code for Myocarditis or Cardiomyopathy (N=150,717). Surgical complexity was stratified using the RACHS score as assigned by PHIS (10). Extracorporeal membrane oxygenation (ECMO) was determined by ICD9 procedure code 39.35.

Only subjects with a RACHS score >1 and the surgical procedures listed in Appendix 1a were included in further analysis (N=95,253). We defined the patient's first cardiac surgery as the primary surgery for the hospital admission. If the primary surgery was not identifiable by procedure day of service, age at time of surgery, or diagnosis code the patient was excluded (n=21,106). GC classified by ICD9 codes included; T21, T13/18, 22q11 deletion syndrome, Turners syndrome, Klinefelters syndrome, Sex chromosome disorder not otherwise specified, Cri du chat, Prader Willi, Microdeletion syndrome, Marfans syndrome, General deletions, Autosomal deletions, Fragile X syndrome, Neurofibromatosis, Tuberous Sclerosis, and Multiple congenital anomalies (See Appendix 1b). Genetic conditions were grouped as T21, T13/18, 22q11 deletion syndrome, and the rest were combined as "other" GC using group consensus with input from a geneticist (SBI). These groups were compared to subjects with no known GC.

Subject level data including congenital heart defect, cardiac surgical procedure, co-existing medical conditions/complications (i.e. prematurity, low birth weight, intraventricular hemorrhage, bronchopulmonary dysplasia, primary and secondary pulmonary hypertension, acute renal failure, pulmonary hemorrhage, stroke, intracranial hemorrhage, and cardiac arrest), and additional procedures were based on ICD9 codes. Cardiac anatomic diagnosis and surgery was validated by two investigators (JFD, SB) and discrepancies resolved by a third investigator (VA).

Primary Comparison

We compared subjects with GC to those without to determine if their odds of death without ECMO, use of ECMO, or mortality with ECMO differed when adjusted for complexity of surgery and other confounders.

Secondary Comparisons

We reported cardiac surgery rates by known GC over time.

Statistical Analysis

Data are reported as frequencies (n) and proportions (%) or as median values with interquartile range (IQR). To identify risk factors for ECMO and death, univariate analysis were performed using the χ^2 or Wilcoxon rank-sum test. Variables associated with in hospital death or ECMO were considered in a multivariable logistic regression models using forward stepwise regression with inclusion $p \leq 0.1$ and exclusion criteria $p \leq 0.05$. The final models included factors that remained independently associated with mortality or ECMO. Complications that occur during ECMO were excluded from the model for odds of ECMO. Significance was defined as $p \leq 0.05$ and when pairwise comparisons were made between study groups a Bonferroni adjustment was used. IBM SPSS (v. 25 for MAC; Armonk, NY) was used for analysis.

Results

After exclusion for patients who did not a RACHS category score in the perioperative period, 95,253 cardiac surgery cases from 43 of the PHIS hospitals met the study criteria. Of these 2,680 (2.8%) received ECMO during the same hospitalization. Cases with a GC comprised 15% (N=14,713) of the study population; represented by T21 (N=9473, 10%), T13/18 (N=156, 0.2%), 22q11 deletion syndrome (N=715, 0.75%) and “other” GC (N=4369, 5%). The subsets of the “other” GC group included 2305 (53%) with multiple congenital anomalies syndromes, 1171 (27%) with single gene defects, 646 (15%) with sex chromosomes disorders, and 248 (6%) with copy number variants (excluding 22q11).

Patient Characteristics

Select cardiac case characteristics are compared by GC in Table 1. Age differed by study groups. The greatest difference was among patients with T21, 68% were age 2–12 months compared to 20–40% among the GC groups and 29% among patients without a GC. The distribution of RACHS categories also varied by study groups (Table 1, Figure 1). Patients with T21 had the largest proportion of RACHS 3 surgeries (Atrioventricular Canal Repair n=6210, 66%), those with T13/18 had greater proportion of RACHS 2 surgeries (Ventricular Septal Defect Repair n=15, 10%).

