

A prospective cohort study to assess the risk factors of failed extubation in mechanically ventilated pediatric patients admitted to the intensive care unit

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Keypoints

Failed extubation is more common in young children, in patients with respiratory illness, and those receiving prolonged mechanical ventilation.

Abstract

Introduction

Failed extubation is a challenge in the intensive care unit. It can cause increased morbidity, and mortality in addition to higher costs due to prolonged hospital stay. We aimed to determine the risk factors of failed extubation and predictors of weaning success among mechanically ventilated children.

Material and Methods

It was a prospective cohort study for children on mechanical ventilation for longer than 24 hrs where they were followed up for 48 hrs after extubation. Failed extubation is the need for tube reinsertion within 48 hrs post-extubation. Demographic characteristics and mechanical ventilation parameters were evaluated. Arterial blood gas values and rapid shallow breathing index (RSBI) were assessed on admission, before weaning from mechanical ventilation, and during weaning.

Results

Failed extubation was seen in 17.5% of patients; 53.9% of them were \leq one year and 26.9% were between one and five years while 19.2% were

\geq 5 years. Of patients with a failed extubation, respiratory illnesses were the principal cause of ventilation (50%) followed by cardiac surgery ventilated cases (23% each), neurological (15.4%), envenomation (7.7%), and lastly drug intoxication cases (3.8%). Duration of ventilation, PaCO₂, and RSBI were significantly higher in cases with failed extubation than others. Body Weight, Glasgow Coma Scale, tidal volume, PaO₂, and PaO₂/FiO₂ were significantly higher with extubation success. PaCO₂ < 45 showed the highest sensitivity followed by RSBI, breaths/min/ml/kg < 7 for extubation success.

Conclusion

Based on the result of this study, failed extubation is more common in young children, in patients with respiratory illness, and those receiving prolonged mechanical ventilation. Close monitoring of oxygenation indices, and PaCO₂ can avoid hazardous premature extubation. PaCO₂ < 45 and rapid shallow breathing index with a threshold of < 7 breath/min/ml/kg are good predictors for extubation

success and dependable parameters for extubation timing in children.

Keywords

Risk factors; Failed extubation; Mechanical ventilation

Introduction

Invasive mechanical ventilation (IMV) is a frequently used tool of management for more than 30% of critically ill patients admitted at pediatric intensive care units.⁽¹⁾ Despite the universally accepted benefits of mechanical ventilation for children suffering from respiratory distress, invasive support is directly associated with a series of complications. Reduction of IMV time is essential to minimize the risk of these hazards such as airway damage and ventilator-induced pneumonia.⁽²⁾

On the other hand, premature extubation may require emergency reintubation⁽³⁾ and lead to respiratory failure and death.⁽⁴⁾ After resolving of the condition requiring intubation, the decision to extubate, followed by planned weaning should be undertaken as soon as possible to avoid delayed extubation.

Even after an extensive evaluation of potential extubation, however, 10% to 19% of patients fail extubation and require reintubation shortly after extubation.^(5,6) Risk factors of extubation failure include impaired muscle strength and gas exchange⁽⁷⁾ in addition to prolonged duration of mechanical ventilation⁽⁸⁾. Furthermore, disturbed level of consciousness and the inability to manage secretions may be etiological factors.⁽⁹⁾ Both failure to recognize the optimum time of extubation readiness and unsuccessful trials at extubation lead to prolonged length of stay, higher costs, and increased mortality.⁽⁷⁻⁹⁾

Identification of patients who may be successfully extubated can be done by extubation readiness tests where the child is placed on minimal ventilator settings and is observed for signs of distress or impaired gas exchange.⁽¹⁰⁾ It is important to assess the different factors that may predict the outcome of weaning.

This will be useful to shorten the duration of mechanical ventilation, reduce the risk of reintubation, improve the outcome, and provide clearer weaning guidelines.⁽⁹⁾ Like *Abdelnaser et al. Failed extubation in ICU pediatric patients*

other researchers,^(11,12) in addition to studying predictors of failed extubation, we tried to investigate the possible factors by which can predict extubation success as respiratory frequency-to-tidal volume (the rapid shallow breathing index), dynamic compliance, and arterial oxygenation parameters.

Material and Methods

A prospective cohort study was conducted from June 2019 to April 2021 at pediatric intensive care and post-operative critical care units of South Valley University Hospital in Qena Governorate.

