A spontaneous breathing trial with pressure support overestimates readiness for extubation in children

Lee P. Ferguson, MBChB; Brian K. Walsh, RRT-NPS; Daphne Munhall, RRT-NPS; John H. Arnold, MD

Objective: **To evaluate the performance of an extubation readiness test based on a spontaneous breathing trial using pressure support.**

Design: **Retrospective chart review.**

Setting: **Pediatric intensive care unit.**

Patients: **All infants and children admitted to the pediatric intensive care unit requiring intubation from July 2007 to December 2008 were eligible for this study.**

Interventions: **Routine use of an extubation readiness test using pressure support set according to endotracheal tube size to determine completion of weaning and readiness for extubation.**

Measurements and Main Results: **A total of 755 extubation readiness tests were performed in 538 patients with a pass rate of 83%. Of 500 children who passed the extubation readiness test and were extubated without planned noninvasive ventilation use, the extubation failure rate was 11.2% (5.8% required reintubation). Extubation failure was defined as need for noninvasive ventilation or reintubation within 24 hrs of planned extubation. Logistic regression analysis revealed a significant association between duration of mechanical ventilation and extubation failure. Children ventilated for over 48 hrs had an 18.5% failure rate despite passing an extubation readiness test before extubation and the extubation readiness test was not a significant predictor of extubation success. Most extubation failures were the result of inadequate gas exchange attributable to lower respiratory tract dysfunction.**

Conclusions: **A spontaneous breathing trial using pressure support set at higher levels for smaller endotracheal tubes overestimates readiness for extubation in children and contributes to a higher failed extubation rate. The objective data obtained during an extubation readiness test may help to identify patients who will benefit from extubation to noninvasive ventilation. (Pediatr Crit Care Med 2011; 12:e330–e335)**

KEY WORDS: extubation readiness test; spontaneous breathing trial; weaning; children

Although mechanical ventilation may be a lifesaving intervention, it can be associated with complications such as nosocomial pneumonia, ventilator-induced lung injury, sedative dependency, and upper airway injury (1). It is important that patients should be extubated as soon as the reasons for intubation and mechanical ventilation have resolved and the patient is capable of sustaining spontaneous ventilation.

Many children do not require gradual weaning and can successfully extubate after a spontaneous breathing trial (2, 3). In the majority of pediatric intensive care units (PICUs), the decision to extubate relies on clinical judgment without routine measurement of pre-extubation respiratory mechanics (4). Although overall extubation failure rate is typically <10% in most PICUs, the failure rate is significantly higher in patients intubated for >10 days and in those with pre-existing respiratory or neurologic conditions (4). Children failing extubation have longer intensive care and hospital stays, greater hospital costs, and increased mortality rate (3, 4). Most failures take place within the first 12 hrs after extubation (4).

An accurate predictor of successful weaning and extubation would likely shorten duration of ventilation, decrease length of intensive care unit stay, and reduce morbidity from unsuccessful extubation attempts. In 2002, a study by Randolph et al (2) developed an extubation readiness test (ERT) to identify eligible patients for inclusion in a randomized trial of weaning strategies in children with acute respiratory failure. Subsequently in our PICU, unless meeting an exclusion criterion, children and infants undergo an ERT with a spontaneous breathing trial (SBT) using a pressure support set according to endotracheal tube size before extubation. The test has been used consistently by all respiratory therapists and attending physicians in our unit to guide timing of extubation.

The primary goal of this study was to assess the value of routine application of an ERT in predicting extubation success in a large unselected cohort of critically ill children. The secondary goal of the study was to evaluate the association between ERT and the use of planned noninvasive ventilatory support on extubation.

MATERIALS AND METHODS

This retrospective study was approved by the institutional review board of Children's Hospital, Boston. All patients aged <19 yrs who were admitted to the 29-bed medical–surgical pediatric intensive care unit from July 2007 to December 2008 and underwent mechanical ventilation through an endotracheal tube were included. The unit provides critical care services to all infants and children except those after cardiac surgery. The ERT has been used as part of the routine care of all intubated children since 2002.

Extubation Readiness Test. Attending physicians and respiratory therapists were encouraged to perform an ERT daily on all intubated patients with spontaneous respiratory effort who required F_{IO_2} of ≤0.5 and who had not required escalation in ventilator support

From the Division of Critical Care Medicine, Department of Anesthesia, Children's Hospital, Boston, MA.

