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Original Article

Predictors of Failed Extubation in Mechanically Ventilated Children: Single Center Experience

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Abstract:
Background: Extubation failure is failure to maintain normal spontaneous breathing after a period of mechanical ventilation with the need for reintubation within 24–72 hours. It has multiple risk factors such as deconditioned muscles, upper airway edema and others.
Aim of the Work: To study the frequency and causes of extubation failure in mechanically ventilated children.
Patients and Methods: This is an observational prospective study that included all admitted children in Pediatric Intensive Care Unit (PICU), Cairo University Children Hospital who underwent mechanical ventilation (MV) through endotracheal tube for more than 48 hours (145 child) with Glasgow coma scale above 8. They were subdivided into successfully extubated (78 children) and failed extubation (67 children).
Results: The mean ± SD age of the cohort was 13.5 ± 15.15 months (range1.3-48, median= 8 months). Of them 80 (55.17%) were males, and 65 (44.8%) were females. The commonest underlying diagnosis was pneumonia in 38 (26.2%), bronchial asthma in 32 (22%), encephalopathy in 32 (22%), and aspiration in 11 (7.58%). Failed extubation was encountered in 67 (46.2%) children. The encountered risk factors of extubation failure were: sedation in 12 (16.7%) (p=0.001), excessive tracheal secretion of more than 200 ml /24 h in 14 (18.7%) (p=0.03), accidental extubation in 27 (40.3%) (p=0.01) and the need for higher setting on MV in all 67 children with failed extubation. Among failed extubated patients, the mean± SD for peak inspiratory pressure (PIP), positive end-expiratory pressure (PEEP), and fraction of inspired oxygen (FiO_2) were 14.5± 1.8 /cm H2O, 5.5± 0.5/cm H_2O, and 27.5± 6.1% respectively. While, PIP, PEEP, and FiO_2 in the successfully extubated group were 12.8± 1.6 /cm H_2O, 4.1± 0.4/cm H_2O, and 24.8± 5.3%, (p= 0.01, p=0.001 and p= 0.001) respectively. Patients who underwent gradual withdrawal of ventilatory support had a higher frequency of successful extubation than those extubated accidentally (p= 0.01). Sensitivity, and specificity of above mentioned indices for successful extubation were 53.79%, and 28.72% respectively.
Conclusion: Causes of extubation failure are the need for long duration of sedation, excessive tracheal secretion, and need for high setting on MV. Furthermore, gradual weaning decreases the frequency of extubation failure. There is a need for a more sensitive and specific comprehensive objective indicator(s) for successful timely extubation.

Level of Evidence of Study: IV (*1*).
Keywords: Extubation failure; mechanical ventilation; ventilation weaning; children.
Abbreviations: ABG: arterial blood gases; bpm: breath per minute; CVP: central venous pressure; DCL: disturbed conscious level; DKA: diabetic ketoacidosis; EF: extubation failure; ETT: endotracheal tube; FiO_2: fraction of inspired oxygen; FB: foreign body; GBS: Guillain-Barre syndrome; ICU: Intensive care unit; K: Serum potassium; MIP: Maximum inspiratory pressure; MV: mechanical ventilation; OSI: oxygen saturation index; P0. 1: occlusion pressure; PICU: Pediatric intensive care unit; PO4: serum phosphorus; PIP: peak inspiratory pressure; PEEP: Positive end-expiratory pressure; SBT: spontaneous breathing trial; SMA: spinal muscle atrophy; SpO_2: Oxygen saturation; VE: Minute ventilation ; VT: tidal volume.

