Risk factors for prolonged mechanical ventilation after surgical repair of congenital heart disease

Experience from a single cardiac center

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ABSTRACT

الأهداف: التعرف على العوامل المؤدية الى إطالة التنفس الصناعي في مركز واحد لأمراض القلب.

الطريقة: أجريت دراسة استرجاعيه للتعرف على العوامل التي حدثت في الماضي وتم عمل البحث بعد الحصول على موافقة من قبل لجنة الأبحاث لمركز القلب. جميع الأطفال تتراوح أعمارهم بين 14–0 عام وخضعوا لعملية اصلاح أمراض القلب الخلقية من يناير 2014م إلى يونيو 2016م تم اضافتهم في البحث. تم تعريف إطالة التنفس الصناعي: إذا تخطى التنفس الصناعي مدة 72 ساعة.

النتائج: تم إضافة عدد 257 مريض في الدراسة؛ منهم 219 (85.2%) مريض استمروا على التنفس الصناعي لأقل من 72 ساعة، و 38 (14.8%) مريض استمروا على التنفس الصناعي لأكثر من 72 ساعة. العمر (29.9 مقابل 11.95 سنة) والوزن (9.6 مقابل 5.9 كجم) وقت قطع الشريان الرئوي (53.6 مقابل 71.8 دقيقة) ووقت المجازة القلبية الرئوية (80.98 مقابل 124.36 دقيقة) ومدة البقاء في العناية المركزة للأطفال (10.4 مقابل 27.2 يوم)، وجود العدوى (12.8% مقابل 42.1%)، مدة بقاء جرح العملية مفتوح (0.9% مقابل 13.2%)، إعادة ادخال انبوب التنفس الصناعي (19.2% مقابل 39.5%)، زيادة الضغط الرئوي (10.9% مقابل 31.6%)، ضعف في عضلة القلب (10.1% مقابل 23.7%)، كل هذه العوامل السابقة لها علاقة بإطالة التنفس الصناعي. إشاره إلى تصنيف تغيير المخاطر في عملية اصلاح أمراض القلب الخلقية، غالبية المرضى كانوا ينتمون لمجموعة 1 و 2. المرضى المنتمين للمجموعة 4 (18.4%) كان لديهم تنفس صناعي لمدة طويلة.

الخاتمة: العمر والوزن ووقت المجازة القلبية الرئوية ووقت القطع وزيادة الضغط الرئوي وضعف في عضلة القلب والعدوى هي عوامل تؤدي الى إطالة التنفس الصناعي ويجب أن تكون هذه العوامل في عين الاعتبار عند أخذ قرار العملية والتنويم في العناية المركزة للأطفال

Objectives: We studied these predictors at a single cardiac center.

Methods: A retrospective cohort study was carried out after obtaining approval from the institutional review board. All patients (age, 0-14 years) who underwent congenital heart disease (CHD) surgery from January 2014 to June 2016 were included. Prolonged mechanical ventilation (PMV) was defined as >72 hours of ventilation.

Results: A total of 257 patients were included, among whom 219 (85.2%) were intubated for ≥72 hours and 38 (14.8%) were intubated for ≥72 hours. Age (29.9 versus 11.95 years), weight (9.6 versus 5.9 kg), cross-clamp time (CCT) (53.6 versus 71.8 min), cardiopulmonary bypass time (CBP) (80.98 versus 124.36 min), length of stay in the pediatric intensive care unit (PICU) (10.4 versus 27.2 days), infection (12.8% versus 42.1%), open sternum (0.9% versus 13.2%), re-intubation (19.2% versus 39.5%), pulmonary hypertension (10.9% versus 31.6%), and impaired heart function (10.1% versus 23.7%) were associated with PMV. In terms of Risk Adjustment in Congenital Heart Surgery (RACHS) classification, only patients with RACHS 4 (18.4%) were associated with the risk for PMV.

Conclusions: Age, weight, CBP, CCT, pulmonary hypertension, impaired cardiac function, and sepsis are risk factors for PMV. These factors should be considered when deciding surgery and in providing PICU care.

