Title: Risk Factors for Extubation Failure following Neonatal Cardiac Surgery

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Abstract

Objective: Extubation failure after neonatal cardiac surgery has been associated with considerable postoperative morbidity, though data identifying risk factors for its occurrence are sparse. We aimed to determine risk factors for extubation failure in our neonatal cardiac surgical population.

Design: Retrospective chart review

Setting: Urban tertiary care free-standing children's hospital

Patients: Neonates (0-30 days of age) who underwent cardiac surgery at our institution between 1/2009-12/2012 was performed.

Interventions: Extubation failure was defined as re-intubation within 72 hours after extubation from mechanical ventilation. Multivariate logistic regression analysis was performed to determine independent risk factors for extubation failure.

Measurements & Main Results: We included 120 neonates, of which 21 (17.5%) experienced extubation failure. On univariate analysis, patients who failed extubation were more likely to have genetic abnormalities [24% versus 6%, *P*=0.023], hypoplastic left heart [43% versus 17%, *P*=0.009], delayed sternal closure [38% versus 12%, *P*=0.004], postoperative infection prior to extubation [38% versus 11%, *P*=0.002], and longer duration of mechanical ventilation [median 142 hours versus 58 hours, *P*=0.009]. On multivariate analysis, genetic abnormalities, hypoplastic left heart and postoperative infection remained independently associated with extubation failure. Moreover, patients with infection who failed extubation tended to receive fewer days of antibiotics prior to their first extubation attempt as compared to patients with infection who did not fail extubation [4.9±2.6 versus 7.3±3, *P*=0.073].

Conclusions: Neonates with underlying genetic abnormalities, hypoplastic left heart, or postoperative infection were at increased risk for extubation failure. A more conservative approach in these patients, including longer pre-extubation duration of antibiotic therapy for postoperative infections, may be warranted.

Introduction

Improvements in surgical techniques and perioperative management have made early extubation from mechanical ventilation (e.g. in the operating suite or shortly after arrival to the intensive care unit) relatively common in pediatric cardiac surgery [1-3]. Many children however, particularly neonates, continue to require mechanical ventilator support for several days or even weeks postoperatively [4-5]. The determination of readiness for extubation from mechanical ventilation in critically-ill infants and children in general continues to be challenging for pediatric intensive care providers [6]. In the adult population, measures of pulmonary function and weaning indices have been developed and standardized to increase the likelihood of extubation success, but the results from applying similar weaning indices in pediatric patients have been inconsistent [7-8] and have not been readily implemented by current pediatric critical care physicians [9].

Extubation outcomes of infants and children following cardiac surgery can be especially unpredictable, given the complex interplay between the recovering respiratory and cardiovascular systems that is often present. Extubation failure is often tumultuous in these patients, and can be associated with considerable postoperative morbidity and prolonged length of stay in the intensive care unit, especially in neonates [10]. To date, existing literature that has reported risk factors for extubation failure specific to patients recovering from pediatric cardiac surgery have been either large heterogeneous groups of children that ranged widely in age [11-12] or smaller studies focused on specific lesions [13-15]. We hypothesized that a study focused solely on neonates but inclusive of all neonatal cardiac lesions would not only identify patient characteristics associated with extubation failure but would also identify specific cardiac defects at increased risk for this undesirable outcome. We therefore aimed to determine the frequency of and identify risk factors for extubation failure in our neonatal cardiac surgical population.

Materials & Methods

Study Population

This study was approved by the Institutional Review Board at Wayne State University and the Detroit Medical Center. We performed a single center retrospective chart review of neonates (0-30 days of age) who underwent cardiac surgery between 1/2009-12/2012 at Children's Hospital of Michigan and recovered in the pediatric intensive care unit. Premature infants undergoing ligation of a patent ductus arteriosus were excluded. Children's Hospital of Michigan is a 260-bed tertiary care where two pediatric cardiovascular surgeons perform approximately 300-350 operations per year on patients with congenital heart lesions in all of the complexity levels. The cardiac surgical patients recover in our 26-bed PICU, where care is provided by multidisciplinary team consisting of cardiovascular surgeons and pediatric intensive care physicians.

