Prediction model for length of intubation with assisted mechanical ventilation in pediatric heart surgery

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Abstract

***Objective*: To establish a prediction model for intubation time in children undergoing heart surgery.**

***Design*: Retrospective chart review.**

***Setting*: A tertiary care pediatric cardiac intensive care.**

***Intervention*: None**

***Measurements and Main Results*: This retrospective cohort study included all patients undergoing cardiac surgery with cardiopulmonary bypass (CPB) and age of less than 18 years in the period of October 2011 through November 2012. Multivariate linear regression was used to determine the predictive model of intubation time. A total of 401 pediatric patients admitted to cardiac intensive care unit after cardiac surgery with cardiopulmonary bypass and survived to hospital discharge. Mean age was 57.8 months (95% confidence interval of mean 52.0 - 63.7). Mean duration of mechanical ventilation was 23.7 (18.6 – 28.9) hours. Among 126 (31.4%) and 323 (80.5%) patients were respectively extubated within 6 and 24 hours after surgery. Age less than 11.5 months (sentitivity and specificity of 83.3% and 54.5%, AUC 0.81 (0.75-0.87)), CPB time longer than 72.5 minutes (sentitivity and specificity of 54% and 29.1%, AUC 0.38 (0.30-0.46)), Pediatric Risk of Mortality (PRISM) III score higher than 3.5 (sentitivity and specificity of 46.3% and 43.6%, AUC 0.41 (0.33-0.50)) were all significant factors to predict intubation time longer than 24 hours after cardiac surgery.**

***Conclusions*: Younger age, longer CPB time, greater severity of illness at post-operative admission are predictive factors for longer intubation time in pediatric cardiac surgery.**

Key words: Intubation time, pediatric cardiac surgery, predictive model, cardiac surgical procedures.

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Introduction

Length of intubation is one of many clinical parameters to define morbidity and predict outcome in pediatric cardiac surgery. (1,2) Many influencing factors such as the underlying disease, the general condition of the patient, anesthetic and surgical techniques and factors, cardiopulmonary bypass (CPB) machine, postoperative management, the availability of experienced staff and the day-to-day routine in the Pediatric Cardiac Intensive Care Unit (PCICU) should be considered for the decision of extubation. (3)

Complex guidance algorithms for decision making of extubation has been described previously. (3,4) In general, simple and instructive postoperative protocols should be determined to guide clinicians for weaning and extubation after pediatric cardiac surgery. Early extubation (extubation in operating room [OR] or 6 hours after surgery) has received renewed attention, however this strategy is not followed by all centers, due to differences in patients population profile, quality of surgery and general postoperative management strategy. (5-7) Our National Cardiovascular Center Harapan Kita (NCCHK), is the main referral for pediatric cardiac service in Indonesia and performs approximately 700 cardiac surgeries per year, with mean basic complexity (Aristotle) score of 6.25 and mortality rate of 5.56%. (8) Most patients present late before surgery compared to other countries, complicated by malnutrition and recurrent chest infection. (9) Human resources, equipment and technology in NCCHK are still limited compared to centers in more developed countries. These settings made our strategy for postoperative management unique for this center. Perhaps the setting in our center is comparable to other centers and therefore this strategy can also be applied for other centers in developing countries. Based on the specific findings in this unique setting our strategy for the timing of extubation after pediatric cardiac surgery needed to be elaborated.

With the paper presented, we want to establish a predictive model for intubation time in our unit after pediatric cardiac surgery. Based on published data, parameters such as age, (3) Aristotle score, (10) Pediatric Risk of Mortality (PRISM) III score, (11) type of ventricular physiology (biventricular or single ventricle physiology), (7) CPB and cross clamp time, (3,7) postoperative lactate and central venous oxygen saturation (ScvO2) levels (12) were identified as predictive factors for the length of intubation. We hypothesized that this model can predict length of intubation and can be a guidance for clinicians or a basis for future protocols to decide when to extubate patients in the postoperative pediatric cardiac surgery setting.

Methods

This retrospective cohort study was approved by the committee on Clinical Investigation at NCCHK. Based on the retrospective character the requirement for written informed consent was waived. Data were retrieved by using our institutional database, which includes all the perioperative details and outcome data of our patients. Postoperative lactate and ScvO2 values were retrieved by retrospective analyzing of perfusion files in the PCICU.