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For information regarding this article, E-mail: lee.ferguson7@nuth.nhs.uk

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in the last 6 hrs. Compliance with performance of a daily ERT was enhanced by its inclusion in a bedside checklist that was completed on morning rounds. All patients underwent testing before extubation unless meeting an exclusion criterion.

Patients were excluded from testing if there was a plan to extubate to noninvasive ventilatory support either as a result of chronic use before the PICU admission or at the discretion of the attending physician based on the likely trajectory of the patient's course. Newborns with congenital diaphragmatic hernia, children with unrepaired or palliated cyanotic congenital heart disease, or with single ventricle physiology, or in whom a decision to withdraw or limit life support was in place were also excluded.

The ERT was based on the spontaneous breathing trial described by Randolph et al (2). Our test involved changing the F_{IO_2} to 0.5 (left at current setting if already <0.5 with saturation by pulse oximetry ≥95%) and decreasing positive end-expiratory pressure to 5 cm H_2O. The ventilator mode was changed to pressure support ventilation in patients with spontaneous respiratory effort and able to maintain saturations ≥95%. Pressure support was set according to endotracheal tube (ETT) size (3.0–3.5 mm = pressure support of 10 cm H_2O, 4.0–4.5 mm = pressure support of 8 cm H_2O, ETT ≥5.0 = pressure support of 6 cm H_2O). Patients were monitored during the test for 2 hrs and were classified as failing the test if at any time in the 2-hr period their exhaled tidal volume was <5 mL/kg body weight, SpO_2 <95%, respiratory rate was outside of acceptable range for their age (for age <6 months, 20—60/min; 6 months to 2 yrs, 14–45/min; 2–5 yrs, 14–40/min; >5 yrs, 10–35/min), there was hypoventilation resulting from sedation or neurologic impairment, or there was excessive work of breathing based on physician assessment (marked retractions, diaphoresis, or nasal flaring).

All patients were managed with flow-triggered pressure support during performance of the ERT (Avea ventilator; CareFusion Corp, San Diego, CA). Both the trigger and flow termination were set to optimize patient–ventilator synchrony by the respiratory therapist at the start of the ERT. In patients <10 kg, tidal volume was measured with a pneumotachometer at the endotracheal tube (COSMO Plus; Novametrix Medical Systems Inc, Wallingford, CT). In larger patients, tidal volume was measured at the exhalation valve with automatic compensation for the compressible gas volume. Patients in whom excessive endotracheal tube leak precluded pressure support ventilation as a result of autotriggering or resulted in inaccurate exhaled tidal volume measurements were excluded from ERT.

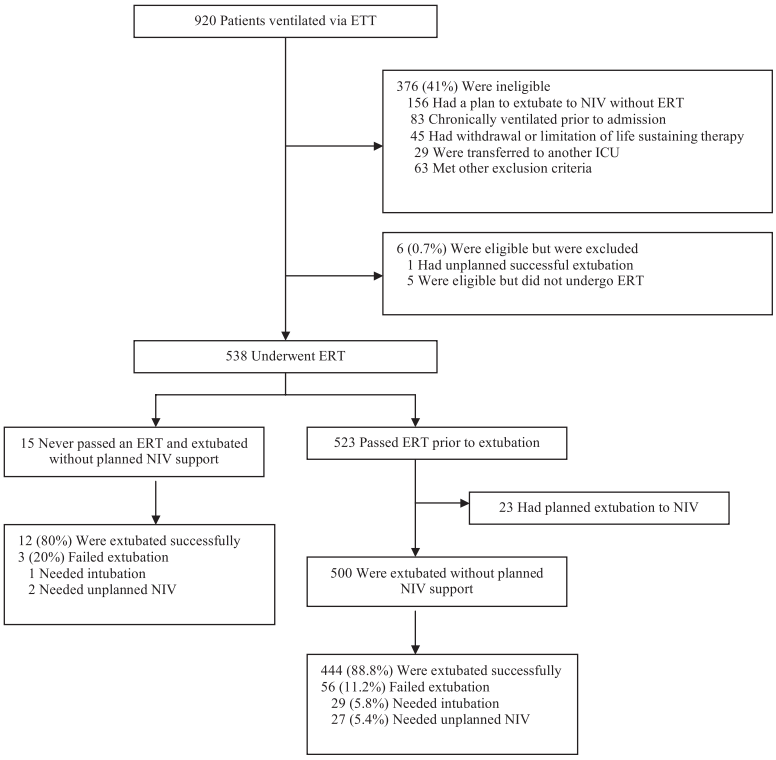

Figure 1. Flow diagram of patients in the study. *ETT*, endotracheal tube; *ERT*, extubation readiness test; *ICU*, intensive care unit; *NIV*, noninvasive ventilation.

