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Accuracy of an extubation readiness test in predicting successful extubation in children with acute respiratory failure from lower respiratory tract disease

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Abstract

OBJECTIVE—Identifying children ready for extubation is desirable to minimize morbidity and mortality associated with prolonged mechanical ventilation and extubation failure. We determined the accuracy of an extubation readiness test (*RESTORE* ERT) in predicting successful extubation in children with acute respiratory failure from lower respiratory tract disease.

DESIGN—Secondary analysis of data from the *RESTORE* clinical trial, a pediatric multicenter cluster randomized trial of sedation.

SETTING—17 pediatric intensive care units in the intervention arm.

PATIENTS—Children 2 weeks to 17 years receiving invasive mechanical ventilation for lower respiratory tract disease.

INTERVENTION—ERT in which spontaneously breathing children with oxygenation index ≤ 6 were placed on FiO_2 of 0.50, positive end expiratory pressure of 5 cm H_2O , and pressure support.

MEASUREMENTS AND MAIN RESULTS—Of 1,042 children, 444 (43%) passed their first ERT. Of these, 295 (66%) were extubated within 10 hours of starting the ERT, including 272 who were successfully extubated, for a positive predictive value of 92%. Among 861 children who were extubated for the first time within 10 hours of performing an ERT, 788 passed their ERT and 736 were successfully extubated for a positive predictive value of 93%. The median time of day for extubation with an ERT was 12:15H compared with 14:54H for extubation without an ERT within 10 hours ($p < 0.001$).

CONCLUSIONS—In children with acute respiratory failure from lower respiratory tract disease, an ERT, as described, should be considered at least daily if the oxygenation index is ≤ 6 . If the child passes the ERT, there is a high likelihood of successful extubation.

Keywords

critical care; endotracheal intubation; endotracheal extubation; mechanical ventilation; pediatrics; predictive value of tests; work of breathing

BACKGROUND

Identifying intubated children who are ready for endotracheal extubation is desirable to minimize the morbidity and mortality associated with prolonged mechanical ventilation and extubation failure. Prolonged mechanical ventilation and extubation failure are associated with biopsychosocial risks, increased hospital costs, and prolonged pediatric intensive care unit (PICU) stay.⁽¹⁾

Extubation readiness tests (ERTs) aid in identifying who may be successfully extubated. In most ERTs, the child is placed on minimal ventilator settings and is observed for signs of distress or impaired gas exchange.^(2, 3) For example, Randolph *et al* used an ERT in which children who were relatively awake and spontaneously breathing on stable minimal ventilator settings were placed on pressure support ventilation with FiO_2 of 0.50 and positive end expiratory pressure (PEEP) of 5 cm H_2O for 2 hours.⁽⁴⁾ This ERT had a positive predictive value (PPV) of 87% for predicting successful extubation.⁽⁴⁾

We recently completed *RESTORE* (Randomized Evaluation of Sedation Titration for Respiratory Failure), a multicenter cluster randomized trial of sedation in children.⁽⁵⁾ The sedation protocol for the intervention arm included an ERT, modified from the ERT by Randolph *et al* and used in the pediatric prone positioning trial in order to apply to children with lower respiratory tract dysfunction.^(4, 6) In this secondary analysis of data from *RESTORE*, we determined the accuracy of this modified ERT in predicting successful extubation in children with acute respiratory failure from lower respiratory tract disease.

METHODS

The primary aim of *RESTORE* was to determine whether critically ill children, managed with a nurse-implemented, goal-directed sedation protocol, would experience fewer days of mechanical ventilation than children receiving usual care.⁽⁵⁾ The trial was conducted from June 2009 to December 2013. Of the 31 United States PICUs that participated, 17 were randomized to the intervention arm and comprised the children used in this secondary analysis. *RESTORE* was approved by the institutional review board at each participating site and parental permission was obtained for all subjects.

Subjects

RESTORE enrolled children aged 2 weeks to 17 years receiving invasive mechanical ventilation for acute airways and/or parenchymal lung disease and excluded those whose length of mechanical ventilation was unlikely to be altered by sedation management, such as mechanical ventilation only for postoperative care. In all analyses, we excluded children admitted with tracheostomies or those with new tracheostomies.

Extubation Readiness Test

The *RESTORE* ERT was a core element of the research intervention (Table 1).⁽⁶⁾ All children were screened daily for ERT eligibility, which included presence of spontaneous breathing and an oxygenation index (OI) or oxygen saturation index (OSI).^{6, (7)} This modification of Randolph *et al* provided an assessment of lower respiratory tract function.^(4, 6, 7) Children were placed sequentially on FiO₂ of 0.50, PEEP of 5 cm H₂O, and a ventilator mode of continuous positive airway pressure and pressure support. The level of pressure support was based on endotracheal tube size and was applied above PEEP. Children were monitored for up to 2 hours for passing physiologic parameters, that is, oxygen saturations ≥ 95%, exhaled tidal volumes ≥ 5 mL/kg ideal body weight, and acceptable respiratory rates for age. Clinicians used their judgment when evaluating parameters in a child with a large air leak. The bedside team worked to optimize the child's capacity to pass the ERT. Specifically, the team assured that the child's endotracheal tube was clear of secretions and that routine cares were completed before the ERT.