Subjects

This study was conducted in our 13-bed PCICU in NCCHK over 1 year in the period from October 2011 to November 2012. We enrolled all pediatric patients (younger than 18 years) undergoing cardiac surgery with the use of cardiopulmonary bypass. We excluded patients undergoing a cardiac surgical procedure that could not be classified using Aristotle method and patients who underwent tracheostomy during their intensive care unit (ICU) stay. We also excluded from primary analysis the patients who were died immediately after surgery that are almost always still intubated at the time of death.

Data collection

The following data were collected from institutional database or direct analysis of the perfusion files: age (months), weight (kg), gender, type of surgical operation with Aristotle complexity score (10) and the type of ventricular physiology (divided into biventricular physiology and single ventricle physiology). Length of CPB and cross clamp time were also recorded. All patients admitted in our PCICU were calculated for their PRISM III score within the first 24 hours after admitted to the PCICU. (11) Based on our protocol, all postoperative patients were measured for arterial and central venous blood gas analysis at one and four hours after ICU admission. Samples were drawn from arterial line and central venous catheter. Blood gas analysis was measured using bedside i-stat technology. Blood samples for measuring lactate were collected from central venous catheter and measured at first and fourth hour ICU admission. Lactate trend was measured as lactate difference between fourth and first hour after admission. We used Lactate Pro Test Strip (lactate oxidase and potassium ferricyanide) with enzymatic assay from Arkray to measure lactate levels.

Outcome data

The only outcome data was the mechanical ventilation time as measured in hours. Mechanical ventilation time (intubation time) was defined as time from the first hour when the patient was admitted to the PCICU until the time when the first extubation occurred. If the patients required re-intubation, the intubation time was calculated as the sum of total time on mechanical ventilation until the second or subsequent extubation. The amount of reintubation and ICU length of stay were also reported.

Statistical analysis

SPSS 19 software (IBM, Armonk, NY, USA) was used for statistical analysis. Continual variables are reported as mean (95% confidence interval) and categorical variables are reported as proportion (%). Linear regression analyses were performed to see relationships between perioperative variables and lenght of intubation. Potential predictors with a p value of <0.2 in univariate analyses were considered for inclusion in the multivariate linear regression analyses. Enter stepwise regression models were used to determined adjusted relationship between predictors and outcome. A p value of <0.05 was used to determine whether a variable would enter or leave the model. If the a variable that left the model made >20% difference of unstandardized coefficient (B) from the previuos model before the variable was left, this variable can be concerned as confounding and then should still be included in the model. The final model resulted as an equation that predicted intubation time. ROC curves were made to calculate area under the curve (AUC) of each significant predictor to predict the chance of extubation within 24 hours after surgery.

Results

Study population

From October 2011 to November 2012, 716 patients were admitted to the PCICU after cardiac surgery, 416 of whom were assigned by the inclusion criteria as patients who underwent surgery with CPB and aged below 18 years. After excluding 15 patients who died before hospital discharge the final study population contained 401 patients. Demographic data and perioperative characteristics of study population are shown in **Table 1**. We only had 7 (1.7%) neonates and the mean age of study population was 57.8 (52.0-63.7) months. Most of our study patients had biventricular physiology (90.8%) with mean (95% CI) Aristotle score of 6.8 (6.6-6.9) that can be classified as level 2 (moderate) in Aristotle basic complexity score. (13) In our cohort, the most frequent surgeries done were isolated ventricular septal defect closure in 157 (38.8%) patients, tetralogy of Fallot repair in 78 (19.4%), atrial septal defect closure in 53 (13.2%), bidirectional cavopulmonary shunt in 16 (3.9%), interrupted aortic arch repair in 11 (2.7%), complete atrioventricular septal defect repair, total anomalous pulmonary venous drainage repair, arterial switch operation for transposition of the great arteries each in 10 (2.5%), Blalock-Taussig shunt in 10 (2.4%), atrioventricular septal defect repair in 8 (2%) and 6 (1.5%) patients with Fontan operation. The most difficult case was Norwood operation, done in 1 patient with hypoplastic left heart syndrome (HLHS).