Introduction

Almost 24-60% of admitted patients to pediatric intensive care (PICUs) need mechanical ventilation (MV) (*2*). Liberation from MV is called the weaning process, in which reduction of respiratory support should be made gradually and steadily over a duration almost 40-50% of the total duration of MV to allow the patient to take his spontaneous breath independently (*3–5*). At removal of the endotracheal tube i.e. extubation, the patient must be assessed carefully to determine whether he can breathe spontaneously. Specific measures for successful extubation are mandatory, including the ability to protect the airway and the management of secretions (*6*). Extubation failure (EF) represents a specific condition at which reintubation and MV must be restored and usually occur within the first 24–72 h after endotracheal tube removal (*7*). Many factors may influence extubation failure, such as deconditioned muscles, upper airway edema, inability to clear secretions, and decreased consciousness level due to persistent effects of sedatives and analgesics (*8*). Extubation failure has been independently associated with increased mortality and prolonged hospitalization (*9*). Therefore, identifying risk factors associated with extubation failure may help reduce the duration of mechanical ventilation and improve outcomes. Several criteria, such as maximum inspiratory pressure (MIP), minute ventilation (VE), rapid shallow breathing index, and tidal volume (VT), respiratory rate (*8*, *10*) are often used as indicators for extubation. Other parameters may also aid in making the decision of extubation, such as: occlusion pressure (P 0.1), work of breathing, esophageal pressure, transdiaphragmatic pressure, electro-myographic activity of diaphragm, and physiological dead space (*11*).

We aimed to study the frequency and causes of extubation failure in mechanically ventilated children in our unit.

Subjects and Methods

This observational prospective study was carried out in the PICU in Cairo University Children Hospital over a period of 6 months. The research was approved by the Faculty of Medicine, Cairo University Health Ethics Review Board (IRB Approval Number: MS371-2019). The study conforms with the Code of Ethics of the World Medical Association (Declaration of Helsinki) for experiments involving humans (*12*).

Participants

This study included consecutive 145 critically ill patients admitted to PICU with acute hypoxemic respiratory failure who were ventilated for more than 48 hours. Only those with a Glasgow Coma Scale of> 8 were included. Of those with neurological disease only acute cases of Guillain-Barre syndrome were included, while we excluded others who were previously diagnosed with chronic neuromuscular disorder in need of more than 21 days of mechanical ventilation, as spinal muscle atrophy.

Methods

Data were collected 24 hours prior to spontaneous breathing trials. All children underwent spontaneous breathing trial (SBT) for 48 hours prior to extubation. For all cases, demographic data were analyzed, including age, gender, detailed medical history, and examination findings. In addition, diagnosis on admission, cause of ventilation, duration of ventilation, modes and settings of MV before extubation, number of extubation trials, level of consciousness, inotropic support if present, tracheal secretion volume, and fluid balance (calculated as fluid input minus output over 24 hours). Pulmonary indices (oxygen saturation index (OSI) were calculated for all patients and recorded using the following equation MAP x FiO_2 x 100/SpO_2 (*13*). Calculated OSI for mild, moderate, and severe ARDS are 5->7.5, 7.5-<12.3 and >12.3 respectively.

The SBT was based upon achievement of the following parameters: respiratory rate (RR) according to age (20-60 breath per minute (bpm) < 6 months; 15-45 < 2 years; 15-40 < 5 years; 10-35 > 5 years); tidal volume (VT of 6-8ml/kg); the assessments of vital signs (with goals of age related heart rate, respiratory rate, and systolic blood pressure); ventilator criteria (PEEP ≤ 5 cmH_2O, pressure support ≤ 10 cmH_2O and FiO_2 ≤ 40%); and calculated OSI<5.

The data collected post-extubation were the frequency of extubation failure, and causes of extubation failure. Extubation failure was considered if their was inability to maintain spontaneous breathing after a period of mechanical ventilation and the need arises for reintubation within 24–72 h [4]. Chest X-ray findings and laboratory investigations (blood gases and serum levels of K and PO_4) before and after extubation were collected.