Table 2 compares patients by receipt of ECMO and by in hospital survival. Neonates were the most likely to receive ECMO and die prior to hospital discharge. Comorbid conditions and medical complications were elevated in similar proportions in those receiving ECMO and in those who died.

Comparing rates of ECMO use and ECMO Mortality by Genetic Condition

Compared to cardiac surgical cases without a GC, those with T21 received ECMO significantly less, while those with “other” GC received ECMO more frequently (Table 1). Patients with multiple congenital anomalies syndromes within the “other” GC group were treated with ECMO significantly more than children without a GC (3.5%) ($p=0.0003$), while use of ECMO did not significantly differ for the remaining subsets.

Among children treated with ECMO in the “other” GC group, the risk of death was significantly greater than in children without a GC on ECMO (RR 1.1 95% CI 1.0–1.3). However, subgroup analysis shows that only disorders of sex chromosomes were associated with a significant increased risk of death with ECMO support (RR 1.34; 95% CI 1.00–1.78). Increased risk of death without ECMO; however, was significantly greater for all subgroups (disorder of sex chromosomes (RR =2.23; 95% CI 1.47–3.37), single gene defects (RR=2.47; 95% CI 1.84–3.30), multiple congenital anomalies (RR=3.00; 95% CI 2.47–3.64), and copy number variants (excluding 22q11) (RR 3.63; 95% CI 2.18–6.05).

Comparing Rates of Surgery over Time

Over the 10-year study period the proportion of patients undergoing cardiac surgery who had GC did not vary over time compared to all patients who had cardiac surgery. The rates for all patients with and without a GC and specifically for children with T13/18 did not significantly increase.

Multivariable Logistic Regression Models for Odds of receiving ECMO and ECMO Mortality

The results of the multivariable logistic regression models used to predict odds of mortality with and without ECMO as well as use of ECMO can be seen in Figure 2. The model to predict odds of death with and without ECMO also controlled for additional medical complications: IVH, acute renal failure, pulmonary hemorrhage, stroke and intracranial hemorrhage. These complications were not included in the regression model to predict odds of receiving ECMO because the database does not specify the timing of medical complications so it is not possible to ascribe the event as result of ECMO or a complication leading to ECMO.

ECMO Use

Compared to patients without a known GC and adjusted for age, surgical complexity, co-morbidities and complications of care (Figure 2, Table 3), the odds of receiving ECMO were significantly lower in T21 (OR 0.54; 95%CI 0. 0.45–0.66). Cases with T13/18 and 22q11 had similar odds of receiving ECMO, while cases with “other” GC’s had greater odds of ECMO receipt (OR 1.22; 95% CI 1.03–1.45).

Adjusted ECMO and non ECMO Mortality

Adjusted for age, surgical complexity, co-morbidities and complications of care, T21 had similar adjusted odds of mortality in those treated with ECMO while those with 22q11 deletion and “other” GC had significantly increased adjusted odds of mortality compared to

children without a GC who received ECMO. All five patients with T13/18 that received ECMO, died prior to hospital discharge.

Compared to children without a GC, the adjusted odds of death among patients not treated with ECMO were significantly greater for cases with T13/18 and cases of those with “other” genetic conditions, but children with 22q11 and T21 had similar adjusted odds of death. The adjusted odds of death without ECMO are roughly 2 fold greater than the adjusted odds of death with ECMO for those with “other” GC.

Discussion

In this large multicenter database study, we found that annual proportions of cardiac surgery for children with known GC versus those without did not increase over the 10 years of study. Our hypothesis that ECMO would be withheld from those with GC who may have benefitted from it was not demonstrated. For instance, children with T21 had significantly lower adjusted odds of receiving ECMO but similar adjusted odds of death with or without ECMO. Children with T13/18 and cardiac surgery die frequently and their ECMO mortality was 100% but the rate they received ECMO does not suggest that they were offered it significantly less. Children with 22q11 had similar odds of ECMO use but had increased odds of dying if they did receive ECMO. The mortality without ECMO in children with 22q11 was similar to those without GC. Finally, the “other” GC group had increased odds of receiving ECMO compared to no GC and increased mortality with and without ECMO, though the odds of death without ECMO was almost twice that of those with ECMO.