Table 1 also shows the laboratory results for lactate, arterial and central venous saturation at first and fourth hour after ICU admission. Mean lactate levels at the first and fourth hour after PCICU admission increased from normal value, that were 3.0 (2.8-3.2) and 3.5 (3.0-4.1) mmol/L respectively, without too much increase in lactate difference between the fourth and first hour ICU admission with mean difference 0.6 (0.04-1.07) mmol/L. Normal lactate value in critical condition is less than 2 mmol/L. (14) Most of our study patients had a biventricular physiology that made their arterial saturation more than 92% with mean ScvO2 at first and fourth hour post admission were 70.1% (68.6%-71.6%) and 69.1 (67.7-70.05), respectively.

Outcome data of study patients is shown in **Table 2**. The median duration of mechanical ventilation was 12 hours (min-max 0-25 days). Most of the study patients (85%) were extubated within 24 hours after surgery. We used muscle relaxant to control ventilation in some of postoperative cases for a mean duration of 6.1 (4.4-7.8) hours. In this study population reintubation was done in 59 (14.7%) patients which mostly occurred more than 6 hours after extubation in 33 (8.2%) patients. Mean ICU length of stay for this cohort was 3 (2.6-3.5) days.

Predictive factors for length of intubation

Univariate analysis was done for age, Aristotle score, CPB time, cross clamp time, PRISM III score, lactate and ScvO2 at first and fourth hour of ICU admission, lactate difference and ventricular physiology as a potential predicting factors for the length of intubation (**Table 3**). Bivariate correlation between these factors and intubation time showed significant correlations except for first and fourth hour lactate levels and lactate difference with p>0.2. Statistical analysis using independent T test to differentiate single vs. biventricular physiology on length of intubation resulted p value of 0.25. Because of only predictive factors with p value of <0.2 were included in multivariate analysis, lactate levels and ventricular physiology were excluded from further analysis. Linear regression with the use of a stepwise regression model included only age, PRISM III score and CPB time in the model, with standardized coefficient (Beta) of -0.21, 0.12 and 0.34, respectively (**Table 4**). First and fourth hour ScvO2 showed p value of >0.05 and tried to be excluded from the model, but their exclusion make >20% changes of unstandardized coefficient (B) to other factors in the model, so these two factors was assumed to be confounding and could not be omitted from the model. Final result for linear regresion equation is showed in the legend of **Table 4**. Adjusted R square of this model was 0.20.

An analysis of ROC curve was performed to evaluate the probability of these factors on predicting the chance of extubation within 24 hours after surgery (**Figure 1**). Age as predictive factor showed the best area under the curve (AUC) with AUC of 0.81 (0.75-0.87); sentitivity and specificity of 83.3% and 54.5%, respectively, for age of 11.5 months as cut of point for extubation within 24 hours (**Table 5**).

Discussion

Our results showed that most of our patients (80,5%) had been extubated within 24 hours after surgery with a reintubation rate of 14.7%; no patient was extubated in OR. Most centers now suggested to perform an early extubation as defined an extubation occurring in the OR or within 6 hours post surgery. In our cohort only 31.4% of our patients were extubated within 6 hours after surgery. Early extubation was known as a safe strategy and is associated with reduction in length of PCICU and hospital stay without adverse effects on morbidity and mortality. (5) Reported early extubation rates in other centers were 37.8-82% with the rate of extubation failure of 0-11%. (15-18)

Our early extubation rate is still less than other centers due to some consideration with our patient population, quality of surgery and postoperative management. Due to failure of early diagnosis, most of our patients came with late presentation complicated with malnutrition, prolonged cardiac failure and pulmonary hypertension due to unrestrictive pulmonary blood flow, and persistent severe cyanosis in cyanotic congenital cardiac lesions. (8,9) Pulmonary hypertension itself has been pointed as a risk factor for prolonged mechanical ventilation. (6) Quality of surgery can be reflected from the occurrence of residual lesion, need for reintervention and bleeding complication due to surgical or medical issue. (7) Although early extubation may be in some centers considered as best practice to manage post cardiac surgery patients, our limitations especially human resources made us be more careful to choose this strategy.

