Cardiology in the Young

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Risk factors for long post-operative hospital stays after cardiopulmonary bypass surgery in full-term neonates

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Abstract

Background: Long hospital stays for neonates following cardiac surgery can be detrimental to short- and long-term outcomes. Furthermore, it can impact resource allocation within heart centres' daily operations. We aimed to explore multiple clinical variables and complications that can influence and predict the post-operative hospital length of stay. *Methods:* We conducted a retrospective observational review of the full-term neonates (<30 days old) who had cardiac surgery in a tertiary paediatric cardiac surgery centre – assessment of multiple clinical variables and their association with post-operative hospital length of stay. *Results:* A total of 273 neonates were screened with a mortality rate of 8%. The survivors (number = 251) were analysed; 83% had at least one complication. The median post-operative hospital length of stay was 19.5 days (interquartile range 10.5, 31.6 days). The median post-operative hospital length of stay was significantly different among patients with complications (21.5 days, 10.5, 34.6 days) versus the no-complication group (14 days, 9.6, 19.5 days), $p < 0.01$. Among the non-modifiable variables, gastrostomy, tracheostomy, syndromes, and single ventricle physiology are significantly associated with longer post-operative hospital length of stay. Among the modifiable variables, deep vein thrombosis and cardiac arrest were associated with extended post-operative hospital length of stay. *Conclusions:* Complications following cardiac surgery can be associated with longer hospital stay. Some complications are modifiable. Deep vein thrombosis and cardiac arrest are among the complications that were associated with longer hospital stay and offer a direct opportunity for prevention which may be reflected in better outcomes and shorter hospital stay.

Over the past decade, advances in congenital heart surgery and perioperative care have significantly improved neonatal survival rates.[1] However, morbidity and prolonged hospital stays persist.[2,3] Long-term mortality, reoperation rates, and low quality of life remain important frontiers that have only been explored to a limited extent.[4,5] Patients with long hospital stays after cardiac surgery have had inferior long-term outcomes – especially patients with single ventricle palliation.[6] A better understanding of clinical factors that affect the post-operative hospital length of stay is critical. Complication profiles after congenital heart surgery are highly variable among centres as demonstrated from the following administrative databases: Kids' Inpatient Database administrative database and Pediatric Hospital Inpatient Sample (administrative databases) and registries: Pediatric Cardiac Critical Care Consortium (intensive care registry) and Society of Thoracic Surgeons (surgical registry).[7–16] Through collaboration and shared knowledge of positive deviance centres, some of these complication rates can be lowered. Lower complication rates will lead to shorter post-operative hospital length of stay, improved short-term survival rates, and potentially improved long-term survival with a higher quality-of-life indicators.[17]

In order to improve hospital length of stay, studies must address it as a primary outcome. Mortality and hospital length of stay share common risk factors and can impact each other. However, the drivers of mortality and length of stay have been demonstrated to diverge in some circumstances. In an analysis of the Pediatric Cardiac Critical Care Consortium database, Dewitt reports that only four covariates are associated with both prolonged critical illness and mortality after cardiac surgery.[2] In addition, Tweddell demonstrated that hospital-acquired infections were associated with nearly a five-fold increase in median length of stay without any difference in mortality.[16] Interestingly, Alten et al reported mortality and length of stay to be associated with hospital-acquired infections.

With the goal of better understanding the effects of complications and length of stay, we reviewed our centre's experience over seven years. We hypothesised that complications are

independently associated with longer hospital stay among survivors to discharge. We were especially interested in modifiable or acquired factors and complications.

Materials and methods

Study population

This study was reviewed and approved by the University of Alabama at Birmingham's Institutional Review Board. Informed consent was waived. A retrospective review of our databases (Pediatric Cardiac Critical Care Consortium, Society of Thoracic Surgeons, and internal cardiac ICU database) was performed on 1613 patients who underwent cardiac surgery with cardiopulmonary bypass over seven years (October 2012–June 2019). Patients older than 30 days (number = 1292) at the time of surgery were excluded. Patients with a gestational age of less than 37 weeks (number = 48) were excluded. Of the remaining patients, 273 patients were full-term and thirty days or younger at the time of surgery. Twenty-two patients (8%) did not survive to hospital discharge and were excluded from our study (Fig 1). Details regarding patient management, data collection, and definitions of terms are reported in supplemental sections.