Previous studies regarding the prevalence of extra-cardiac abnormalities in CHD reported ranges of 17% to 30% (4–5,11–12). A recent analysis of the Society of Thoracic Surgeons Congenital Heart Surgery Database of GC in neonates (<30 days) with a cardiac operation from 2010–13 reported a prevalence of 18.8% (13). We identified a GC in 15% of cardiac surgical patients treated from 2003–14. Our rate may differ because we included all pediatric ages and it also be affected by patients who had multiple procedures over the long study period. Patients with GC would likely have lower rates of multiple palliative procedures but we did not have a unique patient number to link surgical cases to patients.

Children with T13/18 had relatively non-complex surgical repairs (92% RACHS 3 or lower) but still had the greatest rate of surgical mortality. Only 5 patients with T13/18 received a rescue trial of ECMO in the perioperative period and all 5 died. Some patients with T13/18 may not have received cardiac surgery therefore it is difficult to know we identified every patient to accurately predict mortality risk, however we did find a similar amount of patients who received a cardiac procedure (n=154) as a recent publication looking at the Kids’ Inpatient Database from 1997–2009 (14). These results indicate that although the surgical palliation rates are potentially shifting (15–16), both ECMO mortality and non-ECMO surgical mortality remain significantly elevated for these children.

Reluctance to treat T21 patients with ECMO in the past was likely due to a reported higher risk of post ECMO morbidity and mortality reported in 2001 and 2007 (5,8). However, several recent studies confirm our finding of lower adjusted ECMO use but similar ECMO

mortality for T21 patients treated in perioperative period compared to children without known GC. (17–18). In 2015 using the Extracorporeal Life Support Organization registry, Cashen et al found that children with T21 treated with ECMO for both cardiac and respiratory failure did not have increased risk of mortality compared to children without T21 (19).

Use of ECMO was not increased for patients with 22q11 but the risk of death with ECMO was 3.5 fold higher compared to those without a GC; however, the precision of the estimate was poor with a wide confidence interval. Studies directly assessing the association of 22q11 deletion syndrome and perioperative mortality are limited. O’Byrne et al reported similar use of ECMO and hospital mortality of patients with 22q11 compared to other cardiac surgical patients, but significantly worse perioperative outcomes (20). A study using the Extracorporeal Life Support Organization (ELSO) registry of 88 patients with 22q11 deletion treated from 1998–2011 also did not find an increased risk of ECMO use or mortality despite ECMO (21). This is in contrast to our findings, of the 33 patients with 22q11 who died after surgery in our study, 16 (52%) had received ECMO. Of those who did not receive ECMO mortality was only 2%. Our analysis adjusted for surgical complexity and medical complications but in close review we find our patients had a similar surgical case mix in comparison with these previous studies. We cannot say with certainty why the findings of an increase in ECMO mortality are seen in our results but some potential explanations could be that these previous studies had a larger sample size of patients who received ECMO. Further studies would need to confirm this projected increased ECMO mortality risk.

In contrast to those with T21 and 22q11 deletion syndrome, children with “other” GC had significantly greater adjusted odds of receiving ECMO, and both greater odds of death with and without ECMO compared to children without a GC. Similar to our findings, Alsoufi et al reported that despite adjustment for prematurity and low birth weight, children with GC had significantly increased risk of death after cardiac surgery compared to children without a GC (11). Furthermore after surgery, at 10 year follow up survival remained lower among children with a GC compared to those with no GC. Multiple studies describe increased mortality at Stage I palliation for infants with GC. (22–24). It is not surprising that patients with multi-organ system dysfunction would have greater ECMO mortality. Patients with 22q11 syndrome have known impaired immunological function and impaired T-cell production, which increases the risk of infection. The rates of infection on ECMO are reported as high as 11.7% even without the additional factor of an impaired immune system (25). The increased ECMO mortality we identified in those with 22q11 could be secondary to this increased infection risk. In our cohort those with 22q11 had an occurrence of a nosocomial infection of 3.3%, which was three times higher than the rate of nosocomial infection in those with no GC.