We realize that some other factors such as noncardiac structural abnormalities, postoperative healthcare-associated infection, noninfectious pulmonary complications and reintervention had been found to have significant role on prolonged mechanical ventilation (≥7 days) in other studies. (7,19) Due to difficulty to gain information about these significant factors in our database, we were not able to analyze these factors as part of our predictive factors for length of intubation in our model.

Predictive factors such as age, CPB time, PRISM III score and ScvO2 at first and fourth hour of ICU admission were included in the model to determine intubation time after multivariate analysis. These four parameters are easily known for patients undergoing cardiac surgery and can be one of guidance to decide extubation as they reflect cardiac output, the effect of surgery and the potential to recover after surgery. Beside that some other factors should be considered based on problem for each specific cases. (7)

Young age at surgery has been previously known as a significant predictor of prolonged mechanical ventilation and intensive care unit stay. (7,20,21) Neonates and infants have limited cardiorespiratory reserve that make this group of patients vulnerable for failed of extubation. Additionally the metabolism is different, larger halftimes of sedation, anesthesia and opioids. Published data show that almost 10% of failed extubation cases were reported for young patients, with the most common causes were cardiac dysfunction, lung disease and airway edema. (6) Based on the ROC curve in our result, extubation of the patients aged more than 12 months could be predicted within 24 hours after surgery, with AUC of 81%. Only 1.7% of our study population were neonates, therefore we hardly saw that neonatal age had any impact for prolonged intubation. As we discussed earlier most of our patients were presented late before surgical repair because of delayed in early diagnosis. (8) Most of them came in their infants to young child age, and some of our neonatal patients died before they can reach our institution. The cut of point 12 months of age can be a guide to determine extubation within 24 hours for our population and maybe for other centers in developing countries.

Prolonged mechanical ventilation after pediatric cardiac surgery was consistently associated with longer CPB time. (15,16,22) Increased CPB time is required for more complex cases or if unexpected difficulties occur. With longer CPB time there is an increased risk of inflammatory response syndrome with generalized edema, decreased respiratory compliance and coagulopathy that decrease the ability to extubate a patient soon after surgery. (22) A common strategy to prevent this is the use of continuous or modified ultrafiltration during or after surgery, that has been one of our protocol in our unit. In our prediction model for intubation time, CPB time was one of significant factor to predict length of intubation. In the data analysis of ROC curve for CPB time in this study showed CPB time of more than 70 minutes correlated with prolonged extubation, but with low sensitivity and specificity (AUC 0.38 [95% CI 0.30-0.46]). Another study by Mittnacht et al. found CPB time more than 150 minutes was associated with an 11.8-fold increased risk of not being extubated in OR. (22)

PRISM III score has been widely used to predict severity of illness and mortality in population of children admitted to multidisciplinary pediatric intensive care units. (11) In this study and other previous study, (7) higher PRISM III score was also associated with prolonged mechanical ventilation post pediatric cardiac surgery. Aristotle score was independently correlated with length of intubation but this surgical complexity score was not included in the model after multivariate analysis. Other studies using Risk Adjustment in Congenital Heart Surgery-1 (RACHS) scores for complexity score also showed no correlation between this score and prolonged intubation. (7,23) This suggests that usual guidelines for weaning from mechanical ventilation, and not the complexity of the operation are more appropriate in determining extubation readiness. (23)

Lactate levels and ScvO2 are known as parameters of tissue perfusion and cardiac output and a predictive index for major morbidity after pediatric cardiac surgery. (12) This study did not see any correlation between lactate levels and intubation time but lower ScvO2 at first and fourth hour after surgery, however, showed an independent correlation with length of intubation. These findings can be explained through the thought of lactate levels as absolute levels or trend cannot solely reflect tissue perfusion and correlate directly with cardiac output, but an increasing lactate can occur as a result of increased production, decreased excretion and disturbance of enzymatic process in producing lactate. The use of both lactate levels and ScvO2 are preferable to predict morbidity. (12) Lower ScvO2 is one of predictive factors included in the model for intubation time although individually this parameter did not show any significant in multivariate analysis. Concerning about confounding in the statistical analysis during this linear regression model, ScvO2 or better the arteriovenous saturation difference in patients with cyanotic defects still should be included as predictive factor for intubation time. Most of our study patients (91.8%) are biventricular physiology with arterial saturation of more than 92%. This condition made ScvO2 parameter alone can also reflect oxygen extraction ratio in measuring tissue perfusion. (3) Continues monitoring of ScvO2 is warranted to minimize the risk of major adverse event and our study showed ScvO2 parameter also had a role in predicting length of intubation. (24)