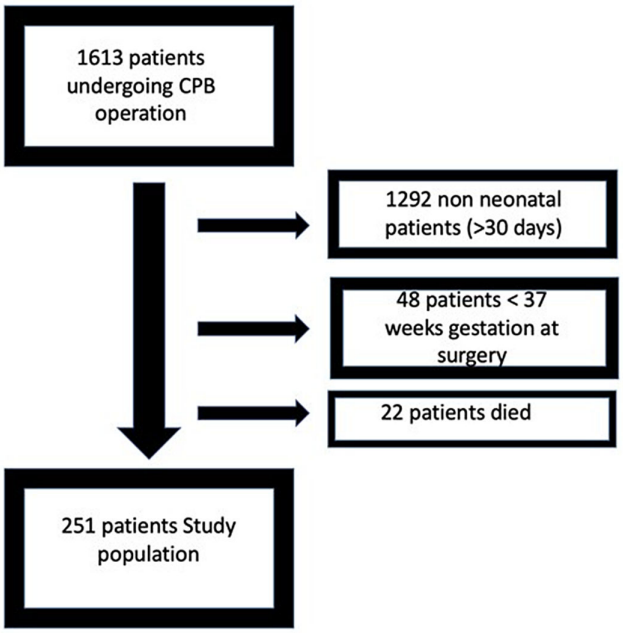

Figure 1. Total patients who were screened for inclusions in our study. Description of the excluded patients is provided.

Statistical analysis

Descriptive analyses were performed. Data are presented as median with interquartile range, mean with standard deviation, and frequency distribution as appropriate. Chi-square, Fisher's exact, Mann–Whitney U-test, Student's t-test, or Kruskal–Wallis test were used as appropriate for initial univariate analyses. Logistic regression was performed to assess risk factors associated with prolonged post-operative hospital length of stay. Generalised linear models were employed to evaluate the risk factors related to the post-operative hospital length of stay. To quantify the risk factors associated with post-operative hospital length of stay, relative risks with their 95% confidence intervals were used. Furthermore, we investigated post-operative hospital length of stay as a dichotomised outcome by dividing our cohort into two groups based on their length of stay. Patients with post-operative hospital length of stay >75th percentile were called prolonged post-operative hospital length of stay. Univariate and multivariate analyses were performed to evaluate associations of selected variables with the prolonged post-operative hospital length of stay. Variable selection was performed by a stepwise initial variable selection carried out with the subject's baseline. Other relevant clinical characteristics and variables with p-value less than or equal to 0.15 were included in the final multivariate models. All hypothesis tests were two-tailed, and a p-value <0.05 was used to indicate statistical significance. All analyses were performed in SAS for windows version 9.4 (Cary, North Carolina).

Results

Overall, 251 patients were included in the study. Demographic data are summarised in Table 1. In our cohort, the median post-operative hospital length of stay was 19.45 days (10.46, 31.58). Patients with complications had significantly longer hospital stay compared to patients in the no-complication group (21.3 days interquartile range: 10.5, 31.6 versus 14.0 days interquartile range 9.6, 19.5 with $p < 0.01$). Descriptive analysis of the cohort's post-operative hospital length of stay is detailed in Supplemental Table S1. The univariate analysis of post-operative hospital length of stay as a continuous outcome is detailed in Table 2.