Operative Protocol and Postoperative Management

All patients received intra-operative methylprednisolone 30 mg/kg prior to surgical incision. Cardiopulmonary bypass was instituted with target flow rate of 3.0 L/min/m^2. Acid-base status was managed using a pH stat blood gas strategy. After cross clamp removal, zero balanced ultra-filtration was performed. Twenty minutes of modified ultra-filtration was initiated after terminating cardiopulmonary bypass.

Postoperatively, patients received intravenous fluids for daily maintenance and electrolyte requirements; packed red blood cells to maintain hematocrit > 30% in acyanotic patients and 36-40% in patients with cyanotic lesions; fresh frozen plasma and platelets as needed to reverse post-surgical coagulopathy; 5% albumin administration for additional fluid resuscitation as deemed necessary by the ICU team; and prophylactic cefazolin. Patients returned to the

ICU on pressure-targeted synchronized intermittent mandatory ventilation. No formal protocol for assessment of extubation readiness was used for the patient cohort reviewed for this study. In general, extubation from ventilator support was attempted when patients were breathing comfortably with good gas exchange and without metabolic acidosis on the following settings: respiratory rate ≤ 5 breaths per minute, pressure support ≤ 10 cmH2O, positive end-expiratory pressure ≤ 5 cmH2O, and fraction of inspired oxygen concentration ≤ 0.4. The decision to extubate was ultimately at the discretion of the ICU attending physician. Peri-extubation (within 24 hours prior to extubation) intravenous dexamethasone 0.5mg/kg every 6 hours was provided to patients at the discretion of the ICU team. Leak assessment prior to extubation was not routinely performed. Upon extubation, all patients were placed on oxygen via nasal cannula, the flow of which was also at the discretion of the ICU team.

Data Collection and Definitions

Preoperative data collection included age, sex, weight, underlying cardiac diagnosis, gestational age at birth, presence of genetic anomalies, preoperative creatinine measurement, and presence or absence of mechanical ventilation prior to the surgical repair or palliation. We collected the following perioperative data: surgical procedure performed, duration of cardiopulmonary bypass and aortic cross clamping, need for deep hypothermic arrest, and intra operative fluid balance. We estimated intraoperative fluid balance in the following manner: [Intravenous crystalloid + intravenous colloid + blood product] – [modified ultrafiltration + urine output]. With regards to postoperative data, we recorded the following: ventilator settings and arterial blood gas measurements; vasoactive medication requirements; number of postoperative drainage tubes (e.g. mediastinal, pleural, and peritoneal, if present); need for inhaled nitric oxide therapy; and fluid balance prior to the first extubation attempt. We also recorded the occurrence of any postoperative arrhythmia or infection prior to the first extubation attempt. Postoperative infection was defined as clinically relevant positive blood, urine, respiratory, or wound cultures;

medically or surgically-treated necrotizing enterocolitis; or culture-negative sepsis (i.e. systemic inflammatory response syndrome with suspected infection) treated with ≥ 7 days of antimicrobial therapy. This latter definition has been used previously [16]. Samples for respiratory cultures were obtained using non-bronchoscopic broncheoalveolar lavage (mini-BAL). Respiratory cultures that were not considered clinically relevant (i.e. not treated with antibiotic therapy by the primary care team) and short courses of antibiotics < 7 days for "rule-out sepsis" episodes were not included in the analyses.

Extubation failure was defined as the need for re-intubation within 72 hours of first attempted extubation from mechanical ventilation. This definition was based on a review of the literature and internal quality assurance initiatives. For those patients who failed extubation, presumed reason for extubation failure was recorded from the medical record. We also recorded mechanical ventilation, and intensive care unit length of stay.

Vasoactive medication requirements were standardized using the vasoactive-inotropic score (VIS), which was calculated according to following formula [17-18]: VIS = Dopamine (μg/kg/min) + dobutamine (μg/kg/min) + 100 X epinephrine (μg/kg/min) + 10 X milrinone (μg/kg/min) + 10,000 X vasopressin (U/kg/min) + 100 X norepinephrine (μg/kg/min). Ventilation support was quantitated using the ventilation index (VI), which was calculated according to the following formula [19]: VI= RR X (PIP-PEEP) X $PaCO_2$ / 1000, where RR is respiratory rate, PIP is peak inspiratory pressure; PEEP is positive end-expiratory pressure. Ventilation index was calculated at the time of admission and prior to the first extubation attempt using the data from the first arterial blood gas obtained after admission and the last arterial blood gas obtained prior to extubation, respectively.

