The Cardiothoracic Surgeon

RESEARCH

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Are neonatal age and small weight predictive of in-hospital death and prolonged hospital stay in children undergoing heart surgery?

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Abstract

Background: The effect of young age and low weight on outcomes of congenital heart disease surgery is controversial. It is still widely believed both by parents and referring cardiologists that they do have a significant deleterious effect and may prohibit surgical care. This study was intended to determine the independent predictors of in-hospital death and prolonged hospital stay in pediatric patients undergoing cardiac surgery. The effects of age and weight were the focus of analysis. To adjust for heterogeneity and complexity, the Risk Adjustment in Congenital Heart Surgery (RACHS-1) system and other factors were used.

Results: All patients between birth and 18 years of age who underwent cardiac surgery with or without the use of cardiopulmonary bypass from April 1, 2011, to September 30, 2019, were included. Patients undergoing isolated patent ductus ligation were excluded. For the analysis of in-hospital death, a multivariable logistic regression model was used. For the analysis of length of stay, a generalized linear regression model with Poisson distribution and a multivariable logistic regression model were used. The RACHS-1 categories were used to adjust for complexity.
The study included 934 index operations. Neonates (age < 28 days) accounted for 11% of the operations. After adjusting for complexity and other operative variables, we found that age and weight were not significant predictors of in-hospital death or prolonged hospital stay. RACHS category and cardio-pulmonary bypass time were, however, significant predictors of in-hospital mortality, p value 0.009, and 0.002, respectively. The complexity of the operation was also predictive of prolonged hospital stay.

Conclusion: Age and weight are not significant predictors of in-hospital death or prolonged hospital stay. Except for severe prematurity and prohibitive genetic or metabolic disease, patients with CHD should get appropriate and expeditious surgical care regardless of age and weight.

Keywords: Age, Bodyweight, Congenital cardiac surgery

Background

The outcomes of surgery for congenital heart disease (CHD) have markedly improved in the last 20 years [1, 2]. It is difficult to pinpoint a singular event or strategy that lead to this improvement. However, it is widely believed that improvements in surgical strategy, timing, and techniques, as well as postoperative care, additively led to this improvement. It is also still widely believed that neonates and very young infants, as well as low weight for age children, have worse outcomes [3]. This belief leads to delaying corrective or palliative surgical care in many children who are born with low weight or who fail to grow to satisfy arbitrary age or weight limits [4, 5]. In this study, we sought to investigate whether age or weight was independent predictors of surgical outcomes in a wide array of surgical procedures for CHD.

Methods

All children from age 0 to18 years who underwent surgery for CHD at our pediatric cardiac center between

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April 1, 2011, and September 30, 2019, were included. Only the first operation of the index admission was included. Patients who underwent isolated patent ductus ligation were excluded, as the length of stay and mortality in those patients were dependent on other factors not related to the cardiac pathology. We have also excluded patients with significant prematurity (< 28 weeks of gestation) and extreme small weight. Those patients may indeed be at higher risk due to technical and technological limitations of the current state of surgical and technological methods and tools.

The data was harvested from our prospective electronic database. The primary outcome of interest was operative mortality defined as death in the index admission at any time. The secondary outcomes were prolonged hospital stay more than 14 days and length of stay in hospital. Age and weight at the time of operation were the main predictors of interest. Other variables included to account for heterogeneity were gender, preoperative hospital stay, redo operation, cardiopulmonary bypass (CPB) time, aortic cross-clamp time, deep hypothermic circulatory arrest (DHCA) time, and the Risk Adjustment in Congenital Cardiac Surgery (RACHS) classification, version 1 [6]. Prematurity, birth weight, and the presence of extra-cardiac or chromosomal anomalies were not included as these variables were not reliably recorded in the prospective database. In patients who underwent surgery without CPB, CPB time was recorded as zero. Similarly, if the patient did not require aortic clamping or DHCA, the respective time variable was recorded as zero.

The surgical methods may vary as two surgeons contributed to the data; however, 98% of the operations were performed by a single surgeon (the author). In general, patients who required CPB were placed on bypass by aortic and bicaval or atrial cannulation as needed. Before June 2015, cold intermittent antegrade blood cardioplegia was used, and cold antegrade DelNido cardioplegia was used thereafter [7]. If DHCA was needed, it was established at 18°. Antegrade cerebral perfusion was applied at 30 ml/kg/min. Delayed sternal closure was used as needed.