Table 3 describes the results of the multivariate analysis. Neonates with genetic syndromes had 70% longer post-operative hospital length of stay. Tracheostomy placement was associated with a three-fold increase in post-operative hospital length of stay. Cardiac arrest, single ventricle physiology, gastrostomy tube placement, and deep vein thrombosis were independently associated with an approximately 50% increase in the post-operative hospital length of stay. When the interaction effect of cardiac arrest and single ventricle physiology was explored, patients with cardiac arrest and single ventricle physiology compared to patients with biventricular physiology without cardiac arrest had a two-fold increase in post-operative hospital length of stay (relative risk 2.06, confidence interval 1.43, 2.97, $p < 0.01$). Other complications were not associated with longer post-operative hospital length of stay. On univariate analyses, an elevated vasoactive inotropic score on POD 3 and later was associated with complications, and an elevated vasoactive inotropic score by POD 1 or later was associated with longer post-operative length of stay. All tracheostomy tube placements were done post-operatively with median post-operative day of placement to be 34 (19,99). Two patients had airway anomalies diagnosed before surgery and had tracheostomy prior to a trial of extubation. Two patients had airway problems after surgery needing ENT procedures and ultimately tracheostomy tube placement, and three patients had tracheostomy placement after multiple failed extubations.

Supplemental Tables S2 & S3 show the univariate and multivariate analysis of the association of several variables and complications with the outcome of prolonged post-operative hospital length of stay as defined by length of stay >75th percentile. Of note, as we clustered all infections in one variable, patients with the incidence of any infection were four times more likely to have prolonged post-operative length of stay (Table S3).

The timing of our complications in relation to the time of surgery is described in detail in Supplemental Tables S4 & S5 and

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Table 1. Patients' characteristics, comparing patients with complications versus patients without complications excluding patients with mortality

Characteristics	Complications (n = 208)	No complications (n = 43)	p-value
Age at surgery (days)	7 (5, 11)	8 (6, 13)	0.13
Weight at surgery (kg)	3.16 ± 0.49	3.08 ± 0.58	0.36
Syndrome, n (%)	25 (12)	0 (0.0)	0.01
CPB (minutes)	111.0 (87.5, 140.5)	98.5 (74.0, 127.5)	0.09
ACC (minutes)	59.0 (34.0, 75.0)	51.5 (32.5, 77.0)	0.81
High complexity surgery*, n (%)	154 (75.0)	24 (56.0)	0.01
Single ventricle, n (%)	76 (37.0)	5 (12.0)	<0.01
Mechanical ventilation duration (days)	12.4 (9.0, 19.4)	2.7 (1.6, 4.5)	<0.01
Pre-operative hospital LOS	5(3,8)	5(2,7)	0.4
PHLOS (days)	21.5(10.5, 34.6)	14 (9.6, 19.5)	<0.01
VIS Day 0	0 (0, 5)	0 (0, 3)	0.45
VIS Day 1	4.8 (0, 9.7)	3 (0, 6.7)	0.11
VIS Day 2	1.8 (0, 6.0)	0 (0, 2)	0.03
VIS Day 3	0 (0, 3.0)	0 (0, 1)	0.05
VIS Day 4	0 (0, 1)	0 (0, 0)	0.03
VIS Day 5	0 (0, 0)	0 (0, 0)	0.04

Data presented as means ± standard deviation or medians (interquartile range)
Comp: patients with any complication. No comp: patients without any complications.
*High complexity surgery – STAT (Society of Thoracic Surgeons-European Association for Cardiothoracic Surgery) 4 and 5
CPB: cardiopulmonary bypass; ACC: aortic cross-clamp; PHLOS: post-operative hospital length of stay; VIS: vasoactive inotropes score

illustrated in Figure 2. Comments on these tables are provided in the supplemental sections.

Discussion

Neonates with congenital heart surgery have had higher survival rates over the past decade.[18,19] However, progress in reducing the length of hospital stay remains a challenge. Across centres and studies, 5–10% of patients experience a prolonged hospital stay following cardiac surgery.[20,21] Our analysis shows that among survivors, the following factors/complications were independently associated with longer post-operative hospital length of stay: single ventricle physiology, genetic syndrome, tracheostomy, cardiac arrest, gastrostomy tube placement (a surrogate for feeding difficulty), and deep vein thrombosis. These are important findings as some represent modifiable or preventable factors that could be amenable to quality improvement interventions. Similar to previous reports, our neonates with single ventricle physiology are among the group of neonates who have a prolonged hospital stay.[3,7] In fact, single ventricle physiology and cardiac arrest revealed a significant interaction where cardiac arrest had a more substantial impact on post-operative hospital length of stay. However, even in single ventricle patients, we observed a hospital course without complications was associated with a shorter stay. This is of great importance as shorter hospital stays have been associated with better neurodevelopmental outcomes and quality of life.[6]