Per protocol, the child's phase of illness based on the clinical team's determination of required respiratory support guided prescribed levels of sedation.⁽⁵⁾ Children passing the daily ERT screen began ERT testing anytime before multidisciplinary walk rounds (typically between 04:00H to 08:00H). If the child passed the ERT, extubation was recommended within 6 hours of completing the test. If the child failed the ERT, the child was returned to

pre-ERT ventilator settings and re-tested the next morning provided that the child met criteria for the ERT. If excessive sedation precipitated ERT failure, the team was instructed to wean sedation and repeat the ERT later during the day. Management of the child post-extubation, particularly with the use of non-invasive ventilation (NIV), was left to the care team's discretion.

Outcome Measures and Statistical Analysis

Our primary cohort included children who had a planned extubation within 10 hours of starting their *first ERT*. For our secondary cohort, we used the *first planned extubation* and the ERT performed prior to this extubation if done within 10 hours of the extubation. The 10-hour limit covered the day shift in participating PICUs.

Our primary outcome was successful extubation defined as discontinuation of invasive mechanical ventilation for at least 24 hours. Our secondary outcome was successful extubation without the use of NIV, *i.e.*, biphasic positive airway pressure or continuous positive airway pressure ≥ 5 cm H₂O, immediately post-extubation. For both cohorts and outcomes, we calculated the diagnostic accuracy of the ERT, *i.e.*, PPV, negative predictive value, sensitivity, and specificity, in predicting successful extubation.

For both cohorts, we compared characteristics of children who passed vs failed the ERT, and children successfully extubated vs reintubated within 24 hours. We also compared children extubated within 10 hours of passing their first ERT vs not extubated for the primary cohort, and children who were extubated with an ERT vs extubated without an ERT for the secondary cohort. Characteristics included demographic variables, baseline Pediatric Cerebral Performance Category (PCPC) and Pediatric Overall Performance Category (POPC) scores(8), Pediatric Risk of Mortality (PRISM) III-12 score(9), type of lung disease, early neuromuscular blockade use, length of mechanical ventilation, sedative exposure, severity of lung disease(10), and State Behavioral Scale.(11) For those extubated, we also compared the use of NIV post-extubation.

Groups were compared using linear, logistic, and cumulative logit regression accounting for PICU as a cluster variable using generalized estimating equations for log-transformed continuous, binary, and ordinal variables, respectively. Stepwise multivariable logistic regression was performed to predict the probability of ERT failure and extubation failure (reintubation within 24 hours) in both cohorts, using the characteristics above as potential covariates. A *p*-value of <0.05 was required for a covariate to enter and stay in the model. For the secondary cohort, the times of day for extubation for children with and without ERTs were compared using the Wilcoxon rank sum test for location shift and the Siegel-Tukey test for variability shift. All tests were performed using SAS, version 9.4 (SAS Institute Inc, Cary, NC) at a two-sided $\alpha=0.05$ to determine statistical significance.

RESULTS

Of 1,225 children in the intervention arm of *RESTORE*, we excluded 24 with tracheostomies and 159 who never had an ERT after passing the screen (Figure 1). The remaining 1,042 children had at least one ERT performed (median: 2, interquartile range

[IQR]: 1–3, maximum: 19) for a total of 2,735 ERTs. Of these, 444 (43%) passed their first ERT. Compared with children who passed their first ERT, those who failed were younger, more likely to have an obstructive lung disease, less likely to have received early neuromuscular blockade, and on mechanical ventilation for fewer days prior to their first ERT and had lower PRISM III-12 scores, less sedative exposure on the day prior to the ERT, and more severe lung disease on the day of the ERT (Table 2). In multivariable analysis, younger age at PICU admission and lower opioid exposure on the day before the first ERT were associated with higher risk of ERT failure. The most common reason for failing the first ERT was respiratory rate out of range (38%). Of 704 children with more than one ERT, 333 (47%) passed their second ERT, while 192 of 409 children (47%) passed their third ERT. (Supplemental Digital Content Tables 1, 2)

Of the 444 children who passed the first ERT, 295 (66%) were extubated within 10 hours of starting the test. The most common reasons for not extubating were physician preference (26%) and excessive secretions (25%). Children who were not extubated were younger and more likely to have received early neuromuscular blockade and had more severe lung disease on the day of the ERT than those who were extubated (Supplemental Digital Content Tables 3, 4).