We acknowledge that the “other” GC group is heterogeneous but evaluation by subgroups still showed an increase in unadjusted risk of receiving ECMO and increased risk of death if ECMO was not used among all subgroups. The subgroup that comprises the greatest percentage of the “other” category is multiple congenital anomalies. The ICD9 code for multiple congenital anomalies is used for genetic conditions that comprise complications of

multiple organ systems (i.e. CHARGE syndrome, VACTERL association etc). It is likely inaccurate to conclude that every GC in our “other” group has equal elevated risk of ECMO use and slightly increased ECMO mortality. Despite the fact that the mortality among surgical cases not supported with ECMO is substantially elevated (4.4%), if the child does not have other complications making successful rescue with ECMO likely, the current 50% ECMO mortality should not dissuade increased use for patients with these GC until more sufficient granular information regarding ECMO mortality is available.

Although the data in this study does not provide sufficient information to judge proper ECMO candidacy among cardiac surgery patients the information provided can be used to help clinicians evaluate risk versus benefit. Because ECMO is usually employed as a rescue therapy the decision to use it is time sensitive, therefore a better understanding of additional risk factors for mortality is important.

Limitations

This study is subject to limitations applicable to all retrospective observational studies including human error for data entry despite quality control measures and use of multiple ICD9 diagnostic and surgical codes for a single patient. We excluded surgical cases that did not have clear cardiac anatomic diagnosis and surgery to reduce diagnostic bias but we were unable to account for the fact that some patients had multiple procedures over the long study period. While we can conclude that the proportion of patients with GC and cardiac surgery compared to all patients who had cardiac surgery per year did not significantly increase over time, this conclusion does not account for patients whose families chose non-surgical options or patients who were not offered surgery. Therefore the proportion of children with GC receiving cardiac surgery remains unknown. Another limitation is the ability to categorize the timing of the co-morbidities on ECMO. It is unknown whether these events occurred prior to initiation of ECMO or as a consequence of ECMO because ICD9 CM codes are collected primarily for billing purposes and are not assigned to a specific hospital day. In our description of patient characteristics and outcomes, we were limited by the variables collected in PHIS which do not include physiologic information to calculate to severity of illness scores or progression of organ dysfunction during hospitalization.

Conclusions

The presence of most GC, excluding T21, have increased mortality with cardiac surgery. Children with T13/18 had the highest mortality rate and in our study the small number of patients who received ECMO had 100% mortality. ECMO was employed as a rescue therapy among all GC groups during their surgical care, but ECMO mortality was significantly greater for those with 22q11 deletion and “other” GC. Children with “other” GC have increased odds of ECMO use and dying with or without ECMO utilization. GC should be considered a potential risk factor for greater hospital mortality with cardiac surgery and when considering ECMO to rescue patients in the perioperative period. Future evaluation should include delineations of “other” GC in more detail to better identify their cardiac surgery and ECMO mortality risks.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Figure 1.
RACHS: Risk Adjust Classification for Congenital Heart Surgery¹⁰

Figure 2.

Multivariable logistic regression models for odds of ECMO (a) and odds of mortality with (b) and without ECMO (c). All models controlled for age, RACHS score, GC, prematurity, and comorbid conditions. The reference groups in the models were: Age 0–30 days, RACHS 1–2, No GC, and no comorbidity. Odds Ratios (OR), 95% Confidence Intervals (CI).

Demographic and Clinical characteristics of Patients Characterized by Genetic Condition or No Genetic Condition