All patients after September 2016 were cared for in a dedicated pediatric cardiac intensive care unit. Before that date, patients were cared for in a general pediatric intensive care unit.

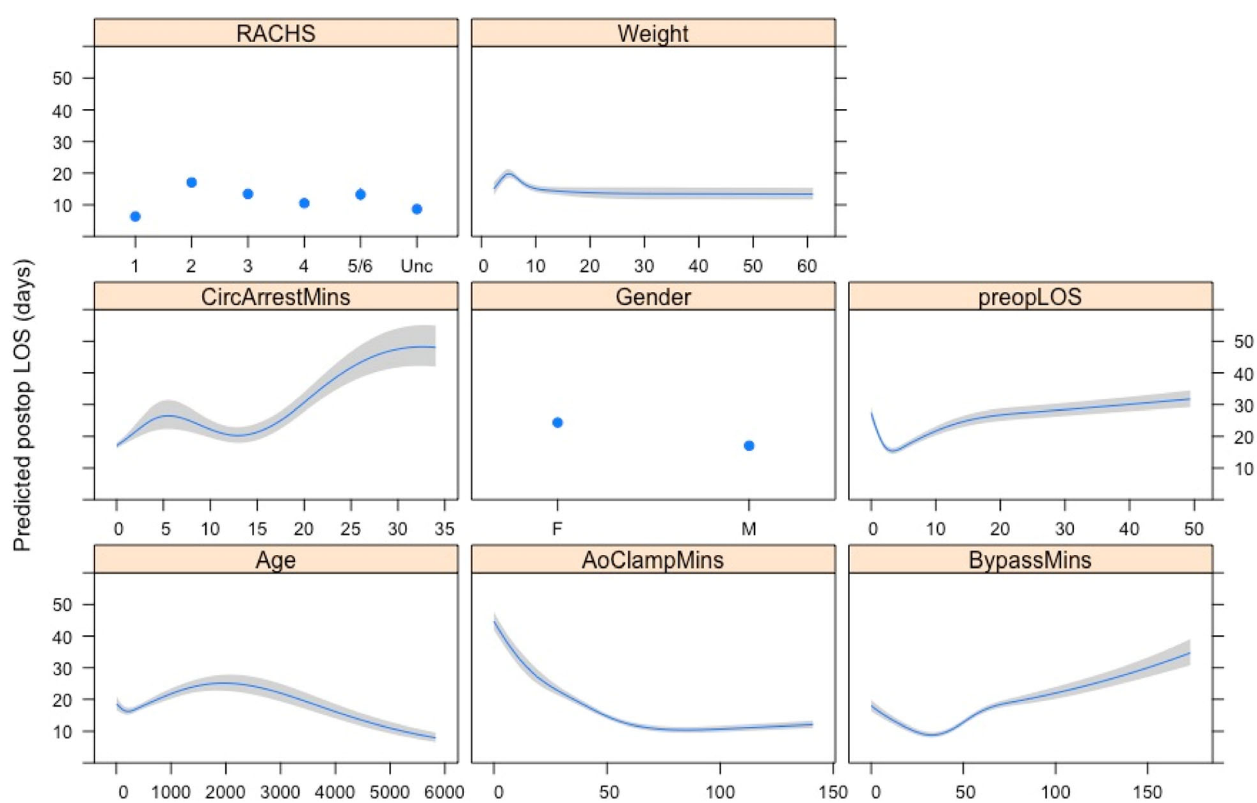

Fig. 1 Graphical description of the relationship between postoperative length of stay in days (*y*-axis) and age at operation in days, aortic clamp time in minutes (AoClampMins), CPB time in minutes (BypassMins), DHCA time in minutes (CircArrestMins), gender, preoperative length of stay in days (preopLOS), RACHS category, and weight in kg as predicted by a generalized linear model with Poisson distribution and 95% confidence bands for continuous variables

Statistical analysis

The data which was imported from the prospective electronic database into the R statistical system with the following packages was used for analysis: rms, Hmisc, and survival [8–11]. Categorical variables were described as frequency and percent. Continuous variables were described as median and upper and lower quartiles. For descriptive purposes, the data was divided into neonates, defined as age less than 28 days, and post-neonatal children age 29 days to 18 years. For statistical modeling, age was used as a continuous variable and the neonatal status was included as a separate variable as appropriate. The normality and linearity of continuous variables were tested, and the appropriate transformation was used. A restricted cubic spline function was used where non-linear association was identified. For the primary outcome of in-hospital mortality, logistic linear regression was used. For the postoperative length of stay, the analysis was restricted to survivors and a generalized linear regression model with Poisson distribution was used due to the skewed nature of the length of stay (Fig. 1). This model was used to graphically study the association between length of stay and the predictive variables. For ease of interpretation and clinical relevance, prolonged hospital stay was defined as a total postoperative length of stay of greater than 14 days. A logistic regression model was used to study factors associated with a prolonged hospital stay. A p value of 0.05 was accepted as significant.