Multiple studies have reported the association of pre-operative factors and, more broadly, non-modifiable risk factors that affect post-operative hospital length of stay. Mori described neonates with a hospital stay longer than 30 days following cardiac surgery. Genetic syndromes and extracardiac malformations formed a significant portion of the studied cohort; however, these comorbidities did not impact mortality. Of note, these patients encountered a high rate of post-operative complications.[5] Similarly, Dewitt reported extracardiac abnormalities, prematurity, and surgical complexity were associated with prolonged length of stay.[2] Even after our multivariate analysis, being diagnosed with a syndrome was associated with a longer hospital stay.

In addition, similar to previous reports the vasoactive inotropes score was a relevant marker for an increased hospital length of stay early in the post-operative course.[22] Persistence of higher vasoactive inotropes score at POD 3 was independently associated with prolonged post-operative hospital length of stay. Whether this association reflects a poor response to cardiopulmonary bypass increased surgical complexity inadequately described by Society of Thoracic Surgeons-European Association for Cardiothoracic Surgery categories, repeated cardiopulmonary bypass runs or residual lesions and would be better explored in a multicenter, prospective manner. These findings could lead a congenital cardiac team to investigate residual lesions earlier and counsel the family concerning abnormal convalescence and prolonged stay.

Conversely, a growing body of data demonstrates multiple modifiable risk factors – largely complications – that are associated with prolonged hospitalisation in neonates. In a study reviewing the length of hospital stay across centres participating in the national paediatric cardiology quality improvement collaborative, Baker-Smith and colleagues reported that patients with single ventricle physiology after the Norwood procedure are prone to prolonged hospital length of stay if complicated by a central line infection or failed extubation.[3] Dewitt et al reported delay in enteral feeds, chylothorax/pleural effusion, deep surgical site

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Table 2. Univariate analysis of the association of potential risk factors with post-operative hospital length of stay

Risk factor	Relative risk	95% confidence interval	p-value
Syndrome	1.76	(1.15, 2.68)	<0.01
Tracheostomy	4.87	(3.66, 6.49)	<0.01
Gastrostomy tube	1.78	(1.39, 2.28)	<0.01
Single ventricle	1.88	(1.49, 2.38)	<0.01
Deep vein thrombosis	2.17	(1.52, 3.11)	<0.01
Cardiac arrest	2.13	(1.61, 2.81)	<0.01
CPB (for 10 minutes increase)	1.01	(0.99, 1.03)	0.32
Age	1.01	(0.99, 1.03)	0.17
ACC	1.00	(0.99, 1.01)	0.43
Weight	0.74	(0.60, 0.92)	<0.01
High complexity surgery	1.55	(1.11, 2.15)	<0.01
Failed extubation	1.56	(1.22, 2.00)	<0.01
ECMO	1.76	(1.30, 2.38)	<0.01
Catheterisation lab	2.08	(1.54, 2.81)	<0.01
Acute kidney injury	1.28	(0.97, 1.69)	0.09
Vocal cord paralysis	0.77	(0.55, 1.07)	0.12
CLABSI	1.65	(1.14, 2.40)	<0.01
Arrhythmia	1.34	(1.02, 1.78)	0.04
VIS Day 0	1.002	(0.98, 1.03)	0.88
VIS Day 1	1.05	(1.02, 1.08)	<0.01
VIS Day 2	1.05	(1.04, 1.07)	<0.01
VIS Day 3	1.09	(1.06, 1.11)	<0.01
VIS Day 4	1.08	(1.06, 1.10)	<0.01
VIS Day 5	1.06	(1.04, 1.07)	<0.01