Statistical Analysis

Data are represented as means and standard deviation for continuous normally distributed variables, medians and range for continuous skewed variables, and counts and percentages for categorical variables. Patients who died without any extubation attempts were excluded from these analyses. In order to determine the risk factors associated with extubation failure, we performed a univariate analysis by comparing variables in patient who required re-intubation within 96 hours to those who extubated successfully on their first attempt using t-tests, Mann Whitney U tests, χ-square tests and Fisher's exact test as appropriate for individual variables. All variables with *P*-values < 0.1 on univariate analysis were considered for inclusion in our multivariate logistic regression model. Variables with *P*-values < 0.05 after multivariate analysis were then identified as independent risk factors for extubation failure after neonatal cardiac surgery.

Results

During the study period, 123 neonates underwent cardiac surgery, 3 of which died prior to an extubation attempt and were excluded. Twenty-one of the 120 neonates (17.5%) included in the study experienced extubation failure within 72 hours of their first extubation attempt. Median time to re-intubation was 26.8 hours, with a range of 0.5 to 70 hours post-extubation. The number of patients who failed extubation in each 24-hour time period up to 72 hours post-extubation is illustrated in Figure 1. Only one patient in the study cohort required re-intubation between 72 and 96 hours post-extubation, related to a large pericardial effusion. Based on our definition, this patient was not categorized as an extubation failure.

The presumed causes and timings of extubation failure are summarized in Table 1. The majority of patients (67%) had primary respiratory etiologies for their extubation failures. In 9 patients, the suspected cause of extubation failure was apparent either upon re-intubation or immediately thereafter on chest x-ray. In 8 other patients, the suspected etiology of extubation

failure became apparent with additional studies: echocardiogram to diagnose cardiovascular pathology (n=3), fluoroscopy to diagnose diaphragmatic paresis (n=3), and bronchoscopy to diagnose airway compression or narrowing (n=2). (One of these latter neonates, recovering from repair of interrupted aortic arch, was found to have pulsatile compression of the right mainstem bronchus on bronchoscopy and follow-up computed tomography scan revealed compression of the left mainstem bronchus between the pulmonary artery and descending aorta. The other neonate was post-repair of aortic coarctation and noted to have narrowing of the distal portion of the trachea on bronchoscopy. This narrowing was ascribed to tracheomalacia versus extrinsic vascular compression but no further imaging was performed to delineate the cause of the narrowing. Both patients were eventually extubated successfully.) In the remaining four patients, extubation failure was ascribed to the non-specific diagnosis of cardiopulmonary insufficiency. Extubation failure in the three patients with cardiac disease identified by echo had extubation failure greater than 24 hours post-extubation. Otherwise, no association or pattern between suspected cause of extubation failure and timing of failure could be identified.

Patients who failed extubation were compared to those patients extubated successfully on their first attempt in Table 2-4. Table 2 summarizes the various cardiac lesions that were repaired or palliated in the patients included in the study. Patients with single ventricle anatomy were more likely to fail extubation, with patients with hypoplastic left heart syndrome or one of its variants representing the majority of extubation failures within this sub-group. On the other hand, patients with d-transposition of the great vessels were significantly less likely to fail extubation as compared to patients with other congenital cardiac lesions included in the study. Patient demographics, pre-operative, intraoperative and immediate postoperative variables are compared in Table 3. Of these factors studied, only the presence of genetic anomalies was

associated with failed extubation, and all five patients with genetic abnormalities that failed extubation had DiGeorge syndrome.

Pre-extubation and post-extubation data are compared in Table 4. Post-operative delayed sternal closure, longer duration of mechanical ventilation, and development of a postoperative infection prior to the first extubation attempt were significantly associated with failed extubation. Three of the five patients with DiGeorge syndrome were being treated for post-operative infections at the time of the first extubation attempt. The majority of patients in the study, including all those who failed extubation, received pre-extubation dexamethasone, and patients who failed extubation received a significantly greater amount of high-flow nasal cannula upon their first extubation attempt. In other words, peri-extubation maneuvers to increase patients' likelihood of success were not more common in those patients who successfully extubated.