Table 1

Variable	No known Genetic Condition N=80540	Trisomy 21 N=9473	Trisomy 13/18 N=156	22 q11 N=715	Other Genetic Conditions N=4369
Age in months ^a (Median, IQR) Age Groups (n, %)	7 (1, 47)	5 (3, 10)	3.5 (0, 8)	3 (0, 28)	6 (0, 41)
0–1 months	22540 (28)	1011 (11)	58 (37)	319 (45)	1355 (31)
2–12 months	23179 (29)	6437 (68)	65 (42)	172 (20)	1283 (30)
13–60 months	18488 (23)	1243 (13)	20 (13)	90 (13)	884 (20)
5–10 years	7192 (9)	419 (4)	9 (6)	87 (8)	383 (9)
>10 years	8485 (11)	335 (4)	4 (3)	74 (11)	434 (10)
Missing Age	656 (1)	28 (<1)	0	3 (<1)	31 (1)
Male (%) ^a	45816 (57)	4385 (46)	51 (33)	366 (51)	2140 (49)
Race (n, %) ^b					
White	42391 (53)	4977 (53)	81 (52)	373 (52)	2373 (54)
Black	9842 (12)	1139 (12)	24 (15)	86 (12)	460 (11)
Latino	13749 (17)	1774 (19)	23 (15)	133 (19)	850 (20)
Asian	2556 (3)	205 (2)	3 (2)	27 (4)	96 (2)
Other	9252 (12)	1076 (11)	13 (8)	75 (11)	444 (10)
Missing Race	2750 (3)	302 (3)	12 (8)	21 (3)	147 (3)
RACHS-I Categories (n, %) ^a					
RACHS 1	8819 (11)	398 (4)	8 (5)	11 (2)	429 (10)
RACHS 2	27852 (35)	3089 (33)	74 (47)	215 (30)	1623 (37)
RACHS 3	30889 (38)	5771 (61)	61 (39)	288 (40)	1687 (39)
RACHS 4	9227 (12)	187 (2)	11 (7)	188 (26)	477 (11)
RACHS 5	133 (<1)	8 (<1)	0	5 (1)	6 (<1)
RACHS 6	3620 (5)	20 (<1)	2 (1)	8 (1)	148 (3)
ECMO (n, %)	2353 (3)	134 (1)	5 (3)	21 (3)	167 (4)*
ECMO Mortality (n, %)	1092 (1)	66 (<1)	5 (3)	16 (2)*	87 (2)
Non ECMO Mortality (n, %)	1252 (2)	128 (1)	15 (10)*	17 (2)	187 (4)

Variable	No known Genetic Condition N=80540	Trisomy 21 N=9473	Trisomy 13/18 N=156	22 q11 N=715	Other Genetic Conditions N=4369
In Hospital Death (n, %)	2344 (3)	194 (2) *	20 (13) *	33 (5) *	274 (6)

Continuous variables summarized by Median and Interquartile Range: 50th (25th-75th).

Categorical variables summarized by % (n).

^a Statistically significant difference between every group compared to no GC, p<.008

^b Statistically significant difference between T21 and 22q11, compared to no GC, p<.008

* Statistically significant difference compared to no GC, p<.008.

Table 2

Select Demographic and Clinical Features Comparing Pediatric Patients who Received ECMO vs. no ECMO and those who Died Prior to Discharge vs. those who Survived

Variable	Received ECMO N=2680	No ECMO N= 92573	Died Prior to Hospital Discharge N= 2865	Survived to Hospital Discharge N= 92388
<i>Age Groups (n, %)</i>				
Age 0–1 month	1791 (66)	23491 (26)	2052 (72)	23230 (25)
Age 1–12 months	513 (19)	30623 (33)	481 (17)	30655 (33)
Age 2–5 years	229 (9)	20496 (22)	189 (7)	20536 (22)
Age 15–10 years	47 (2)	8013 (9)	47 (2)	9013 (9)
Age 10–18 years	96 (4)	9236 (10)	89 (3)	9243 (10)
Missing Age	7 (<1)	714 (1)	7 (<1)	711 (1)
Male (n, %)	1494 (56)	51263 (55)	1541 (54)	51216 (55)
<i>Race (n, %)</i>				
White	1346 (50)	48848 (53)	1277 (45)	48917 (53)
Black	360 (13)	11191 (12)	373 (13)	11178 (12)
Other	829 (31)	29447 (32)	1040 (36)	29236 (32)
Missing Race	145 (5)	3087 (3)	175 (6)	3057 (3)
<i>Comorbid Conditions and Complications (n, %)</i>				
Prematurity (<35 weeks)	94 (4)	1586 (2)	215 (8)	1465 (2)
Low Birth Weight	222 (8)	2798 (3)	409 (14)	2611 (3)
Interventricular Hemorrhage	244 (9)	974 (1)	263 (9)	955 (1)
Bronchopulmonary Dysplasia	73 (3)	1112 (1)	168 (6)	1017 (1)
Secondary Pulmonary Hypertension	310 (12)	5827 (6)	349 (12)	5788 (6)
Primary Pulmonary Hypertension	46 (2)	560 (1)	42 (2)	564 (1)
Acute Renal Failure	912 (34)	3055 (3)	1105 (39)	2862 (3)
Pulmonary Hemorrhage	108 (4)	194 (<1)	96 (3)	206 (<1)
Stroke	310 (12)	1121 (1)	264 (9)	1167 (1)
Intracranial Hemorrhage	213 (8)	542 (1)	175 (6)	580 (1)
Cardiac Arrest	1427 (53)	10768 (12)	1263 (44)	10932 (12)