Children failing the ERT were classified as unlikely to successfully extubate and continued ventilation was recommended by the unit guideline. The attending physician made the ultimate decision regarding timing of extubation.

Data Collection and Analysis. Demographic data, including age, gender, source of admission, admission diagnosis, and duration of ventilation, were recorded for all intubated patients. All patients were observed for 24 hrs after extubation and the need for noninvasive ventilatory support including continuous positive airway pressure or need for reintubation was recorded. The timing and results of all ERTs performed were collected. If an ERT was not performed before extubation, the reason was recorded.

Extubation failure was defined as reintubation or initiation of unplanned noninvasive ventilation within 24 hrs of planned removal of an ETT. Each extubation failure was assigned by the PICU attending to one or more of five causes: upper airway obstruction, inadequate gas exchange resulting from lower respiratory tract problem, respiratory muscle weakness, apnea, or neurologic impairment. The assignment was subjective but often supported by objective clinical findings and radiologic studies. Extubation failure rate was defined as the number of patients who failed extubation despite passing the ERT divided by the number of patients who passed the ERT and were extubated without planned use of noninvasive support. Patients in whom a decision to extubate to noninvasive ventilation (NIV) was made after ERT were excluded from the analysis of extubation outcome. In cases of unsuccessful extubation, only the ERT(s) in relation to the first extubation attempt were considered.

Logistic regression analysis was performed to identify variables related to extubation outcomes. Backward stepwise analysis was undertaken to identify independent risk factors for extubation failure. A p value of <.05 was used as the criterion for retention in the model. The odds ratio and the 95% confidence interval (CI) were calculated for tested variables. Fisher's exact and chi-squared tests were used to compare groups. A $p < .05$ was considered statistically significant. The sensitivity, specificity, and positive and negative predictive values of passing or failing the ERT and extubation success were determined.

RESULTS

Demographics. A total of 920 patients <19 yrs of age underwent mechanical ventilation through an ETT during the study period. Of these, 544 were eligible for an ERT and 538 (58%) underwent testing before extubation (Fig. 1). Reasons for ineligibility for testing were chronic noninvasive ventilation in 83 (9%), physician's decision to extubate to noninvasive support without an ERT in

156 (17%), decision to withdraw or limit life-sustaining therapy in 45 (4.9%), transfer to another unit in 29 (3.2%), and other reasons in 63 (6.8%). Five patients meeting inclusion criteria were extubated without testing, and one unplanned successful extubation occurred.

The 538 patients who underwent extubation readiness testing had a median age of 48 months at admission to the PICU and a mortality rate of 1.3%. Neonates (aged <28 days) and infants (aged 28 days to 1 yr) comprised 1.7% and 20% of this population, respectively. The median duration of intubation in this group was 1.5 days. Twenty-six percent of patients were admitted from the operating room (Table 1).

Extubation Readiness Testing. A total of 755 ERTs was performed in 538 patients. Of the 755 tests, 627 (83%) tests were passed. Reasons for ERT failure were related to SpO_2 in nine (7%), tachypnea in 13 (10%), exhaled tidal volume in 64 (50%), excessive work of breathing in eight (6%), apnea in ten (8%), hypoventilation in nine (7%), and multiple reasons in 15 (12%).

Of the 538 patients who underwent testing, 523 (97%) children passed an ERT and 371 patients were extubated after passing the ERT on the first attempt. Seventy-five children passed more than one ERT before extubation and of these, 20 children passed three or more tests before extubation. Fifteen (2.8%) patients were extubated without successfully passing an ERT despite testing.

Twenty-three patients were extubated to NIV support despite passing an ERT. None of these children required reintubation within the first 24 hrs. These patients were excluded from evaluation of ERT performance in predicting extubation outcome.