Extubation failure was associated with worse clinical outcomes (Table 4). Median intensive care unit length of stay was significantly longer and postoperative mortality was significantly greater in those patients who failed extubation. Though duration of mechanical ventilation prior to the first extubation attempt was significantly longer in patients who failed extubation, intensive care unit length of stay *after the first extubation attempt* was also significantly longer in patients who failed extubation as compared to those who were extubated successfully [99 days (intraquartile range: 29-154) versus 8 days (intraquartile range: 5-15), respectively ($P<0.001$)].

The results of our multivariate logistic regression analysis are provided in Table 5. Hypoplastic left heart syndrome, DiGeorge syndrome, and the occurrence of postoperative infection were independently associated with extubation failure after neonatal cardiac surgery. As a result of the latter finding, we decided, *post-hoc*, to review etiologies of and antibiotic courses for the post-operative infections. Causes of infection in all patients are listed in Table 6. Patients who

failed extubation tended to receive fewer days of antibiotic therapy prior to their first extubation attempt as compared to patients with postoperative infections who extubated successfully [4.9 ± 2.6 versus 7.3 ± 3, *P*=0.073].

We also performed a *post-hoc* sub-analysis on the 41 patients with single ventricle anatomy. In this subgroup, patients who failed extubation were more likely to require delayed sternal closure, develop post-operative infections, and have a longer duration of mechanical ventilation prior to their first extubation attempt. No other variables deemed potential risk factors for extubation failure were significantly different within this subgroup (data not shown). A multivariable logistic regression analysis performed on this subgroup incorporating the three aforementioned variables revealed only the occurrence of postoperative infections prior to the first extubation attempt as a significant risk factor for extubation failure. This sub-group analysis is summarized on Table 7. Within this subgroup, similar to the results of the analysis of all study patients, both total intensive care unit length of stay [112 days (intraquartile range: 46-197) versus 15.5 days (intraquartile range: 8.5-28), (*P*<0.001)] and intensive care unit length of stay following the first extubation attempt [111 days (intraquartile range: 40-165) versus 13 days (intraquartile range: 5-24), (P<0.001)] were significantly longer in patients who failed extubation.

Discussion

Extubation failure continues to be one of the more frustrating clinical scenarios in contemporary pediatric cardiac critical care for both the pediatric intensive providers and the families of the affected patients. In our study, extubation failure occurred in nearly one-fifth of neonates, which is consistent with the range of 10-27% reported in other studies of children recovering from pediatric cardiac surgery [10-15]. The definition of extubation failure has varied in prior studies examining extubation failure in children with cardiac disease [10-15], with some defining extubation failure as the need for re-intubation within 24-48 hours while others have used 96

hours as their definition. Authors who have employed the latter definition [13-15] have asserted that extubation failure in patients with underlying cardiac disease can be slow to evolve and thus the time frame for extubation failure should be expanded beyond 48 hours. We agreed with this latter sentiment though we opted to limit the definition to 72 hours based on anecdotal observations from quality assurance efforts at our institution, in which we have found extubation failure beyond 72 hours to be uncommon. Based on the results of our study, this time interval appears appropriate. Indeed, one third of patients who failed extubation in our study did so between 48-72 hours (Figure 1) and the presumed etiologies of their extubation failures were relatively similar to patients who failed extubation within 0-48 hours (Table 1), while only one patient in the study cohort (with a unique pathophysiologic cause of extubation failure) required re-intubation within the ensuing 72-96 hour time period. The time frame of 0-72 hours post-extubation may therefore be reasonable for future studies on this important subject.

In our study, over half of the patients who failed extubation had single ventricle anatomy and physiology, and the majority of these children had hypoplastic left heart syndrome or one of its variants. This finding was not surprising, given the higher mortality rate in these infants relative to other cardiac lesions that persists in contemporary pediatric cardiac intensive care. In two recent studies, both from the same center, extubation failure occurred in 22% of patients who underwent the Norwood procedure and 27% of infants with univentricular physiology who underwent shunt placement for ductal-dependent pulmonary blood flow [13,15], frequencies that are not as high as observed in our study yet still representative of a considerable portion of the study population.

Of the eight patients with two-ventricle anatomy in our study who failed extubation, five of these patients had DiGeorge syndrome. An association between DiGeorge's syndrome and structural airway abnormalities has been previously described [20-22]. Patients with DiGeorge's

syndrome frequently have laryngeal abnormalities [20-21] and have also been shown to have shorter tracheas with reduced numbers of cartilage rings [22], likely making them prone to various degrees of laryngomalacia and tracheobronchomalacia, respectively. It is possible that some of these conditions were present in our patients, as even mild versions of these abnormalities coupled with residual edema or post-cardiopulmonary bypass lung injury could contribute to the development of post-extubation stridor, wheezing, atelectasis, or alveolar hypoxia.