The study included all patients aged between 1 month and 16 years who were admitted to the PICU, continued on MV for a time equal to or greater than 24 hours, be ready to undergo extubation, and followed up to 48 hrs after extubation. Exclusion criteria included all cases of unplanned extubation and patients with tracheostomy. Failed extubation was defined as the need for re-intubation within the first 48 hours after extubation and extubation success as the patient's ability to maintain spontaneous ventilation without respiratory support for 48 hours following extubation.

A total of 148 mechanically ventilated patients admitted to the pediatric ICU were eligible for the study. The factors affecting the timing of weaning and extubation include the patient's clinical condition, blood gas analysis, and parameters of ventilator support.

Demographic data collected at the time of extubation were the patient's age, weight, sex, admitting diagnosis, date of intubation, and extubation and coma scale. Modified Glasgow coma scale, which is Sharples' adaptation (personal communication) of the James' adaptation of the Glasgow coma scale (JGCS) was used to overcome the problem of intubation.

This score developed a grimace score to replace the verbal component in intubated children.⁽¹³⁾ Additional collected data were pre-extubation arterial blood gases, peak inspiratory airway pressure (PIP; cmH₂O), positive end-expiratory pressure (PEEP; cmH₂O), corrected exhaled tidal volume from mechanical ventilator breaths (vVt;

ml/kg), and inspired oxygen fraction concentration (FiO₂). Dynamic compliance (C_{dyn}, ml/kg/cm H₂O) was calculated using the formula: $vVt / (PIP - PEEP)$. The rapid shallow breathing index (RSBI breaths/ml/kg) was calculated as RR/sVt. Patients were assessed and examined daily, checking for the possibility of changing the initiated controlled ventilatory pressure mode to spontaneous breathing trial (SBT) using a T-tube (T-piece) or reducing the applied airway pressure to provide low levels of pressure support (PS) (5 to 10 cmH₂O).

Pressure support was set according to endotracheal tube size (for tube size of 3.0–3.5 mm, pressure support of 10 cmH₂O, for the size of 4.0–4.5 mm, pressure support of 8 cmH₂O, and for the size of 5.0 mm, pressure support of 6 cmH₂O).

The usual practice for SBT decision is the resolution of the condition that necessitated IMV, hemodynamic stability, and suitable ventilator parameters including Fio₂ < 50%, PIP < 20 cmH₂O, PEEP below 5 cmH₂O and respiratory frequency of ventilator rate 6 to 8 breath/min before extubation.

The primary physician considers a failure of SBT if any sign of poor tolerance appeared as increased respiratory rate or heart rate than normal value for a given age, signs of increased respiratory distress, diaphoresis, deteriorated mental status, hypotension, and oxygen saturation lower than 90% measured by a pulse oximeter or partial pressure of arterial carbon dioxide higher than 50 mmHg.

Before re-institution of mechanical ventilation for those, rescue noninvasive ventilation (rNIV) was tried through a full-face mask or oronasal mask to prevent the reimplementation of IMV. NIV failure was defined as the need for endotracheal intubation within the first 48 hours manifested by hemodynamic alterations, progression of respiratory distress non-invasive hypoxemia.

Patients were considered as having passed the SBT if there were no changes in any of the parameters assessed. The institutional ethics committee of our university approved the study and parents provided informed consent.

Statistical analysis

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Statistical analyses of the data collected from the two outcome groups (extubation success and failed extubation) were compared using SPSS version 20 for Windows. Continuous variables were expressed as mean \pm standard deviation, and categorical variables were expressed as frequency.

Pearson's chi-square was used for the comparison of categorical data between groups and t-test used for comparison of means.

A p value < 0.05 was considered statistically significant. The sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV) were calculated for each variable.

Pearson's correlation was used to assess the correlation between different variables and a logistic regression model was used for clinically relevant significant variables to assess the relative effect of risk factors on the outcome.

Results

Our study included 148 mechanically ventilated patients who met the inclusion criteria.

The general characteristics of the patients were reported in Table 1. Failed extubation was seen in 26 patients, corresponding to 17.5% of the total; 53.9% of them were less than one year and 26.9% were between one and five years while 19.2% were more than 5 years in contrast to the patients with successful extubation.