Extubation. The extubation failure rate of the 500 patients extubated after passing the ERT without planned use of NIV was 11.2% (n = 56), of which 5.4% (n = 27) needed NIV and 5.8% (n = 29) required reintubation. The most common reason for failure was lower respiratory tract dysfunction (Table 2). Three of the six children failing extubation as a result of upper airway obstruction were infants. Of the 15 patients eligible for testing and who were extubated without passing an ERT, three (20%) had unsuccessful extubations (one required intubation, two needed NIV). There was no significant difference in the odds of successful extubation between eligible patients extubated after passing and those extubated without passing an ERT (odds ratio [OR] 0.8; 95% CI 0.2–3.9). Successful completion of the ERT had a 97% sensitivity for predicting successful extubation with a positive predictive value of 89%. The specificity of the ERT was 5% and negative predictive value of a failed ERT for failed extubation of 20%.

There was no significant association between extubation outcome and gender, age, diagnostic category on PICU admission, or success in ERT before extubation (Table 3). Only the duration of mechanical ventilation was identified as an independent risk factor on the multivariable logistic regression. The odds of extubation failure increased by 9.6% (95% CI 4.6% to 14.8%) for every 24-hr increase in duration of mechanical ventilation. Children failing extubation had a median duration of ventilation before the first extubation attempt more than four times greater than those successfully extubated (failed, 107 hrs; successful, 26 hrs). In patients intubated for >48 hrs and extubated after passing an ERT (n = 211), the rate of extubation failure was 18.5% (n = 39) with 10% (n = 21) needing reintubation and 8.5% (n = 18) requiring NIV support.

In patients ventilated for >48 hrs, there was no association between passing the ERT and extubation success (OR 1.13; 95% CI 0.23–5.5). There was no significant association between the number of failed ERTs and extubation failure (p = .19). There was a trend toward attending physician decision to extubate to NIV with the number of unsuccessful ERTs before extubation (OR 1.53; 95% CI 0.92–2.6).

Table 1. Characteristics of the extubation readiness test study population (excludes patients subsequently extubated to planned noninvasive ventilation, n = 23)

Characteristic	Successful Extubation (n = 457)	Unsuccessful Extubation (n = 58)
Gender, no. (%)		
Male	252 (55)	33 (57)
Female	205 (45)	25 (43)
Age, median months (range)	49.6	34.8
Age distribution in months, no. (%)		
<1	7 (2)	2 (3)
1–6	44 (10)	8 (14)
>6–12	51 (11)	2 (3)
>12–24	74 (16)	11 (19)
>24–72	83 (18)	15 (26)
>72–144	76 (17)	8 (14)
>144	122 (27)	12 (21)
Percent Paediatric Index of Mortality 2 risk of mortality, median (interquartile range)	1.4 (0.6–3.6)	1.0 (0.8–3.4)
Duration of intubation, median hrs (range)	26.5 (0.7–744)	96.9 (5.5–692)
Reason for pediatric intensive care unit admission, no. (%)		
Acute respiratory failure		
Acute respiratory distress syndrome	10 (2)	0 (0)
Asthma	9 (2)	0 (0)
Bronchiolitis	9 (2)	2 (3)
Pneumonia	27 (6)	4 (7)
Upper airway	72 (16)	5 (9)
Other	11 (2)	5 (9)
Hematology/oncology	11 (2)	5 (9)
Neurologic dysfunction	84 (18)	8 (14)
Postoperative		
General surgery	74 (16)	8 (14)
Spinal fusion	37 (8)	12 (21)
Other surgery	2 (0.4)	1 (2)
Sepsis	4 (1)	2 (3)
Trauma	22 (5)	0 (0)
Other	85 (19)	6 (10)

Table 2. Causes of extubation failure in children extubated after successful extubation readiness test

Cause of Extubation Failure	No. (%)
Lower respiratory tract	30 (54)
Upper airway obstruction	6 (11)
Respiratory muscle weakness	2 (4)
Neurologic	6 (11)
Apnea	1 (2)
Combination of above	11 (20)

Table 3. Multiple logistic regression model with extubation failure within 24 hrs as the dependent variable

Variable[a]	Odds Ratio (95% Confidence Interval)	*p*
Duration of mechanical ventilation >48 hrs	3.1 (1.8–5.6)	<.001

[a]The following variables were removed from the model because of nonsignificance: male gender, $p = .82$; age[b], $p = .87$; Paediatric Index of Mortality 2 risk of mortality, $p = .64$; indication for pediatric intensive care unit admission: upper airway disease, $p = .17$; neurologic condition, $p = .62$; oncologic/hematologic condition, $p = 0.05$; admission from operating or recovery room, $p = .74$; extubation readiness test passed before extubation, $p = .79$; [b]age categories tested: <1 yr, 1–4 yrs, >4 yrs.