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Mechanical ventilation (MV) is a common treatment in the intensive care medicine, whether for neonates, children, or adults. Regardless of the underlying disease, this supportive treatment is associated with many complications that may delay weaning, such as ventilator-associated lung injury and pneumonia.[1] Every child undergoing surgery for congenital heart disease (CHD) will need MV, which may be extended for different periods after the surgery. Prolonged MV (PMV) after CHD surgery in children is associated with high postoperative morbidity and mortality, as well as increased use of pediatric intensive care units (PICUs) and hospital resources. There are few published data identifying the predictors of PMV after CHD surgery. These data show inconsistencies in many parameters across different centers.[2-14] There are limited published data on PMV in the United States, Asia, and Europe. There is only 1 published paper in Saudi Arabia; however, the data are limited to only patients with Down syndrome.[15] Taking into consideration the lack of data in the Saudi Arabian region and the differences in the reported risk factors for PMV among different studies, we decided to investigate patients who underwent CHD surgery at our institution to identify the possible predictors.

Methods. The protocol of this retrospective cohort study was approved by the Institutional Review Board of Madinah Cardiac Center, and the need for patient consent was waived.

Patients' demographic data and procedural details were retrieved from the hospital information system. This database contains patients' demographic data, dates of admission, procedures and discharge information, diagnoses according to International Classifications of Disease 10th revision codes, imaging findings, and laboratory data. The collected patient data included the following: date of birth, gender, date of admission, date of discharge, date of procedures, and length of stay in the pediatric intensive care unit (PICU). Individual patient records were then revised for further details, including history and physical examination findings, associated diseases, echocardiography notes, operative notes, and progress notes in the PICU. Complications related to procedures during the operation or within the PICU were also revised.

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The duration of MV was calculated from the time of arrival to PICU until extubation. Patients were divided into 2 groups according to MV duration: PMV group (≥72 hours) and non-PMV group (≥72 hours). This definition of PMV was based on previous studies,[3,6,16] in which the median ventilation duration after pediatric cardiac surgery was 3 days.

All patients aged one day to <14 years who underwent surgical repair and admitted to the PICU at our institution were included. Patients older than 14 years were excluded.

From January 2014 until the end of 2016, a total of 262 patients underwent surgery for CHD and were admitted to the PICU. Five patients were excluded from the study because they were older than 14 years. These patients were considered adult CHD cases operated on by our surgeons and admitted to the PICU for postoperative care. Thus, 257 patients remained as the study cohort. The patients were classified according to the Risk Adjustment in Congenital Heart Surgery (RACHS-1) system into 6 categories, to adjust for the patient mix when comparing in-hospital mortality.[17-19] Surgical procedures were classified into one of 6 categories. Risk category one has the lowest in-hospital mortality, whereas risk category 6 has the highest mortality. Patients who underwent >1 cardiac surgical procedure were placed in the highest risk category.

Statistical analysis. All data were analyzed using the Statistical Package for Social Sciences, Version 22.0; (IBM Corp., Armonk, NY, USA). Descriptive statistics were expressed as means and standard deviations for continuous variables and percentages and frequencies for categorical variables. Unpaired t-test was used for comparison of continuous variables, and the Chi-squared test was used for categorical variables. A *p*-value of <0.05 was considered significant.

Results. During the study period, 257 patients aged <14 years were retrieved. The demographic data of the patients are shown in **Table 1**. The mean patient age was 27.1 months; the proportion of male patients (57.6%) was slightly higher than that of female patients; and the mean weight of the patients was 9.1 kg.

Among all patients, 219 (85.2%) were intubated for <72 hours and 38 (14.8%) were intubated for ≥72 hours. With respect to the type of CHD, ventricular septal defect was the most common anomaly (38.5%) and double outlet right ventricle was the least common (2.7%) (**Table 2**). During the operation, the mean cardiopulmonary bypass time (CPB) was 86.8 min and the cross-clamp time was 56.3 min.

Table 1 - Characteristics of patients included in the study (N=257).

Parameter	Value
Age (months), mean (interval)	27.1 (0.3 - 187.6)
Weight (kg), mean (SD)	9.1 (7.96)
Gender (male), n (%)	148 (57.6)
Cross-clamp time (min), mean (interval)	56.3 (1.9 - 59.5)
CPB time (min), mean (interval)	86.8 (15 - 263)
PICU stay (days), mean (interval)	13.2 (1 - 109)
MV (h), mean (interval)	55.3 (0 - 1800)

CPB - cardiopulmonary bypass, PICU - pediatric intensive care unit, MV - mechanical ventilation

Table 2 - Distribution of congenital heart diseases among patients.

Type of congenital heart	n (%)
Tetralogy of Fallot	29 (11.3)
Transposition of great arteries	4 (1.6)
Ventricular septal defect	99 (38.5)
Atrial septal defectCOA	33 (12.8)
Coarctation of aorta	16 (6.2)
Patent ductus arteriosus	31 (12.1)
Atrioventricular septal defect	21 (8.2)
Aortic prolapse	9 (3.5)
Aortic stenosis	5 (1.9)
Double outlet right ventricle	7 (2.7)
Pulmonary atresia	13 (5.0)
Others	104 (40.5)

A patient may have more than one defect.