Taken together, patients with either single ventricle anatomy or DiGeorge syndrome accounted for the majority (81%) of extubation failures in our study. Duration of mechanical ventilation, on the other hand, was not independently associated with extubation failure. Our data therefore suggest that, in determining the likelihood of extubation success in neonatal cardiac surgical patients, underlying disease and co-morbidities are likely more important than the length of time mechanically ventilated. If confirmed in a larger, prospective study, these findings could support a focus more so on optimizing the physiologic state of these high risk neonates (e.g. fluid balance, infectious burden, afterload reduction) and diagnosing other potential hazards (e.g. diaphragm paresis, residual lesions) rather than expeditiously liberating them from mechanical ventilation. A recent pilot study has reported promising results with the use of near-infrared spectroscopy in conjunction with spontaneous breathing trials to predict extubation outcome in infants and children recovering from pediatric cardiac surgery [23]. Future research aimed at assessment of extubation readiness in these high-risk patient populations will hopefully prove helpful in improving their current (less than optimal) clinical outcomes.

We also identified the occurrence of postoperative infection prior to the first extubation attempt as an independent risk factor for extubation failure. Though not previously reported, this finding does seem intuitive in that patients with less than optimal cardiopulmonary reserve would have

more difficulty remaining extubated if also recovering from or in the midst of an acute infectious process. *Post-hoc*, we recorded the number of days of antibiotic therapy received by these patients prior to extubation and found that patients who failed extubation tended to receive fewer days of antibiotic therapy as compared to those who extubated successfully. We cannot assert based on our limited data that longer courses of antibiotic therapy prior to extubation would have prevented the observed extubation failures, nor can we make recommendations as to how long these complicated patients should be treated prior to extubation in the future. Rather, we can only assert that, for patients being treated for infection, it is important to determine if infection-related challenges to successful extubation have been thoroughly mitigated, especially in patients with a known underlying immunodeficiency such as DiGeorge syndrome. Biomarkers such as c-reactive protein, serum amyloid A, and procalcitonin have been shown to be effective tools for assessing and monitoring the inflammatory burden imposed upon neonates with nosocomial infections and necrotizing enterocolitis [24-25]. These biomarkers have potential to be helpful in determining extubation readiness in infants who develop postoperative infections while recovering from cardiac surgery and represent an exciting area for future research.

In regards to the use of high flow of oxygen via nasal cannula in this patient population, those patients who failed extubation were more likely to be placed on higher flows of oxygen via nasal cannula upon extubation than those who extubated successfully. We speculate that this finding was, at least in part, due to selection bias, such that patients presumed to be higher risk for extubation failure by the primary team were placed on higher flows upon extubation. Use of high flow oxygen via nasal cannula for administration of supplemental oxygen in neonates has become ubiquitous in contemporary pediatric intensive care, primarily because of its ease of application and better tolerability relative to nasal continuous positive airway pressure (CPAP). High flow of oxygen via nasal cannula however has not yet been shown to be equivalent to or

superior to non-invasive CPAP [26]. Moreover, a recent study demonstrated a possible protective effect of prophylactic application of CPAP to infants recovering from cardiac surgery upon extubation [27]. Again, further investigations of these modalities in the high-risk patient populations identified in this report are needed.

We acknowledge that our study has several limitations. This study represents the experience at a single center, which may limit the generalizability of the findings. For example, the assessment of extubation readiness varies greatly in pediatric intensive care units from center to center, with many centers conducting more formal spontaneous breathing trials prior to attempting extubation. To our knowledge however, data demonstrating superior effectiveness of these trials as compared to clinical assessment on low levels of ventilator support (as was practiced in this study) in this age group has not been published. Moreover, length of stay in neonates who failed extubation was markedly longer than the rest of the study patients. This finding was more related to the fact that the group of patients who failed extubation contained a disproportionate number of patients with hypoplastic left heart and thus more reflective of the challenges in discharge planning associated with high-risk infants in an urban inner-city setting, rather than due to the extubation failure itself. On the other hand, there are some consistencies among our findings and other reports from single centers, suggesting that our results might reflect what is also being experienced at other centers. The study also has limitations inherent to its retrospective nature. For example, the delineation of the exact cause for extubation failure for many of these patients was difficult to deduce from the medical records. Additionally, even though the number of patients reviewed in our study was relatively high compared to many other studies in the literature that have focused on neonates post-cardiac surgery, our results should be confirmed in a larger multi-centered setting.