Of the patients with a failed extubation, respiratory illnesses were the principal cause of ventilation (50%) followed by cardiac surgery ventilated cases (23% each), neurological (15.4%), envenomation (7.7%), and lastly drug intoxication cases (3.8%). The use of sedatives > 5 days, duration of ventilation, length of hospital stay and mortality were significantly higher in cases with failed extubation than others with success.

Noninvasive ventilation was tried for cases of failed extubation who deteriorate and required reintubation and 11 of them succeeded and escaped MV.

Table 1. Demographic characteristics of ventilated patients.

Variable	Extubation success (n= 122)	Failed extubation (n= 26)	P value
Age (years)	8.07 ± 1.57	3.82 ± 1.90	<0.001
< 1 year	23(18.8%)	14(53.8%)	
>1y-<5y	25(20.4%)	7(26.9%)	
>5 years	74(60.8%)	5(19.3%)	
Indications for ventilation	Respiratory diseases	13(50%)	<0.05
	Cardiac surgery	13(10.7%)	6 (23%)
	Neurological	13(10.7%)	4 (15.4%)
	Envenomation	8(6.5%)	2(7.8%)
	Drug intoxication	3(2.5%)	1(3.8)
Sex (male/female)	65/57	12/14	NS
Weight (kg)	23.35 ± 2.91	14.24 ± 4.42	<0.001
Use of sedatives > 5 days	42/122 (34.4)	14/26 (53.8%)	<0.01
Use of inotropes > 5 days	51/122 (41.8%)	12/26(46%)	NS
Duration of ventilation (days)	6.63 ± 2.08	12.84 ± 2.27	<0.001
Length of hospital stay (days)	10.43 ± 1.72	16.30 ± 3.87	<0.001
Mortality	10 (8%)	6 (23%)	<0.01

Significant P value at P <0.05, NS; Non-Significant

Table 2 shows the comparison of pre-extubation parameters between patients with successful and failed extubations. The group of failed extubation showed significantly lower values of GCS, tidal volume, PaO₂, and CDYN, and higher PIP and PaCO₂ compared with the successful group. Pre-extubation spontaneous breathing parameters show a significantly lower ventilator respiratory rate, and spontaneous respiratory rate, and higher RSBI.

Table 2: Pre-extubation ventilation parameters

Variable	Extubation success (n= 122)	Failed extubation (n= 26)	P value
Ventilator respiratory rate breaths/min	8.95 ± 2.44	8.03 ± 1.45	<0.05
Glasgow Coma Scale	10.76 ± 1.23	8.12 ± 1.62	<0.05
Tidal volume	10.77 ± 4.87	7.92 ± 2.15	<0.05
PEEP cm H ₂ O	4.23 ± .86	4.38 ± .57	NS
PIP cm H ₂ O	21.27± 1.81	23.73± 1.61	<0.001
PH	7.39 ± 0.07	7.41 ± 0.06	NS
PaO ₂ mmHg	110.24 ± 19.27	91.42 ± 10.13	<0.001
PaCO ₂ mmHg	40.31 ± 3.75	45.88 ± 6.29	<0.001
(PaO ₂ /FiO ₂)	284.20 ± 87.16	185.23 ± 79.21	<0.001
CDYN mL/cmH ₂ O	0.59±0.24	0.38±0.12	<0.001
Spontaneous respiratory rate breaths/min	35.53 ± 11.48	54.26 ± 16.96	<0.001
RSBI breaths/min /ml/kg	3.17± 0.41	9.90± 1.14	<0.001

PEEP: Positive end-expiratory pressure; PIP.: Peak inspiratory pressure ; PaO₂: partial pressures of oxygen; PaCO₂: partial pressures of carbon dioxide; PaO₂/FiO₂ ratio PaO₂:FiO₂ = oxygenation ratio; CDYN: Dynamic Compliance; RSBI: rapid Shallow Breathing Index; significant P value<0.05 NS; Non Significant

In **Table 3** sensitivity, specificity and predictive values of weaning indices for successful extubation were shown. While PaCO₂ < 45 showed the highest sensitivity, RSBI < 7 breaths/min/ml/kg is a good predictor of weaning success.