Statistical Analysis

The data were analyzed using Microsoft Excel 2016 and the Statistical Package for Social Sciences (SPSS) version 26 (IBM Corp., Armonk, N.Y., USA). The mean ± standard deviation

(SD) was used to demonstrate the continuous, normally distributed variables. Moreover, the median with 25% and 75% was used to represent the non-normal variables, and the frequencies and percentages were used for categorical variables. A p-value < or = 0.05 was considered statistically significant. The Student's t-test was performed to compare the means of normally distributed variables between groups, and the Mann-Whitney U test was used for non-normal variables. The Chi-squared test or Fisher's exact test were used to determine the significance of categorical variables between groups. The diagnostic power of ventilatory setting in croup and other causes with failed extubation was evaluated by the receiver operating characteristic (ROC) curve.

Results

Demographics and clinical characteristics of the studied group:

The study included 145 patients whose age mean ± SD was 13.5 ± 15.15 and was (range1.3-48, median 8 months). Of them 80 (55.17%) were males, and 65 (44.8%) were females. The commonest underlying diagnosis was pneumonia in 38 (26.2%) cases, bronchial asthma in 32 (22%), encephalopathy (with GCS>8) in 32 (22%), and aspiration in 11 (7.58%). Only 25 (17.2%) patients were on assisted control mode while 120 (82.7%) were on synchronized intermittent mandatory ventilation. The mean ± SD duration of mechanical ventilation was 4.8±4.7 days (range=0.5-30, median= 3 days), and of the duration of weaning from mechanical ventilation was 2.4± 2.3 days (range=0.5-15, median= 1 day). Failed extubation was encountered in 67 (46.2%) children. Clinical characteristics of the studied group are shown in tables 1 and 2. The successfully extubated group had a mean ± SD age of 12.3 ±17.5 months (range= 1.3-36, median= 9.5months), of them 33 (42%) were females, and 45 (57.7%) were males. The failed extubation group had a mean ± SD age of 12.8 ±12.4 months (range= 1.3-48, median= 7.5 months), of them 32 (47.7%) were females, and 35 (52.2%) were males. There was no significant difference in age and gender distribution between both groups (p=0.2) and (p= 0.5) respectively. (Table 1).

Table 1. Demographics and clinical characteristics of the studied group of 145 mechanically ventilated children.

	Cohort N=145		Successfully extubated N=78		Failed extubation N=67		P-value
Age (months)							
Range	1.3-48		1.3-36		1.3-48		0.2
Mean	13.6		14.3		12.8		
SD	15.15		17.5		12.4		
Median	8		9.5		7.5		
Duration on MV (days)	4.8±4.7		4.8 ± 6.3		4.6 ± 2.6		0.4
MV weaning duration of (days)	2.4± 2.3		2.4 ±3.2		2.3±1.3		0.4
	Number	%	Number	%	Number	%	
Gender							
Males	80	55.1	45	57.7	35	52.2	0.5
Females	65	44	33	42.3	32	47.7	0.5
Diagnosis							
Pneumonia	38	26.2	18	23.1	20	29.8	0.2
DCL (GCS>8)	32	22	15	19.5	17	25 .3	0.2
Bronchial asthma	32	22	15	15.4	17	25.3	0.2
Aspiration	11	7.58	9	11.5	2	2.9	0.05
ARF	3	2	3	3.8	0	0.00	0.1
GBS	6	4	6	7.7	0	0.0	0.8
DKA	3	2	3	3.8	0	0.0	0.1
Others*	20	14	12	15.4	8	11.9	0.4
MV mode							
A/C mode	25	17.2	12	15.4	12	18	0.6
SIMV mode	120	82.7	66	84.6	55	82	

*Others includes: Fallot tetralogy with cyanotic spell, hydrocephalus, Post Kasai biliary atresia, metabolic acidosis, and foreign body aspiration. A/c mode: Assisted control mode; ARF: Acute renal failure; DCL: disturbed conscious level; DKA: Diabetic ketoacidosis; GBS: Guillain barre syndrome; GCS: Glasco coma scale; MV: mechanical ventilation; SIMV mode: synchronized intermittent mandatory ventilation.