Conclusions

Our data support the hypothesis that prompted our study, that neonates with certain cardiac lesions or risk factors, namely those with single ventricle anatomy, underlying genetic abnormalities, and post-operative infections, have a greater risk for extubation failure as compared to other neonates. A more cautious approach to weaning and assessment of extubation readiness in the high-risk infants identified in our study may be appropriate.

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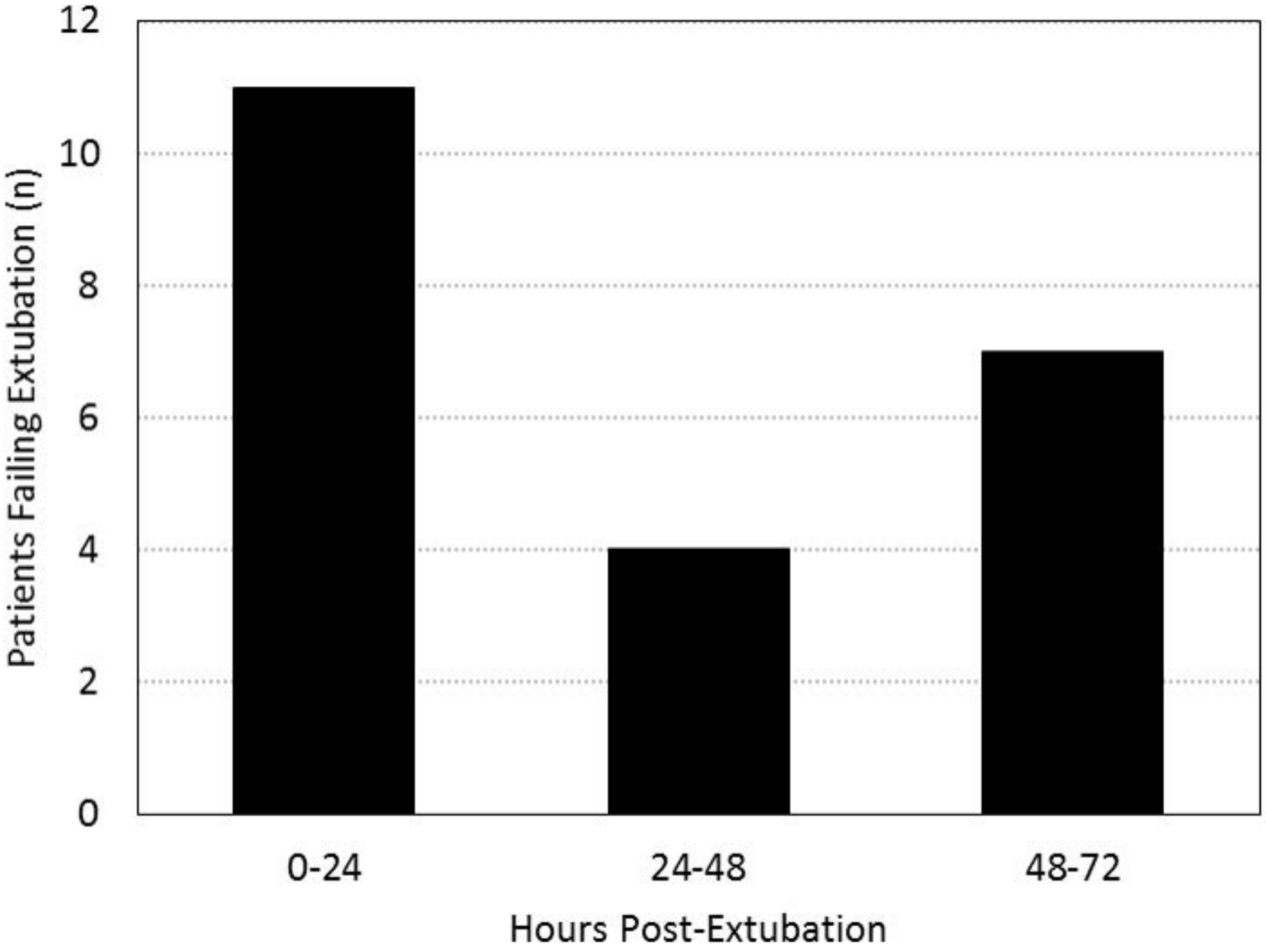
Figure Legends

Figure 1. Frequency of patients who failed extubation in each 24-hour time period post-extubation.