Note: in this univariate analysis, one predictor at a time was analysed in the model with PHLOS being the outcome.
Covariates with p-value <0.15 were initially considered for variable selection method for multivariable analysis of the outcome post-operative length of stay.
High complexity surgery – STAT (Society of Thoracic Surgeons-European Association for Cardiothoracic Surgery) 4 and 5; CPB: cardiopulmonary bypass; ACC: aortic cross-clamp; ECMO: extracorporeal membrane oxygenation; CLABSI: central line-associated bloodstream infection; VIS: vasoactive inotropes score

Table 3. Multivariable analysis of the risk factor associated with post-operative length of stay as a continuous variable

Risk factor (Yes versus No)	Relative risk	95% confidence interval	p-value
Unmodifiable			
Genetic syndrome	1.64	1.16, 2.32	<0.01
Tracheostomy	3.01	2.20, 4.14	<0.01
Gastrostomy tube	1.35	1.11, 1.65	<0.01
Single ventricle	1.48	1.25, 1.76	<0.01
High complexity surgery	1.27	1.04, 1.54	0.02
Weight	0.82	0.71, 0.95	<0.01
Vocal cord paralysis	0.86	0.68, 1.07	0.17
POD 3 VIS	1.0399	1.02, 1.06	<0.01
Modifiable			
Deep vein thrombosis	1.46	1.09, 1.95	0.01
Cardiac arrest	1.39	1.01, 1.90	0.04
Failed extubation	1.10	0.91, 1.34	0.31
Catheterisation study	1.29	0.98, 1.69	0.07
Interaction			
Cardiac arrest and single ventricle	2.06	1.43, 2.97	<0.01

Note: All covariates from the univariate analysis (Table 3 with $p < 0.15$) were considered in the initial multivariable models. Final mode includes all covariates with a p-value <0.15 through a variable selection method. Generalised linear models (negative-binomial regression) were employed to evaluate the risk factors related to the hospital length of stay with 95% confidence intervals.
High complexity surgery – STAT (Society of Thoracic Surgeons-European Association for Cardiothoracic Surgery) 4 and 5; ACC: aortic cross-clamp; VIS: vasoactive inotropes score

infections, and infections, in general, were associated with prolonged critical care stay for neonates with heart surgery.[2] Within our dataset, upon multivariate analysis, deep vein thrombosis and cardiac arrest were morbidities independently associated with longer post-operative hospital stay and potentially preventable.

The association of deep vein thrombosis and length of stay has been highlighted recently; however, patients that remain critically ill with central venous catheters in place are more likely to acquire a deep vein thrombosis as opposed to a deep vein thrombosis causing prolonged hospital stay.[23] The multiple outpatient regimens available to treat deep vein thromboses would support this reasoning. This is the first time that cardiac arrest has been demonstrated to predict prolonged hospital length of stay among survivors from neonatal congenital heart surgery to our knowledge. We propose after cardiac arrests, additional end organ injuries occur along with escalations of support that prolong the length of stay in a way where the patient is not able to return to their original trajectory. Future studies verifying our findings regarding cardiac arrest and focusing on mitigating strategies are warranted.

Placement of a tracheostomy and/or gastrostomy tube is not always modifiable and preventable. Congenital airway anomalies, severe tracheomalacia, and oesophageal anomalies are expected to require these interventions and are not preventable. But, other indications may be preventable and amenable to quality improvement interventions. Upper airway obstruction as indication for tracheostomy represents potential targets for quality improvement interventions.

Timing of complications can be important when designing quality improvement interventions. The majority of early complications identified in our data analysis did not impact the post-operative hospital length of stay, with the exception of the cardiac arrest. Similar to the national paediatric cardiology quality improvement collaborative report, failed extubation and central line-associated bloodstream infection were encountered in our cohort and were more likely to occur 2–4 weeks after surgery.[3] However, both complications were not predictive of longer hospital stay. Among the complications that occurred late in the hospitalisation course, gastrostomy tube placement, deep vein thrombosis incidence, and tracheostomy tube placement were associated with significantly longer hospital of stay.