The successfully extubated group had a mean ± SD age of 12.3 ±17.5 months (range= 1.3-36, median= 9.5months), of them 33 (42%) were females, and 45 (57.7%) were males. The failed extubation group had a mean ± SD age of 12.8 ±12.4 months (range= 1.3-48, median= 7.5 months), of them 32 (47.7%) were females, and 35 (52.2%) were males. Foreign body aspiration had a highly successful extubation rate (p= 0.05), where 9 (11.5%) patients were successfully extubated compared with 2 (2.5%) patients whose extubation failed. (Table 1).

Patients who presented with pneumonia, encephalopathy, bronchial asthma, acute renal failure and Guillain Barre syndrome showed no significant difference as regards the failure rate of extubation (p=0.2), (p=0.2), (p=0.2), (p=0.8) and (p=0.1) respectively. (Table 1).

Risk factors for extubation failure:

Many risk factors contributed to failed extubation; continuous sedation in 12(16.7%) (p=0.001), excessive tracheal secretion >200ml in 30 (23%) (p=0.03), accidental extubation in 27(40.3%) (p=0.01) and higher ventilatory setting in 67(100%), namely: the mean± SD for PIP, PEEP, and FiO_2 were 14.5± 1.8 /cm H_2O, 5.5± 0.5/cm H_2O, and 27.5± 6.1%, respectively (p=0.01), (p=0.001), and (p=0.001) respectively. On the other hand, PIP, PEEP, and FiO_2 in successfully extubated patients were 12.8± 1.6 cm H_2O, 4.1± 0.4cm H_2O, and 24.9± 5.3% respectively (p=0.01), (p=0.001), and (p=0.001) respectively. (Figure 1).

The 12(16.7%) on continuous sedation on MV and the 30 (23%) with the excessive tracheal secretion of more than 200 ml/24 hours had a high extubation failure rate (p=0.001) and (p=0.03) respectively. (Table 2). No significant difference was found between both groups as regards the serum electrolytes (p=0.2), ABG before (p=0.1), or after extubation (p=0.4), or fluid balance (p=0.6). A shorter duration of length of stay on MV was associated with more successful extubation (p=0.05). (Table 2).

Table 2. Risk factors for failed extubation in our studied cohort.

		Successful extubation	Failed extubation	P value
Length of stay on MV(<7)days		69 (88.5%)	57 (77.6%)	0.05
Length of stay on MV>7days		9 (11.5%)	15 (20.8%)	0.05
PIP (cmH_2O)		12.8±1.6	14.5±1.8	0.01
PEEP (cmH_2O)		4.1±0.4	5.5±0.5	0.001
FiO_2%		24.9±5.3	27.8±6.1	0.001
OSI		2.5±1.8	3.3±1.8	0.01
Conscious		75 (96.2%)	60 (83%)	0.01
Continuous sedation		3 (3.8%)	12 (16.7%)	0.001
Tracheal secretion ml/24hr		50.0 (20.0- 100.0)	70.0 (30.0- 200)	0.03
Fluid balance over 24hr		-90.0 (-140.0- 130.0)	-57.0 (-125.0- 119.0)	0.6
Serum K(mmol\L)		3.9±0.5	4.0±0.4	0.2
Serum PO4 (mg\dl)		4.4 (4.1- 4.7)	4.2 (4.0- 4.8)	0.2
Inotropic support	yes	3 (3.8%)	3 (4.2%)	0.6
	no	75 (96.2%)	69 (95.8%)	0.6
ABG before extubation				
PH (mmHg)		7.4±0.1	7.4±0.1	0.1
PCO_2 (mmHg)		44.6±5.8	43.8±8.1	0.5
HCO_3 (mmHg)		24.0 (20.9- 26.0)	21.8 (20.0- 23.6)	0.06
ABG after extubation				
PH (mmHg)		7.4±0.1	7.3±0.1	0.4
PCO_2 (mmHg)		44.0±5.5	44.2±9.7	0.8
HCO_3 (mmHg)		23.0 (22.0- 27.2)	18.9 (17.6- 24.0)	0.1

ABG: Arterial blood gases; FIO_2: fraction of oxygen; MV :mechanical ventilation; OSI: oxygen saturation index; PIP: peak inspiratory pressure; PEEP: positive end expiratory pressure.