12
10
8
6
4
2
0
Patients Failing Extubation (n)
0-24
24-48
48-72
Hours Post-Extubation

Tables

Table 1. Presumed Causes of Extubation Failure (*N*=21)

Presumed Cause of Extubation Failure	n	Timing (hours post-extubation)
Pulmonary edema / pleural effusion	4	2, 3, 50, 70
Stridor / extrathoracic upper airway obstruction	2	0.5, 48
Lobar atelectasis	2	10, 60
Pulmonary hemorrhage	1	3
Cardiovascular lesion / complication	3	
• Partial systemic-to-pulmonary artery shunt occlusion		64
• Severe pulmonary insufficiency, post-repair of truncus		54
• Severe tricuspid insufficiency, post-repair of truncus		28
Left diaphragm paresis	3	1, 26, 30
Airway compression secondary to intracardiac structure(s)	2	2.5, 7
Cardiopulmonary insufficiency of unclear etiology	4	9, 22, 28, 29

Table 2. Extubation Success vs. Failure by Cardiac Lesion

Cardiac Lesion	Extubation Success (n=99)	Extubation Failure (n=21)	*P*-value
D-Transposition of Great Arteries	25	1	0.042
Coarctation of aorta - All	23	5	1.000
On bypass	10	4	0.267
Off bypass	13	1	0.460
Single Ventricle – All	28	13	0.003
Hypoplastic Left Heart - All	17	9	0.009
Norwood	2	5	
Hybrid	7	3	
Variant	8	1	
Hypoplastic Right Heart	6	3	0.192
Heterotaxy	5	1	1.000
RVOT Obstruction – Two ventricle	7	0	0.352
Anomalous Pulmonary Veins	7	0	0.352
Truncus Arteriosus	3	2	0.210
Atrioventricular septal defect s/p PDA ligation	1	0	1.000
Interrupted Aortic Arch	1	0	1.000
Pulmonary artery arising from aorta	1	0	1.000
Aortopulmonary window	1	0	1.000
Aneurysm of the sinus of Valsalva	1	0	1.000
Coarctation with VSD s/p PA band	1	0	1.000

PA: pulmonary artery; PDA: Patent Ductus Arteriosus; RVOT*:* Right ventricular outflow tract obstruction; *VSD*: ventricular septal defect

Table 3. Demographic, Anthropometric, Intraoperative, and ICU Admission Data

Variable	Extubation Success (n=99)	Extubation Failure (n=21)	*P*-value
Age (days)	11.7 (6.8)	10.4 (6.4)	0.417
Weight (kg)	3.3 (0.6)	3.4 (1.3)	0.729
Sex (male)	55 (56%)	15 (71%)	0.180
Prematurity (n)	3 (3%)	0	1.000
Genetic Syndrome (n)	6 (6%)	5 (24%)	0.010
DiGeorge syndrome	3	5	0.004
Down's syndrome	2	0	1.000
Turner's syndrome	1	0	1.000
Preoperative Creatinine (mg/dL)	0.47 (0.21)	0.43 (0.22)	0.412
Preoperative Mechanical Ventilation (n)	54 (55%)	12 (57%)	0.828
Cardiopulmonary Bypass (minutes)	119 (101)	151 (137)	0.214
Aortic Cross Clamp (minutes)	52 (57)	58 (57)	0.641
Deep Hypothermic Circulatory Arrest (n)	45 (45%)	10 (48%)	0.857
Intraoperative Fluid Balance (per kg)	-34 (73)	-16 (62)	0.317
ICU Admit Drainage Tubes (n)[a]	2 (0 - 5)	2 (1 - 4)	0.669
ICU Admit VIS (mg/dL)	12.5 (7.8)	10.9 (5.9)	0.388
ICU Admit Creatinine (mg/dL)	0.62 (0.2)	0.63 (0.2)	0.847
Δ Creatinine (mg/dL)	0.15 (0.23)	0.2 (0.41)	0.413