Mechanical ventilation duration and PICU stay. The mean MV duration for all patients was 55.3 hours. Thirty-eight (14.8%) patients were ventilated for ≥72 hours. The mean duration of PICU stay was 13.2 days.

Predictors of PMV. **Table 3** shows the comparison between patients with and without PMV. Age, weight, cross-clamp time, CPB time, length of stay in the PICU, infection, and open sternum were associated with PMV. There was no association between PMV and gender. Re-intubation of patients was significantly associated with PMV. Re-intubation was performed in 42 patients (19.2%) without PMV and in 15 patients (39.5%) with PMV.

When specific CHDs were compared, we found no significant risk factor for PMV among specific disease entities. With respect to RACHS classification, most of the patients in both groups fell into class 1 and 2. There was no statistical significance with respect to PMV except for the class 4 group, which included 18.4% of patients with PMV and 7.8% of patients without PMV.

Table 3 - Comparison of predictors of prolonged mechanical ventilation.

Parameter	<72 h (n=219)	≥72 h (n=38)	*P*-value
Age (months)	29.9 (0.3-187.6)	11.95 (0.3-158.7)	0.01
Weight	9.6 (2.2-59.5)	5.9 (1.9-40.7)	0.01
Male gender	127 (49.0)	21 (8.0)	0.1
Female gender	92 (36.0)	17 (7.0)	
Pulmonary hypertension	24 (10.9)	12 (31.6)	0.001
Impaired hearing function	22 (10.1)	9 (23.7)	0.017
Cross-clamp time (min)	53.6 (0-169)	71.8 (15-168)	0.009
CPB time (min)	80.98 (15-262)	124.36 (26-263)	0.001
PICU stay (days)	10.4 (1-35)	27.2 (9-93)	0.001
MV duration (h)	14.2 (0-71)	284.3 (72-1800)	0.001
Associated infection	28 (12.8)	16 (42.1)	0.001
Re-intubation	42 (19.2)	15 (39.5)	0.01
Postponed sternal closure	2 (0.9)	5 (13.2)	0.001
Associated disease			
Down's syndrome	36 (16.4)	5 (13.2)	0.6
Failure to thrive	20 (9.1)	2 (2.6)	0.5
Others	37 (16.9)	8 (21.1)	0.5
Type of CHD			
VSD	80 (36.5)	9 (23.7)	0.1
ASD	30 (13.7)	3 (7.9)	0.3
TOF	24 (10.9)	5 (13.1)	0.7
TGA	3 (1.4)	1 (0.5)	0. 1
PDA	26 (11.9)	5 (13.1)	0.8
AVSD	17 (7.8)	4 (10.5)	0.6
Aortic prolapse	9 (4.1)	0	
Aortic stenosis	5 (2.3)	0	
DORV	5 (2.3)	2 (5.3)	0.3
Pulmonary atresia	10 (4.6)	3 (7.9)	0.4
COA	14 (6.4)	2 (5.3)	0.8
Others	112 (51.1)	13 (34.2)	0.5
RACHS 1	22 (10.0)	2 (5.3)	0.32
RACHS 2	108 (44.3)	11 (28.9)	0.12
RACHS 3	72 (32.9)	18 (47.4)	0.25
RACHS 4	17 (7.8)	7 (18.4)	0.04

CPB - cardiopulmonary bypass, PICU - pediatric intensive care unit, MV - mechanical ventilation, CHD - congenital heart disease, VSD - ventricular septal defect, ASD - atrial septal defect, TOF - tetralogy of Fallot, TGA - transposition of great arteries, PDA - patent ductus arteriosus, AVSD - atrioventricular septal defect, DORV - double outlet right ventricle, COA - coarctation of aorta, RACHS - Risk Adjustment in Congenital Heart Surgery

Discussion. In our study, approximately 65% of patients were extubated within 24 hours after CHD surgery. Of the patients, 38 (14.9%) continued to be ventilated after 72 hours and 10 patients (3.9%) continued to be ventilated after 7 days. The results were within the previously reported ranges. The incidence of PMV of >72 hours was 20% and 7 days was 10.7%, in a recent study.[2] The percentage of PMV of >72 hours after CHD was 13.2%,[3] 25%,[4] and 35.4%[5] in other previous studies. In another study, a total of 362 patients were admitted to the cardiac intensive care unit after a cardiac surgical procedure of RACHS, and 41 patients (11%) were ventilated for >7 days.[7]