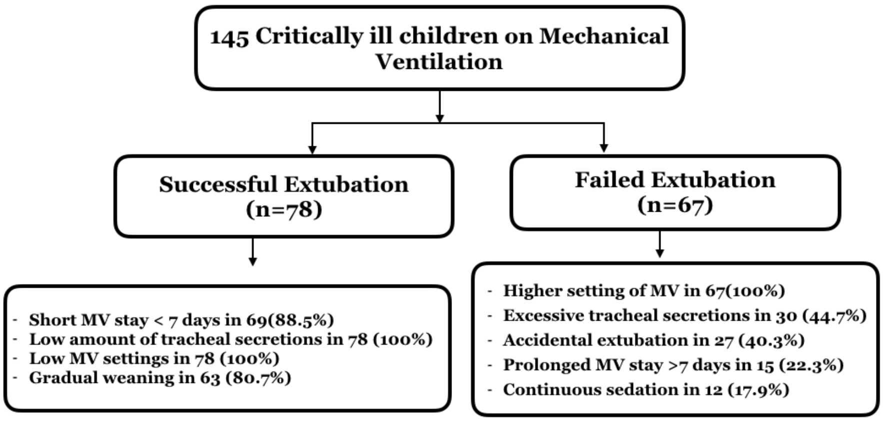

Figure 1. Associations of extubation outcome in our studied cohort.

Cut off value for ventilator settings for the failed extubation group:

The sensitivity and specificity of relying on PIP of > 13 cmH_2O as a cut off to predict failure of extubation were 58.6%and 62.1%, respectively, PEEP of > 5.5 cmH_2O were 58.6% and 100%, respectively and FiO_2 of > 25.5% were 69% and 93.1%, respectively (Table 3).

Table3. Cut off value for ventilator settings for the failed extubation group.

	Cut off point	The area under the curve	95 % confidence interval	Sensitivity	Specificity
PIP (cmH_2O)	13	0.603	0.456-0.750	58.6%	62.1%
PEEP (cmH_2O)	5.5	0.793	0.672-0.915	58.6%	100%
FiO_2%	25.50	0.820	0.706- 0.934	69%	93.1%

FIO_2: fraction of oxygen; PIP: peak inspiratory pressure; PEEP: positive end expiratory pressure

Causes of reintubation:

The most frequent causes of reintubation encountered in this study were laryngeal edema among 31(46.3%) patients, followed by encephalopathy 13 (19.4%), then excessive secretion 12 (17.9%), and hemodynamic instability in 11 (16.4%) (Table 4).

The present study revealed that patients who underwent gradual weaning 63 (80.7%) according to extubation protocol, had a highly successful extubation rate (p =0.01), and those with accidental and unplanned extubation 27(40.3%) had a significantly high extubation failure rate (p value = 0.01). (Figure 2).

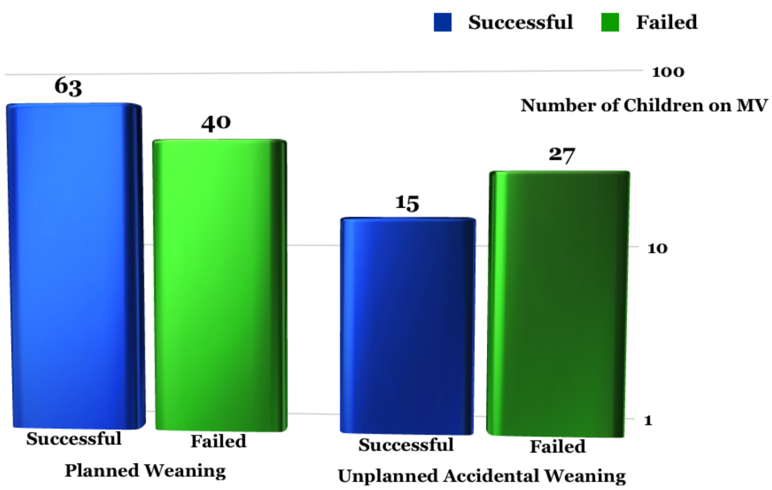

Figure 2. Accidental extubation outcome in our studied cohort.