The study was approved by the local Hospital board of research ethics.

Table 1 Descriptive statistics (N = 934)

	N	Neonate *N* = 103 *a*, *b*, *c*	Post neonate *N* = 831 *a*, *b*, *c*	Combined *N* = 934 *a*, *b*, *c*	*p* value
Age, days	934	8.00, 15.00, 20.50	202.50, 459.00, 1728.50	137.00, 372.00, 1535.75	< 0.001[1]
Gender	934				0.48[2]
F		40% (41)	43% (361)	43% (402)	
M		60% (62)	57% (470)	57% (532)	
Weight, kg	934	2.70, 3.00, 3.50	5.10, 8.30, 14.00	4.30, 7.35, 13.00	< 0.001[1]
Height	885	46.5, 49.0, 52.0	61.0, 74.0, 100.0	58.0, 70.0, 97.0	< 0.001[1]
Body surface area, m^2	887	0.19, 0.20, 0.21	0.29, 0.41, 0.62	0.26, 0.38, 0.60	< 0.001[1]
Type	934				< 0.001[2]
Primary		100% (103)	87% (720)	88% (823)	
Reoperation		0% (0)	13% (111)	12% (111)	
RACHS	934				< 0.001[2]
1		0% (0)	5% (40)	4% (40)	
2		21% (22)	52% (433)	49% (455)	
3		26% (27)	27% (224)	27% (251)	
4		17% (17)	7% (59)	8% (76)	
5/6		11% (11)	3% (22)	4% (33)	
Uncategorized		25% (26)	6% (53)	8% (79)	
CPB time, min	934	51, 77, 94	46 63 86	46 64 87	0.021[1]
Clamp time, min	934	24.5, 49.0, 64.0	23.0, 43.0, 63.0	23.0, 44.0, 63.0	0.42[1]
DHCA time, min	934	0.0, 0.0, 11.5	0.0, 0.0, 0.0	0.0, 0.0, 0.0	< 0.001[1]
Length of stay, days	934	15.5, 22.0, 37.0	9.0, 15.0, 25.0	9.0, 15.0, 26.0	< 0.001[1]
Preop LOS, days	918	2 5 9	1 2 5	1 2 6	< 0.001[1]
Postop LOS, days	918	10.0, 16.5, 29.0	7.0, 11.0, 19.0	7.0, 11.0, 20.0	< 0.001[1]
Result	934				0.14[2]
Death		9% (9)	5% (40)	5% (49)	
Discharged		88% (91)	94% (778)	93% (869)	
Still in hospital		3% (3)	2% (13)	2% (16)	

a b c represent the lower quartile *a*, the median *b*, and the upper quartile *c* for continuous variables. *N* is the number of non-missing values. Numbers after proportions are frequencies

Tests used: [1]Wilcoxon test, [2]Pearson test

Results

There were 934 index operations included in the analysis. Neonates accounted for 11% (103) of the patients. Some patients contributed more than one operation to the data. The youngest patient in the analysis was zero days old. The smallest patient requiring surgery with the use of CPB was 1.25 kg. Table 1 shows the detailed descriptive statistics of the study patients. The operative RACHS category distribution was different for neonates compared to post-neonates, while in neonates 11% underwent category 5/6 operation and 17% category 4 operations, compared to 3% and 7% in post-neonates, respectively. Neonates also had a higher percentage of uncategorized operations, 25% versus 6% in post-neonates. The primary outcome of in-hospital death occurred in 9% (9) neonates and 5% (40) post-neonatal children; this difference did not reach statistical significance in unadjusted univariable testing, p value = 0.14. The median postoperative length of stay was 16.5 days for neonates, and 11 days for post-neonatal children, in unadjusted univariable testing the p value was < 0.001.