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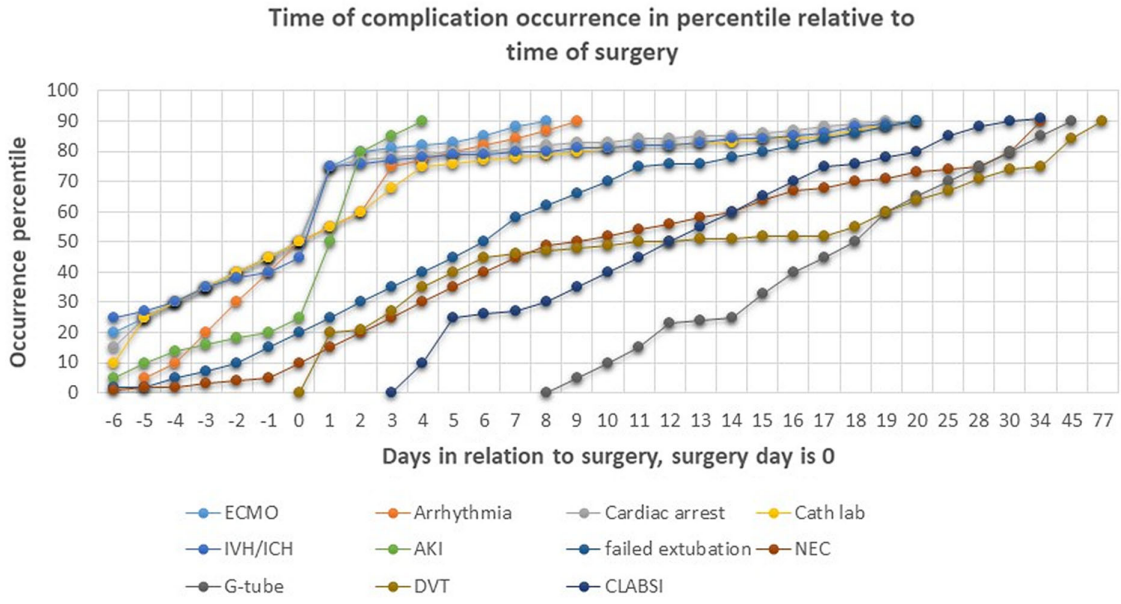

Figure 2. X-axis represents the length of stay in days. Day of surgery is 0, and negative numbers indicate pre-operative period. Y-axis represents the occurrence percentile. ECMO: extracorporeal membrane oxygenation; IVH: interventricular haemorrhage; ICH: intercranial haemorrhage; CLABSI: central line-associated bloodstream infection.

Our study is limited by its single-centre and retrospective nature. We did not have statistical power to show more rare complications associated with length of stay that was rare in our centre during the study period. Even with our system of data collection, it is also possible that some complications were not recorded and could have affected our analysis. We were not able to explore the important impact of surgical residual lesions following surgery and their impact on the hospital length of stay, although we reported the need for catheterisation study incidence and association with the hospital length of stay. Other measures or therapeutic and preventative modalities that could have prevented some of the complications were not accounted for in our analysis, such as inhaled nitric oxide or heparin. In the case of gastrostomy tubes, we did not collect the indication, hence limiting our ability to assess the fraction of modifiable indications associated with gastrostomy tube placement. The reoccurrence of any complication was not accounted for in our analysis, which could have impacted the incidence of other events.

A good understanding of the factors that can impact the hospital's length of stay can provide quality improvement opportunities.[24,25] Several factors can be modified, and other complications can be prevented, which may be reflected in a shorter hospital stay and improved outcomes. Deep vein thrombosis and cardiac arrest are among the complications that offer a direct opportunity for prevention. Other factors like single ventricle physiology or syndromes are not modifiable; however, knowing that patients with these two variables can have a longer hospital stay if they encounter specific complications can help resource allocation in a busy surgical congenital heart centre.

Supplementary material. To view supplementary material for this article, please visit https://doi.org/10.1017/S1047951123000379

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Conflict of interest. None.

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