Rate of extubation failure trial:

In this study, the first time of extubation failed in 42 (62.6%) patients, then the second time for re-intubation failed 19 (28.4%)patients, and the third time trial failed 6 (8.2%) patients. Sensitivity and specificity of our protocol in extubation were 53.79% and 28.72% respectively.

Table 4. Causes of reintubation among our studied cohort.

Causes of extubation failure (Total number= 67)	Number	%
Laryngeal edema	31	46.3
Encephalopathy	13	19.4
Excessive chest secretions	12	17.9
Hemodynamic instability	11	16.4

Encephalopathy causes: hypertensive encephalopathy, hepatic encephalopathy, neurological insult.

Discussion

Indicators for mechanical ventilation weaning and extubation aim to achieve successful extubation (*7*). Many risk factors contributed to failed extubation in our current study; as continuous sedation, excessive tracheal secretion, accidental extubation and higher ventilatory settings.

Our single center study results indicate high extubation failure rate. We rely upon respiratory rate (RR); tidal volume, the assessments of vital signs, ventilator criteria (PEEP $\leq$ 5 cmH_2O, pressure support $\leq$ 10 cmH_2O and FiO_2 $\leq$ 40%); and calculated OSI<5 for weaning and extubation. These indices had modest sensitivity, and specificity of extubation of 53.79% and 28.72% respectively. They were correct in predicting successful extubation in only half the cases, hence more objective indicators are needed to achieve more success of extubation. We did not study the effect of assessment of cuff leak test, cough reflex, lung mechanics (volume, compliance, resistance), diaphragm thickening fraction, diaphragmatic excursion and lung ultrasound score as indices for weaning and extubation.

The preventable commonest cause of failed extubation was accidental extubation. Our study showed that the patients who underwent gradual weaning had a highly successful extubation rate compared to those who extubated accidentally. There are many contributing factors for accidental extubation e.g. patient agitation, inappropriate handling of patients during performance of procedures and inappropriate positioning and fixation of endotracheal tube. All are potentially preventable risk factors, and in turn lead to high extubation failure rate.

Strict measures should be taken to lower the frequency of accidental extubation as much as possible to lower the rate of extubation failure. In addition, proper assessment of the patients who accidentally extubate. Reintubation as early as possible should be taken into consideration if the patients do not fulfill the criteria for extubation. The only benefit for successfully tolerated unplanned extubation is unintentional decrease in the duration of weaning trials, as it has no other measurable beneficial impact on outcome (*14*).

The prolonged use of sedation was another risk factor of failed extubation in our study. The prolonged use of sedation seems possible to control, or fine tune to achieve more successful smooth extubation. Especially that evidence supports that comfort during MV can be achieved with no or very light sedation, and this is associated with lower incidences of delirium, and shorter length of stay (*15*), and there is no difference between deeply sedated patients and those not deeply sedated regarding extubation success (*16*). More research is needed to assess the minimum effective dose, duration, methods of administration whether continuous or interrupted and decrease its empirical unnecessary use as in encephalopathic patients, as it may be of value to decrease the frequency of extubation failure.

Chest care and toilette is an essential component in MV care, which include session of nebulizer followed by percussion and vibration then suction after flushing the endotracheal tube with normal saline and its implementation to address the amount of secretions more than 200cc/24 hours seems to be an important factor to reduce the failed extubation. No proof that a semi-quantitative airway care score (ACS) comprising six parts: spontaneous cough, gag, sputum quantity, sputum viscosity, suctioning frequency and sputum character in brain injured patients was found effective in prevention of failure of extubation (*17*). Hence, more research is needed to define an effective chest toilette that achieves successful extubation.