Adjusting for gender, preoperative length of stay CPB time, aortic clamp time, DHCA time, reoperation, and RACHS category, age, weight, and neonatal status were not found to be independent predictors of in-hospital death or prolonged hospital stay (> 14 days). In fact, only RACHS category and CPB time were the statistically significant predictors of in-hospital mortality, p value 0.0085 and 0.0023, respectively (Table 2). On the other hand, preoperative length of stay, CPB time, aortic clamp time, DHCA time, and RACHS category were independent significant predictors of prolonged hospital stay, p values shown in Table 3.

Table 2 Wald statistics of logistic regression, outcome: in-hospital death

Factor	Chi-square	d.f.	*p*
Age	0.06	1	0.8
Neonate	0.06	1	0.8
Gender	0.00	1	0.9
Weight	0.23	1	0.6
Preoperative LOS	0.08	1	0.8
Reoperation	2.39	1	0.122
Bypass time (min)	9.27	1	*0.0023*
Aortic clamp time (min)	0.84	1	0.3580
DHCA time (min)	0.25	1	0.6
RACHS	15.47	5	*0.0085*

d.f. degrees of freedom, *LOS* length of stay, *DHCA* deep hypothermic circulatory arrest, *RACHS* Risk Adjustment in Congenital Heart Surgery

Discussion

The common practice of corrective surgery for major congenital heart disease lesions during neonatal and young infant life has been established since 1990; however, still many patients are denied care or significantly delayed due to the dogma that the risk of surgery is too high due to the young age or small weight. We have shown that in crude terms, it may appear that neonates have higher in-hospital mortality and prolonged length of stay, in fact with analysis adjusted for the complexity of the operation that does not bare truth. In addition to adjusting for complexity by the RACHS category, we believe that CPB time and DHCA time are also a surrogate for complexity. CPB time may also be a surrogate for operative difficulties or complications.

The limitations of this study include a lack of reliable data about extra-cardiac comorbidity, prematurity, and chromosomal or genetic anomalies. Therefore, it is difficult to assertively comment on the effect of these variables. However, it is more than likely that an important contribution does exist for these and other variables [12]. It is also difficult to account for the urgency of the operation. We included a variable for the preoperative length of stay in hopes of at least partially accounting for some of these effects. We found that the patients with the shortest postoperative length of stay were those who did not have very short or very long preoperative stay. We hypothesize that patient with preoperative length of stay less than 1 day may be a surrogate for urgency and that prolonged preoperative length of stay may be a surrogate for comorbidity requiring medical treatment in preparation for surgery.

We were unable to comment on patients with significant prematurity and extreme small weight as well as patients who underwent patent ductus ligation, as they

Table 3 Wald statistics of logistic regression, outcome: postoperative LOS > 14 days in survivors

Factor	Chi-square	d.f.	*p*
Age	6.42	4	0.17
Nonlinear	1.36	3	0.7
Neonate	0.13	1	0.7
Gender	0.17	1	0.7
Weight	0.31	1	0.6
Preoperative LOS	23.55	1	< 0.0001
Reoperation	0.2	1	0.7
Bypass time (min)	13.87	1	0.0002
Aortic clamp time (min)	14.85	4	0.005
Nonlinear	12.57	3	0.006
DHCA time (min)	10.23	1	0.0014
RACHS	16.17	5	0.006

d.f. degrees of freedom, *LOS* length of stay, *DHCA* deep hypothermic circulatory arrest, *RACHS* Risk Adjustment in Congenital Heart Surgery were not included in this analysis, as stated in the methods.

Conclusions

We did not find age or weight to be independent predictors of in-hospital death or prolonged hospital stay. Except for severe prematurity and prohibitive genetic or metabolic disease, patients with CHD should get appropriate and expeditious surgical care regardless of age and weight.

Abbreviations

CHD: Congenital Heart Disease; CPB: Cardiopulmonary bypass; DHCA: Deep hypothermic circulatory arrest; RACHS-1: Risk Adjustment in Congenital Heart Surgery, edition 1

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Authors' contributions

OOA conducted the literature search; designed the study; was responsible for the data collection and analysis and interpretation of data; conducted the statistical analysis; and drafted the manuscript. The author read and approved the final manuscript.

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Availability of data and materials

Data are available from the author upon request.

Ethics approval and consent to participate

The study was approved by the local institutional review board (IRB), at King Abdulaziz University/and the patients' consent was waived for this retrospective observational study.

Consent for publication

Not applicable

Competing interests

The author declares that he has no competing interests.

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