The median time from first passing an ERT to extubation was 5.5 hrs (range, 0–633 hrs). Of the 524 patients extubated after a successful ERT, extubation was delayed >6 hrs after passing an ERT in 232 (44%) of children. The reasons for these delays were documented in 166 patients and were the result of no ETT leak in 23 (13.9%), excessive sedation in 74 (44.6%), neurologic status in 12 (7.2%), physician decision in 29 (17.5%), secretions in three (1.8%), upcoming procedure in ten (6%), and other reason in 15 (9%).

DISCUSSION

This study describes our experience with the routine use of a SBT in a multidisciplinary PICU to guide timing of extubation and is the largest reported pediatric cohort subjected to extubation readiness testing to date. The study has two major findings. First, the overall extubation failure rate when using an ERT with a SBT using pressure support as part of a routine ventilatory strategy is similar to the failure rate when extubation timing is guided by clinical judgment alone (4). Second, the ERT is unreliable in patients ventilated for >48 hrs who are at higher risk of extubation failure.

In single-site PICU studies, extubation failure rates ranging from 5% to 22% have been reported (5–8). The differences in failure rates are attributable in part to study design with varying inclusion criteria, patient populations, and extubation failure definitions. We chose to define extubation failure demarcated at 24 hrs because >80% of children who fail extubation do so within this time (4). In this study, the reintubation rate of 5.6% is similar to the findings of Kurachek et al (4) who reported a 6.2% reintubation rate at 24 hrs in a large prospective multiple-center study in which the decision to extubate was made primarily using clinical judgment.

Although overall extubation failure has a relatively low frequency, we found duration of ventilation to be strongly associated with extubation failure, which is consistent with other PICU extubation studies (4, 5, 7). In our patients extubated after >48 hrs of ventilation and who passed the ERT, the extubation failure rate was over three times higher than those extubated within 48 hrs of ventilation. The 10% reintubation rate in patients ventilated for >48 hrs in this study compares less favorably with the 8% reintubation rate in the Kurachek et al multiple-center study (4, 9). By far the most common cause of extubation failure was inadequate gas exchange resulting from lower respiratory tract problems suggesting that the SBT with pressure support was masking respiratory insufficiency and contributing to the higher failed extubation rate. In children ventilated for >48 hrs, we found successful completion of an ERT before extubation was not associated with extubation success.

Diaphragmatic function plays an important role in respiration and the patient's ability to coordinate with and liberate from mechanical ventilation. Diaphragmatic fatigue or ventilator-induced diaphragm dysfunction may be primarily responsible for weaning or extubation failures. Recently, a study by Levine and coworkers (10) suggested that even a short period of controlled mechanical ventilation induces oxidative stress that leads to protein degradation and diaphragmatic atrophy within 18–69 hrs. When the mechanical load on the respiratory system is too large or continues for a long period of time, the diaphragm can develop contractile fatigue (11). This may explain why patients have struggled to extubate successfully after 48 hrs of mechanical ventilation.

An ERT aims to assess likelihood of successful extubation by simulating the work of breathing that will be present after extubation. In this study, pressure support during the SBT was applied to overcome the hypothesized inspiratory workload resulting from the inherent resistance of the ETT with increasing empirical levels of pressure support for smaller ETT internal diameters. This approach was supported in the study by Bock et al (12) that found by computed tomographic measurements that endotracheal intubation commonly reduces the radius of the intubated trachea by a factor of 0.4–0.5 and results in an increase in resistance of up to 32-fold. Similarly, a study by Manczur et al (13) in laboratory testing demonstrated increased resistances with smaller ETTs at high flow rates and concluded the use of small-diameter ETT significantly increases the work of breathing.

More recently, there is growing consensus that at clinically relevant flow rates, work of breathing probably does not increase significantly with decreasing ETT size (9, 14). Data from Willis et al (15) indicate both continuous positive airway pressure and pressure support of 5 cm H_2O decrease the work of breathing compared with the extubated state and a study by Keidan et al (16) found work of breathing of anesthetized, spontaneously breathing children undergoing elective surgery to be decreased with the insertion of an ETT. In children intubated for severe croup with a 3.0-mm ETT, esophageal pressure changes and indices of work of breathing return to the normal range after intubation despite the small ETT size (17). Pressure support ventilation reduces respiratory work in proportion to the level of pressure support (18) and even in infants with 3.5- to 4.5-mm ETTs, pressure support >4 cm H_2O reduces work of breathing compared with the extubated state (18).