There are several limitations of this study including that it has a retrospective design that made some of important factors to predict intubation were not available for analysis, and therefore there is no prove of causality between predictive factors and outcome, and we did not have specific guideline for physician practice to decide extubation so there would be variability of physician practice. This model of prediction of intubation was done in order to help the physician when to extubate patients with condition that we had in our unit, so this single institution finding had limited generalizability.

In conclusions, younger age, prolonged CPB time, higher PRISM III score and lower ScvO2 were all significant factors to predict intubation time after pediatric cardiac surgery. Future research could focus on some specific conditions that our population have such as malnutrition, recurrent infection before surgery, severity of pulmonary hypertension or cyanosis and other recognized prolonged intubation factors from previous research whether have roles in predicting intubation time in patients population such ours in developing countries.

Table 1. Demographics, perioperative characteristics, laboratory results for lactate, arterial and central venous oxygen saturation at first and fourth hour after ICU admission for 401 study patients

Preoperative variables	
Male	198 (49%)
Age (months)	57.8 (52.0-63.7)
Neonate	7 (1.7%)
Intraoperative variables	
Single ventricle physiology	32 (8.1%)
Aristotle score	6.8 (6.6-6.9)
CPB time (minutes)	95.5 (90.1-100.9)
Cross clamp time (minutes)	53.9 (49.2-58.7)
Postoperative variables	
PRISM III score	4.3 (3.9-4.8)
Lactate levels at 1st hour ICU admission (mmol/L)	3.0 (2.8-3.2)
Lactate levels at 4th hour ICU admission (mmol/L)	3.5 (3.0-4.1)
Lactate difference	0.6 (0.04-1.07)
SaO2 levels at 1st hour ICU admission (%)	97.5 (96.8-98.2)
SaO2 levels at 4th hour ICU admission (%)	97.2 (96.5-97.8)
ScvO2 levels at 1st hour ICU admission (%)	70.1 (68.6-71.6)
ScvO2 levels at 4th hour ICU admission (%)	69.1 (67.7-70.05)

Legend: CPB=cardiopulmonary bypass; PRISM III=Pediatric Risk of Mortality III; SaO2=arterial oxygen saturation; ScvO2=central venous oxygen saturation. Data are reported as number (%) or mean (95% confidence interval)

Table 2. Outcome data for 401 study patients

Hours of mechanical ventilation	23.7 (18.6-28.9)
≤6 hours in mechanical ventilation	126 (31.4%)
≤24 hours in mechanical ventilation	323 (80.5%)
Length of control ventilation (hours)	6.1 (4.4-7.8)
Reintubation in ≤6 hours	26 (6.5%)
Reintubation in >6 hours	33 (8.2%)
Length of stay in ICU (days)	3 (2.6-3.5)

Legend: Data expressed as number (%) or mean (95% confidence interval)

Table 3. Predictive factors for length of intubation following univariate analyses

Variables	Pearson correlation	p
Age	-0.21	<0.001
Aristotle score	0.31	<0.001
PRISM III score	0.21	<0.001
CPB time	0.34	<0.001
Cross clamp time	0.15	0.004
Lactate levels at 1st hour ICU admission	-0.02	0.76
Lactate levels at 4th hour ICU admission	-0.01	0.88
Lactate difference	-0.001	0.98
ScvO2 levels at 1st hour ICU admission	-0.23	<0.001
ScvO2 levels at 4th hour ICU admission	-0.26	<0.001

Legend: Bivariate analysis for categorical predictive factors were analyzed with independent T test.