Table 3: Predictive value of weaning indices for successful extubation

Variable	Threshold Value	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)
RR, breaths/min	<45	91	73	94	63.3
PaCO ₂ mmHg	<45	98	69	93.7	90
PaO ₂ /FiO ₂ ratio	>200	78.7	54.5	90.5	31.5
Tidal volume ml/kg	>5	82	23.8	82.6	18.5
RSBI, breaths/min/ml/kg	<7	96.7	80.7	95.9	84

RR: respiratory rate; PaCO₂: partial pressures of carbon dioxide; PaO₂/FiO₂ ratio: oxygenation ratio; RSBI: Rapid Shallow Breathing Index; PPV: positive predictive value; NPV: negative predictive value

Table 4 showed logistic regression analysis for predictors of extubation. It revealed a significant association between failed extubation and RR, PaCO₂, FiO₂/PaO₂, RSBI in addition to the duration of mechanical ventilation.

Table 4: Multivariate logistic regression analysis for predictors of failed extubation

Variable	Odds ratio	95% CI	P value	
Higher RR, breaths/min	>50	1.79	0.81-3.66	<0.01
Higher PaCO ₂	>50	2.49	1.36-8.96	<0.001
Lower PaO ₂ /FiO ₂ ratio	<200	1.98	0.91-4.84	<0.001
Higher RSBI breaths/min/ml/kg	>7	3.14	1.46-10.0	<0.001
MV duration (days)	>10	4.72	1.95-16.4	<0.001

RR: respiratory rate; PaCO₂: partial pressures of carbon dioxide; PaO₂/FiO₂ ratio: oxygenation ratio; RSBI: Rapid Shallow Breathing Index; MV: mechanical ventilation

Discussion

In the present prospective study, 17.5% of patients had failed extubation. This finding is consistent with previous studies in which the incidence of failed extubation ranged from 10 to 20%.^(6, 14, 15) Patients who were reintubated within 48 to 72 hours had higher mortality outcomes and longer ICU stays. The increased mortality rate after failed extubation may reflect the critical illness of the studied cases.⁽¹⁴⁾ Younger age and smaller body weight were associated with failed extubation and this agrees with those reporting that the smaller diameter of the upper airway at a younger age is responsible for the risk of failed extubation.⁽¹⁶⁾ Furthermore, we found that a prolonged time of mechanical ventilation is associated with failed extubation. Silva et al. in 2018,⁽¹⁷⁾ reported that MV time of greater than 7 days increased the risk of failed extubation by almost 4 times and this was consistent with Cruces et al., study which found that prolonged MV increased the

risk of failed extubation by almost 7 times compared to extubation success.⁽¹⁸⁾

Similar to previous studies,^(19, 20) we detected that patients with failed extubation had longer ICU stays compared to the extubation success group. Increased length of stay may be related to several factors. Firstly, delayed extubation is associated with an increased risk for ventilator-associated pneumonia. Secondly, the re-intubation may reflect the severity of underlying illness or result in complications during re-intubation that prolong hospital stay. Thirdly, delayed re-implementation of ventilatory support may cause more deterioration and new organ failure. All of these factors lead to the prolongation of ICU stays with its impact on increased costs and increased mortality.

It was appreciated that respiratory causes were the main reason for failed extubation in our study and this was similar to Siva et al.,⁽¹⁷⁾ where respiratory illness constituted 56.67% of cases of failed extubation. This finding is a usual reflection of the frequency of respiratory diseases as an indication for PICU admission in comparison to other indications. Like other researches,^(21, 22) patients with failed extubation were found to be of a lower coma scale than those who succeeded. They concluded that depressed mental status and brain dysfunction can contribute to failed extubation by impairing the capacity to protect the airway, as well as by causing hypoventilation.

We detected a highly statistically significant difference between the studied groups regarding PaO₂, PaCO₂, and PaO₂/FiO₂. This agreed with a study performed by Keyal et al.⁽²³⁾ that documented arterial blood gas analysis as a helpful tool in the identification of patients who can undergo failed extubation. In the study by Venkata Raman⁽²⁴⁾, an association was found between the oxygenation index and the risk of failed extubation. The failed extubation group showed a significant increase in respiratory

rate with a concomitant significant reduction in tidal volume as compared with the success group. Nemer and Barbas,⁽²⁵⁾ found similar results during studying the predictive parameters for weaning from mechanical ventilation.