This study confirms that a SBT using pressure support considered to be "low level" and widely believed to be necessary to overcome the inherent resistance of smaller diameter ETTs amounts to continued mechanical ventilation during testing and leads to overestimation of readiness for extubation and higher failed extubation rates.

The ERT has the advantage of being both an objective and reproducible measure of weaning. Children with ineffective spontaneous efforts as suggested by low spontaneous tidal volume are at high risk of extubation failure (19) and by measuring tidal volume during the SBT, unnecessary extubation failures may be avoided. Low

exhaled tidal volume was the most common reason for failing the ERT and the majority of these patients continued to receive ventilatory support until successfully completing an ERT. NIV may be useful to facilitate weaning from invasive ventilation and extubation but is unproven and ill defined in the pediatric population. Studies in critically ill adults in intensive care, although limited by inclusion of mostly patients with chronic obstructive pulmonary disease, show weaning to NIV is associated with decreased mortality, ventilator-associated pneumonia, and length of stay in intensive care and the hospital (20). In children, NIV has been used successfully in chronic upper airway obstruction (21), cystic fibrosis (22), and neuromuscular disease (23). Despite the lack of evidence of its role in the pediatric critical care setting, NIV is being commonly used (24). In this present study, 19% of intubated patients were electively extubated to NIV. Performance in a routinely applied ERT, particularly in children intubated for >48 hrs, may provide useful objective measures to identify children who may benefit from direct extubation to NIV. The influence of the child's performance in ERT on the attending physician's decision to extubate to NIV is suggested by a trend toward planned use of NIV with increasing number of failed ERTs. Further work is needed define the criteria for extubation readiness test failure and the best predictors of children likely to benefit from extubation to NIV.

Children can be considered ready for extubation after successfully transitioning from ventilatory support to spontaneous breathing and when hemodynamically stable, sufficiently awake with intact airway reflexes, and with adequate cough strength with manageable secretions (9). The aim of routine application of the ERT was for earlier identification of patients who had either completed weaning or who did not require weaning and who could be successfully extubated. However, in common with other SBTs, the ERT inherently fails to identify children who fail extubation as a result of upper airway obstruction and this in part explains the low specificity of the ERT found in this study. An ETT air-leak test was not performed as part of the ERT. Although commonly used to predict upper airway obstruction after extubation, recent data suggest that the majority of patients identified as candidates for extubation but without a leak will successfully tolerate removal of the ETT (25). However, a leak test was permitted at the discretion of the attending physician and in 23 patients, extubation was delayed as a result of the absence of an audible leak. Of these patients, three had extubation failure and this was attributed to upper airway obstruction in two children.

In >40% of children, extubation was delayed >6 hrs suggesting importance of other factors not evaluated in the test but that have influence on the overall timing of extubation. The most common documented reason for delay was excessive sedation. Future studies will need to investigate how these factors influence intubation dependency to facilitate earlier extubation and successfully increase ventilator-free days.

This study has a number of limitations. Although the ERT is standardized, the decisions to extubate, reintubate, or use NIV as a planned measure (with or without testing) or as a rescue therapy were not controlled and were at the discretion of the attending physician. Patients who failed the ERT were not systematically extubated limiting the accuracy of the predictive value of a failed test in predicting need for ventilator support. The effect of commonly occurring delay in extubation after successfully passing the ERT on the failure rate, and hence sensitivity and specificity of the test, is unknown. Patients were not randomized to either daily consideration of ERT or to routine practice and consequently, it is not possible to elucidate whether this screening process contributes to an overall decrease in duration of mechanical ventilation. ETT size data were not collected. However, extubation outcome was analyzed by age group to approximate the three groups of pressure support level set according to ETT size. Finally, the precise cause of extubation failure was defined only in clinical terms by the attending physician at the time of extubation failure and was not independently categorized by the study investigators.

CONCLUSIONS

An ERT based on a SBT with pressure support adjusted according to ETT size overestimates a child's ability to breathe independently. Patients ventilated for >48 hrs continue to be at high risk of extubation failure. Objective data from ERT may be useful to identify patients who may benefit from planned extubation to noninvasive ventilation. Further work is required to develop a quality indicator of successful planned extubation.

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