Assessment of the hydration status of the patients is necessary as dehydration is known to increase the viscidity of secretions, decrease ciliary movement, that increase duration of weaning (*18*). Control of cough reflex and amount of tracheal secretion is important to decrease the reintubation.

High ventilatory setting i.e. high-pressure support (PIP and PEEP) with a high pulmonary index (e.g. OSI) may lead to a volutrauma in which ultra-structural lung injury is occurring because of using high pressure support. Our study supports close follow-up of ventilatory settings to avoid complications and decrease the extubation failure rate (*19*).

Duration of mechanical ventilation is very much related to the indication and rate of improvement of the ventilated child (*20*). Antibiotics, fluids and management of other system affection are all crucial factors in reducing the MV duration and procuring the better extubation. We did not study the effect of nutritional status on the success of extubation, but it is logical to consider that a healthier child would improve in a shorter duration.

Further research is needed to create a new extubation scoring system based on more individualized and non-invasive objective predictors. We have not assessed sensitivity and specificity of other extubation readiness scores (*20*), yet, every effort should be made to introduce effective MV strategies. Neurally adjusted ventilatory assist (NANA) might prove helpful in gradual weaning of patients with a well-trained respiratory therapist (*21*).

Our study had its limitations, we did not study the effect of nutritional status of the patients, their BMI, their enteral feeding cardiac dysfunction, deconditioned muscle effect and the medications prior to extubation.

Conclusions

The most common causes of extubation failure are continuous sedation, excessive tracheal secretion, high ventilatory settings on MV and accidental extubation. Furthermore, research is needed to create a new extubation scoring system based on more individualized and non-invasive objective predictors.

Author Contributions: All authors searched medical literature, databases, conceptualized, conducted the case review and reviewed the final manuscript. All authors have read and agreed to the published version of the manuscript.

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CONFLICT OF INTEREST

The authors declare no conflict of interest in connection with the reported study. Authors declare veracity of information.

References

1. S. Tenny, M. Varacallo, *Evidence Based Medicine.* (StatPearls Publishing; Treasure Island (FL), 2020; https://www.ncbi.nlm.nih.gov/books/NBK470182/).
2. B. Mukhtar, N. R. Siddiqui, A. Haque, Clinical Characteristics and Immediate-Outcome of Children Mechanically Ventilated in PICU of Pakistan. *Pak J Med Sci.* **30**, 927–930 (2014).
3. A. Esteban, N. D. Ferguson, M. O. Meade, F. Frutos-Vivar, C. Apezteguia, L. Brochard, K. Raymondos, N. Nin, J. Hurtado, V. Tomicic, M. González, J. Elizalde, P. Nightingale, F. Abroug, P. Pelosi, Y. Arabi, R. Moreno, M. Jibaja, G. D'Empaire, F. Sandi, D. Matamis, A. M. Montañez, A. Anzueto, Evolution of Mechanical Ventilation in Response to Clinical Research. *Am J Respir Crit Care Med.* **177**, 170–177 (2008).
4. C. Egbuta, F. Evans, Weaning from ventilation and extubation of children in critical care. *BJA Education.* **22**, 104–110 (2022).
5. B. Schönhofer, J. Geiseler, D. Dellweg, H. Fuchs, O. Moerer, S. Weber-Carstens, M. Westhoff, W. Windisch, Prolonged Weaning: S2k Guideline Published by the German Respiratory Society. *Respiration.* **99**, 982–1084 (2020).
6. L. P. Ferguson, B. K. Walsh, D. Munhall, J. H. Arnold, A spontaneous breathing trial with pressure support overestimates readiness for extubation in children: *Pediatric Critical Care Medicine.* **12**, e330–e335 (2011).