Regarding RSBI, our results of significantly higher values ($p < 0.001$) in the failed group were matched with results published by Osman et al.,⁽²⁶⁾ Furthermore, hypercapnia was shown as the most sensitive predictor of failed extubation where PaCO₂ < 45 showed the highest sensitivity followed by RSBI, breaths/min/ml/kg < 7 which also was a good predictor of weaning success. This was in agreement with previous studies^(27, 28) that reported frank hypercapnia as a sign of weaning failure and milder hypercapnia a marker of increased risk for re-intubation. Patients extubated despite hypercapnia (PaCO₂ ≥ 45 mm Hg) had a higher rate of death due to respiratory failure, compared to patients who do not develop hypercapnia during spontaneous breathing test.⁽²⁷⁾

Higher RR, prolonged MV days, lower PaO₂/FiO₂ ratio, and higher RSBI, breaths/min/ml/kg were significantly correlated with extubation failure. These findings were comparable to several previous supporting studies.⁽²⁹⁻³¹⁾ Cases of failed extubation in our study were subjected to a trial of noninvasive ventilation hoping avoidance of IMV and 11 cases succeeded to avoid. Trevisan reported the NIV effectiveness following unsuccessful weaning trials especially if applied shortly after extubation⁽³²⁾ and Nava described that NIV decreased the need for tube reinsertion in cases developing respiratory failure following extubation⁽³³⁾. This finding encourages further future studies using NIV electively during weaning of mechanical ventilated children or directly after extubation.

The strength of the present study is demonstrated in that it was a prospective study and proposes cut-off points for some parameters that are being regularly used in PICU and help for extubation decisions as

PaCO₂ and RSBI. Also, the current prospective study was based on daily clinical practice allowing findings to be beneficial for clinical application for studied cases. Furthermore, despite the observational design, inclusion and MV re-implementation criteria were well defined following our ICU protocol. Several limitations of this study can be appreciated. First, the study was conducted in a single-center, a factor that limits the generalization of our results. Second is the small size of the study, hence a larger sampled study with a greater number of extubation failures potentially could have the power to identify other important risk factors. Lastly, the absence of studying the effect of anesthetic drugs used for cardiac surgery cases could be an important effector on GCS.

Conclusion

Prediction of extubation outcome is of potential importance because both extubation delay and unsuccessful extubation are associated with a poor outcome. Failed extubation is more common in young children, patients with respiratory illness, and those receiving prolonged mechanical ventilation. Duration of ventilation, length of hospital stay, PaCO₂ and RSBI were significantly higher in cases with failed extubation than others. Body Weight, Glasgow Coma Scale, tidal volume, PaO₂, and PaO₂/FiO₂ were significantly higher with extubation success. Close monitoring of oxygenation indices, and PaCO₂ can avoid hazardous premature extubation. PaCO₂ < 45 and rapid shallow breathing index with a threshold of 7 breath/min/ml/kg are dependable parameters for predicting the extubation timing in children. The use of rescue NIV had decreased the need for re intubation in some cases of failed extubation.

List of abbreviations

cdyn: Dynamic compliance

ERTs: Extubation readiness tests

FiO₂: fraction of inspired oxygen

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GCS: Glasgow coma scale

IMV: Invasive mechanical ventilation

JGCS: James' adaptation of the Glasgow coma scale

MV: mechanical ventilation

NIV: noninvasive ventilation

NPV: negative predictive value

PaCO₂: partial pressures of carbon dioxide

PaO₂: partial pressures of oxygen;

PaO₂/FiO₂ ratio: oxygenation ratio

PEEP: positive end-expiratory pressure

PICU: pediatric intensive care unit

PIP: peak inspiratory airway pressure

PPV: positive predictive value;

rNIV: rescue noninvasive ventilation

RR: respiratory rate

RSBI: rapid shallow breathing index

SBT: spontaneous breathing trial

vVt: tidal volume

Declarations:

- **Ethics approval and consent to participate:** this study was approved by the ethical committee of south valley university and consent was taken from parents for participation in the study and publication.

- **Availability of data and materials:** the datasets used and analyzed during the current study are available from the corresponding author on reasonable request.

- **Competing interests:** The authors declare that they have no competing interests. No support from any organization for the submitted work and no financial relations with any organizations.

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Authors contributions:

Mohamed Abdallah Abdelnaser performed the study, analyzed data, and co-wrote the paper. Khaled Abd Allah Abdel Baseer shared in study design, data

collection, co-wrote the paper. All authors read and approved the final version of the manuscript.

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