Table 4. Predictive factors for length of intubation following multivariate analyses

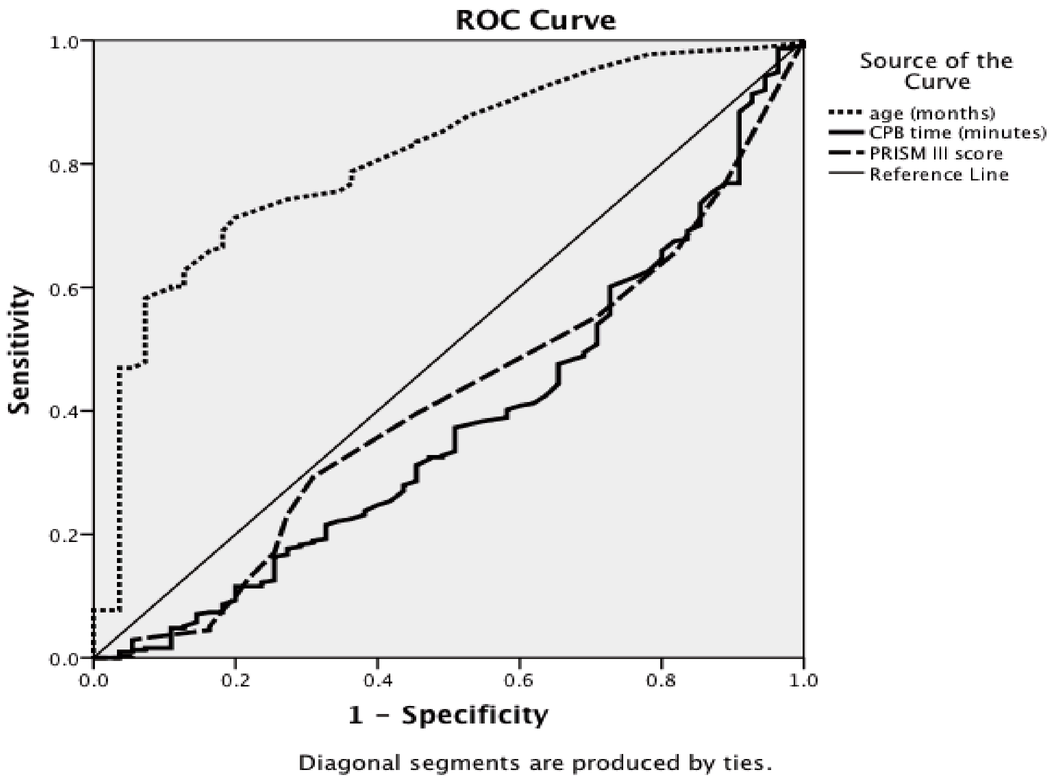
Variables	Unstandardized coefficients (Beta)	Standardized coefficient (Beta)	p
Constant	26.88		0.01
Age in months	-0.13	-0.21	<0.001
PRISM III score	1.02	0.13	<0.001
CPB time in minutes	0.22	0.34	0.009
ScvO2 levels at 1st hour ICU admission (%)	-0.16	-0.06	0.26
ScvO2 levels at 4th hour ICU admission (%)	-0.19	-0.08	0.15

Legend: Formula derived from linear regression analyses: Y=26.88-0.13X1+1.02X2+0.22X3-0.16X4-0.19X5. Y=intubation time (hours); X1=age; X2=PRISM III score; X3=CPB time; X4=ScvO2 levels at 1st hour ICU admission; X5=ScvO2 levels at 4th hour ICU admission.

Table 5. AUC, sensitivity and specifity of age, CPB time and PRISM III to predict extubation within 24 hours after surgery

Variables	AUC (95% CI)	Sensitivity	Specificity
Age	0.81 (0.75-0.87)		
11.5 months		83.3%	54.5%
12.5 months		78.8%	63.6%
13.5 months		76.8%	63.6%
CPB time	0.38 (0.30-0.46)		
72.5 minutes		54%	29.1%
76.5 minutes		49.5%	30%
78.5 minutes		48.2%	32.3%
PRISM III score	0.41 (0.33-0.50)		
3.5		46.3	43.6
4.5		39.5	54.5
5.5		29.3	59.1

Figure 1. ROC curve for age, CPB time and PRISM III score to predict extubation within 24 hours after surgery



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