All variables are summarized by % (n).

Table 3

Multivariable logistic regression models for odds of ECMO (a) and odds of mortality (b,c).

Variable	Adjusted Odds of ECMO Odds Ratio (95% CI)	Adjusted Odds of Death with ECMO Odds Ratio (95% CI)	Adjusted Odds of Death without ECMO Odds Ratio (95% CI)
Age (1–12mo)	0.41 (0.37–0.46)	0.74 (0.59–0.94)	0.37 (0.32–0.43)
Age (1–5 years)	0.26 (0.22–0.30)	0.63 (0.46–0.89)	0.24 (0.19–0.29)
Age (5–10 years)	0.16 (0.12–0.21)	0.83 (0.42–1.51)	0.17 (0.12–0.32)
Age (10–18 years)	0.26 (0.21–0.32)	0.68 (0.44–1.07)	0.23 (0.17–0.31)
RACHS 3–4	2.70 (2.39–3.04)	1.59 (1.23–2.06)	2.13 (1.84–2.46)
RACHS 5–6	5.51 (4.72–6.44)	2.27 (1.65–3.11)	3.82 (3.13–4.65)
Trisomy 21	0.54 (0.45–0.66)	1.29 (0.88–1.89)	1.13 (0.92–1.39)
Trisomy 13/18 ^c	1.01 (0.40–2.55)	-	6.76 (3.78–12.10)
22q11	0.72 (0.46–1.13)	3.44 (1.21–9.79)	0.91 (0.54–1.54)
Other Genetic Conditions	1.22 (1.03–1.45)	1.42 (1.01–1.99)	2.62 (2.20–3.11)
Prematurity (<35 weeks) ^{b, d}	-	-	1.33 (1.02–1.73)
Low Birth Weight	1.22 (1.04–1.43)	1.83 (1.35–2.50)	1.95 (1.59–2.40)
IVH ^{a, d}	-	-	1.50 (1.18–1.89)
BPD ^d	1.34 (1.03–1.74)	-	3.45 (2.74–4.34)
Secondary Pulmonary Hypertension ^d	2.16 (1.89–2.47)	-	2.21 (1.88–2.61)
Primary Pulmonary Hypertension ^d	2.72 (1.95–3.78)	-	1.93 (1.22–3.05)
Acute Renal Failure ^a	-	3.43 (2.89–4.08)	6.57 (5.80–7.43)
Pulmonary Hemorrhage, ^e	-	2.32 (1.48–3.62)	-
Stroke ^{a, d}	-	-	2.84 (2.12–3.80)
Intracranial Hemorrhage ^{a, d}	-	-	2.24 (1.53–3.28)
Cardiac Arrest ^d	6.48 (5.98–7.03)	-	2.99 (2.67–3.35)

All models controlled for age, RACHS score, GC, prematurity, and comorbid conditions. The reference groups in the models were: Age 0–30 days, RACHS 1–2, No GC, and no comorbidity. 95% Confidence Intervals (CI).

^b Excluded from Odds of ECMO model as it was not independently significant.

^c Model performed without Trisomy 13 and 18 included due of small sample size

^d Excluded from Odds of Death on ECMO model as they were not independently significant.

^e Excluded from Odds of Death without ECMO model as they were not independently significant