Early extubation and early weaning of children from MV after CHD surgery lead to rapid ambulation, improve the cardiopulmonary function, and shorten the PICU and hospital stays.[2-14] Addressing the predictors

of delayed extubation is difficult, nevertheless, the ability to define high-risk patients and preoperative, operative, and postoperative risk factors may help modify surgical or medical approaches to enable early weaning from the ventilator. However, the data on the definition and predictors of PMV are not consistent across different studies.[2-10] Simple CHD surgery is associated with early extubation; however, it has been reported that extubation can be achieved within 72 hours even after complex CHD surgeries.[1] Davis et al[8] studied 203 children and adults aged <33 years who underwent 219 surgeries for CHD. They found that complex versus simple procedure and palliative versus complete repair were not associated with the success of early extubation. Of their patients, 47% were extubated within 24 hours after surgery. The main risk factors for PMV were heart failure, pulmonary hypertension, and age <6 months. Our results showed that weight and age are risk factors for PMV. Young age is known to be an important risk factor for PMV and PICU stay.[3,6,20,21] Shu et al[5] showed an extubation failure rate of 13.2% after cardiac surgery for CHD in pediatric patients with a mean age of 64 months. Pulmonary hypertension and impaired heart function are other universal risk factors for PMV.[2-10] Prolonged CPB and cross-clamp times were associated with PMV in our patients. These risk factors are not consistently reported in all studies. Mittnacht et al[14] found that a CPB time of >150 min was associated with an 11.8-fold increased risk of failure to extubate early.[14] Szekely et al[1,5] found an association between the duration of CPB and delayed extubation. In another study, the CPB and cross-clamp times were not significant risk factors for PMV.[2,16] Delayed sternal closure, sepsis, and re-intubation were also associated with PMV in our patients. These results are in agreement with those of other studies.[2-10] Nosocomial pneumonia, fluid overload, and low cardiac output syndrome were associated with PMV of >72 hours.[3] Szekely et al found that of all the studied clinical predictors, pulmonary hypertension, delayed sternal closure, peritoneal dialysis, low output syndrome, and fluid intake were associated with PMV of >61 hours, whereas urea nitrogen (24 hours), postsurgical neurological events, nitric oxide, tracheobronchomalacia, pulmonary hypertension, and cardiac reoperations were identified as determinants of PMV of >7 days.[3] Age is an important risk factor for PMV. Especially, infants with CHD are physiologically different from older children or adults, as they may be still under the effect of low birth weight or preterm birth, have malnutrition, and have frequent infections. Therefore, infants tend to have decreased cardiorespiratory reserve and are at a high risk for PMV.[3,6,20,21] Many previous reports suggested preoperative pulmonary hypertension and respiratory problems including postoperative pneumonia as important risk factors for PMV in children after CHD surgery.[5,6,10] In patients with left-to-right shunt lesions, the pulmonary artery pressure decreases after surgical correction. However, these patients are susceptible to pulmonary hypertension crisis after surgery, which may be due to hypoperfusion of pulmonary tissues during CPB. The pulmonary compliance is reduced in these patients, making them prone to respiratory complications and PMV.[5,6] Impaired cardiac function is an important and constant risk factor for PMV after CHD surgery. Patients with CHD, especially those with complex disease types, have limited cardiac reserve that may worsen during CPB.[16] The presence of impaired cardiac function and low output syndrome after CHD surgery has multifactorial causes and correlates with the severity of cardiac dysfunction before surgery, cross-clamp time, CPB time, and myocardial preservation parameters during the operation.[1,3] When those conditions continue, heart failure manifests, weaning from inotropic support becomes difficult, and using many inotropes at high doses may induce more damage to the myocardium.[3,4,21] The presence of conflicting data about the risk factors for PMV shows that it is not a simple issue. An interaction between systemic and cardiopulmonary factors is responsible for this event, and it is difficult to create a unified list of risk factors for PMV. We believe that the possible risk factors differ from one center to another. These factors should be individually investigated in each center, and each pediatric cardiology center should have its own protocol for the selection, intraoperative management, and postoperative care of such patients.

Study limitation. A retrospective cohort study has its own limitation rather doing a prospective analytical study. Also, human factors during surgical intervention and post-operative management cannot be clearly studied.

In conclusions, age, weight, intraoperative CBP time, cross-clamp time, pulmonary hypertension, impaired cardiac function, and sepsis are risk factors for PMV. These factors should be taken into consideration when deciding surgery and in providing PICU care.

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