7. Ramadan N.N., Reda S.M., Al-Sawah A.Y., Aboud M.A., Arafa R.S., Abdo A.M., Difficult Weaning From Mechanical Ventilation In Pediatric Intensive Care Unit. *Al-Azhar Journal Of Pediatrics*. **21**, 1918–1933 (2018).
8. R. G. Khemani, T. Sekayan, J. Hotz, R. C. Flink, G. F. Rafferty, N. Iyer, C. J. L. Newth, Risk Factors for Pediatric Extubation Failure: The Importance of Respiratory Muscle Strength*. *Critical Care Medicine*. **45**, e798–e805 (2017).
9. S. Chawla, G. Natarajan, M. Gelmini, S. N. J. Kazzi, Role of spontaneous breathing trial in predicting successful extubation in premature infants: Spontaneous Breathing Trial Premature Infants. *Pediatr. Pulmonol.* **48**, 443–448 (2013).
10. M. Karthika, F. Al Enezi, L. Pillai, Y. Arabi, Rapid shallow breathing index. *Ann Thorac Med*. **11**, 167 (2016).
11. P. A. F. Magalhães, C. A. Camillo, D. Langer, L. B. Andrade, M. do C. M. B. Duarte, R. Gosselink, Weaning failure and respiratory muscle function: What has been done and what can be improved? *Respiratory Medicine*. **134**, 54–61 (2018).
12. World Medical Association, WMA Declaration of Helsinki- Ethical Principles for Medical Research Involving Human Subjects (2013), (available at https://www.wma.net/policies-post/wma-declaration-of-helsinki-ethical-principles-for-medical-research-involving-human-subjects/2013/).
13. H. K. Muniraman, A. Y. Song, R. Ramanathan, K. L. Fletcher, R. Kibe, L. Ding, A. Lakshmanan, M. Biniwale, Evaluation of Oxygen Saturation Index Compared With Oxygenation Index in Neonates With Hypoxemic Respiratory Failure. *JAMA Netw Open*. **2**, e191179 (2019).
14. S. K. Epstein, M. L. Nevins, J. Chung, Effect of Unplanned Extubation on Outcome of Mechanical Ventilation. *Am J Respir Crit Care Med*. **161**, 1912–1916 (2000).
15. The Sedation Practice in Intensive Care Evaluation (SPICE) Study Group investigators, Y. Shehabi, L. Chan, S. Kadiman, A. Alias, W. N. Ismail, M. A. T. I. Tan, T. M. Khoo, S. B. Ali, M. A. Saman, A. Shaltut, C. C. Tan, C. Y. Yong, M. Bailey, Sedation depth and long-term mortality in mechanically ventilated critically ill adults: a prospective longitudinal multicentre cohort study. *Intensive Care Med*. **39**, 910–918 (2013).
16. J. M. Schultheis, T. S. Heath, D. A. Turner, Association Between Deep Sedation from Continuous Intravenous Sedatives and Extubation Failures in Mechanically Ventilated Patients in the Pediatric Intensive Care Unit. *The Journal of Pediatric Pharmacology and Therapeutics*. **22**, 106–111 (2017).
17. J. Haruna, H. Tatsumi, S. Kazuma, A. Sasaki, Y. Masuda, Frequent tracheal suctioning is associated with extubation failure in patients with successful spontaneous breathing trial: a single-center retrospective cohort study. *JA Clin Rep*. **8**, 5 (2022).
18. A. E. Tilley, M. S. Walters, R. Shaykhiev, R. G. Crystal, Cilia Dysfunction in Lung Disease. *Annu. Rev. Physiol.* **77**, 379–406 (2015).
19. C. Toida, T. Muguruma, M. Miyamoto, Detection and validation of predictors of successful extubation in critically ill children. *PLoS ONE*. **12**, e0189787 (2017).
20. M. L. Lourenção, W. B. de Carvalho, Pediatric ventilation weaning. *Revista Brasileira de Terapia Intensiva*. **32** (2020), doi:10.5935/0103-507X.20200061.
21. P. Sugunan, O. Hosheh, M. Garcia Cusco, R. Mildner, Neurally-Adjusted Ventilatory Assist (NAVA) versus Pneumatically Synchronized Ventilation Modes in Children Admitted to PICU. *JCM*. **10**, 3393 (2021).