Continuous variables represented as mean (standard deviation) unless otherwise noted; categorical data represented as absolute counts (%)

[a] Mediastinal tube(s) + pleural tube(s) + peritoneal drain in place upon ICU admit; represented as median (range); [b] *VIS*: vasoactive inotrope score; [c] Preoperative creatinine – ICU Admit creatinine

Table 4. Postoperative and Pre-extubation Data

Variable	Extubation Success (n=99)	Extubation Failure (n=21)	*P*-value
Postoperative delayed sternal closure (n)	12 (12%)	8 (38%)	0.004
Postoperative extracorporeal support (n)	2 (2%)	1 (4.8%)	0.442
Postoperative arrhythmia (n)	34 (35%)	6 (29%)	0.610
Postoperative infection (n)	11 (11%)	8 (38%)	0.002
Postoperative nitric oxide (n)	32 (33%)	10 (48%)	0.182
Postoperative fluid balance (mL/kg)	-18 (58)	-26 (55)	0.560
Total fluid balance (mL/kg) [a]	-51 (106)	-42 (97)	0.712
Narcotic infusion use (n)	44 (45%)	13 (62%)	0.146
Maximum narcotic rate (mcg/kg/hour) [b]	0 (0-40)	20 (0-240)	0.959
Midazolam infusion use (n)	22 (22%)	3 (14%)	0.559
Vecuronium use (n)	18 (18%)	4 (19%)	1.000
Pre-extubation respiratory rate (breaths/min)	37 (13)	36 (13)	0.809
Pre-extubation Δ P (mmHg) [c]	17.3 (3.4)	18.3 (3.5)	0.224
Pre-extubation ventilation index	4.7 (2.2)	4.5 (1.1)	0.649
Pre-extubation vasoactive-inotrope score	4.7 (2.2)	4.5 (1.1)	0.642
Pre-extubation dexamethasone (n)	87 (88%)	21 (100%)	0.123
Post-extubation nasal cannula flow (L/min)	3.7 (2.7)	5.3 (2)	0.010
Postoperative mechanical ventilation (hrs) [d]	58 (42-94)	142 (49-186)	0.009
Postoperative length of stay (days) [d]	11 (7-20)	101 (32-168)	<0.001
Mortality (n)	1 (1%)	5 (24%)	<0.001

Continuous variables represented as mean (standard deviation) unless otherwise noted; categorical data represented as absolute counts (%)

[a] Intraoperative + postoperative fluid balance

[b] Morphine equivalents; for patients receiving fentanyl (N=17), fentanyl infusion rate was multiplied by 80

[c] ΔP: Peak inspiratory pressure – positive end expiratory pressure

[d] Represented as median (intra-quartile range)

Table 5. Multivariate Logistic Regression Analysis for Predictors of Extubation Failure

Variable	Odds Ratio	95% Confidence Intervals	*P*-value
DiGeorge Syndrome	13.4	2.3-78.4	0.004
Hypoplastic Left Heart	3.5	1.1-11.1	0.037
Delayed Sternal Closure	3.3	0.7-16	0.142
Postoperative infection	3.7	1.1-13.2	0.043
Duration of Mechanical Ventilation	1.0	0.99-1.01	0.832

Table 6. Summary of Postoperative Infections

Type of Infection	Extubation success (n=11)	Extubation Failure (n=8)
Respiratory:		
E. Coli	1	1
Pseudomonas	1	0
Klebsiella	0	1
Stenotrophomonas	1	0
Bloodstream:		
Moraxella catarrhalis	1	0
Group-B Streptococcus	1	0
Enterococcus	1	0
Urinary Tract Infection	2	0
Necrotizing enterocolitis	1	3
Culture-negative sepsis	2	3

Table 7. Sub-Group Analysis of Patients with Single Ventricle Anatomy

Variable	Extubation Success (n=28)	Extubation Failure (n=13)	Univariate *P*-value	Multivariate *P-value*
Delayed Sternal Closure (n)	2 (7%)	5 (38%)	0.024	0.629
Postoperative Infection (n)	2 (7%)	7 (54%)	0.002	0.015
Duration of Mechanical Ventilation (hrs)	47.5 (39-73)	119 (48-160)	0.044	0.302

Continuous variables represented as median (intraquartile range) and categorical data represented as absolute counts (%)