In addition to the 295 children who were extubated within 10 hours of passing their first ERT, 30 children were extubated within 10 hours of failing their first ERT. Seventeen of these 30 children passed a second ERT prior to extubation. We included these 325 children in our primary cohort.

A total of 1,093 children had a planned extubation. Of these, 861 (79%) had an ERT started within 10 hours of extubation and comprised our secondary cohort. An additional 138 children had an ERT started >10 hours prior to extubation. Children who did not have an ERT within 10 hours of extubation had worse baseline PCPC and POPC scores, were less likely to have an obstructive lung disease, and had more severe lung disease on the day of their first extubation. A total of 788 (92%) passed this ERT. Children who failed the ERT had lower PRISM III-12 scores, were on mechanical ventilation for more days prior to extubation, and had less opioid exposure on the day before extubation than those who passed the ERT. In multivariable analysis, lower PRISM III-12 score and more days on mechanical ventilation prior to extubation were associated with higher risk of ERT failure. The most common reason for failing this ERT was respiratory rate out of range (49%) (Supplemental Digital Content Figure 1 and Tables 1, 2, 5, 6).

Extubation Failures

Among children in the primary cohort who passed their first ERT and were extubated, 23 (8%) failed extubation. The reasons for failing extubation were upper airway obstruction (65%), lower respiratory dysfunction resulting in impaired gas exchange (22%), excessive secretions (9%), and tachypnea (4%). Children who failed extubation were younger, had lower risk of mortality, and had more agitated State Behavioral Scale scores at the start of the ERT than those who were successfully extubated (Table 3). Of 272 children who were successfully extubated, 37 (14%) were placed on NIV post-extubation. One of 30 children (3%) who failed the first ERT but were extubated failed extubation. Of those who passed a

second and third ERT and were extubated within 10 hours of starting the ERT, 21 of 247 (9%) and 5 of 128 (4%) failed extubation, respectively.

Among children in the secondary cohort who passed the ERT prior to their first planned extubation, 52 (7%) failed extubation. Those who failed extubation were younger and had lower PRISM III-12 scores than those who were successfully extubated. Of 736 children who were successfully extubated, 101 (14%) were placed on NIV post-extubation. Of the 73 children (10%) who failed their ERT but were extubated, 7 (10%) failed extubation. (Supplemental Digital Content Table 7)

In multivariable analysis, younger age, worse baseline PCPC score, lower PRISM III-12 score, and use of NIV post-extubation were associated with extubation failure in both cohorts (Supplemental Digital Content Table 8).

Diagnostic Accuracy of the ERT

In our primary cohort, the PPV of the first ERT was 92% (Table 4). The negative predictive value, sensitivity, and specificity were 3%, 90%, and 4%, respectively. When the use of NIV post-extubation was added to the definition of extubation failure, the PPV was 80%.

In our secondary cohort, the PPV of the ERT was 93% (Table 3). When the use of NIV post-extubation was added to the definition of extubation failure, the PPV was 81%.

Timing of Extubation

In the secondary cohort, the ERT was most often (59%) started between 04:00H and 07:59H, while an additional 36% were started between 08:00H and 15:59H. Nearly half (46%) of first planned extubations occurred between 12:00H and 15:59H in children who had an ERT, with an additional 39% extubated between 08:00H and 11:59H. This compares with 34% and 19% for these time periods in children who did not have an ERT. Children who had an ERT were extubated earlier in the day with less variability (median: 12:15H, IQR: 10:45H-14:18H) compared to those who did not have an ERT (median: 14:54H, IQR: 11:42H-16:42H; $p < 0.001$ for location shift and $p < 0.001$ for variability shift). (Supplemental Digital Content Figure 2)

DISCUSSION

In this analysis of data from a large multicenter cluster randomized trial, we report that if a child passed the ERT and was extubated within 10 hours of starting the ERT, the probability of remaining extubated for at least 24 hours was 92–93%. Performing an ERT was associated with extubations occurring earlier during the day. Our findings demonstrate the potential benefits of using an ERT screen and test in practice and in clinical trials.(12)

In our multivariable analyses, we found that younger children were more likely to fail the ERT and fail extubation, which is consistent with other studies.(3, 5) It is unclear if extubation failure in these children is due to patient factors such as weight, motor strength, or smaller airways. We also found that lower PRISM III-12 score was associated with ERT and extubation failure, although these associations may be statistically but not clinically

significant. Lower opioid exposure on the day before the first ERT was also associated with ERT failure, which may reflect the complex relationship of wakefulness, pain, and agitation that was demonstrated in the *RESTORE* trial.(5)

Our study provides some insight into potential barriers to the routine use of ERT screening and testing. The most common reasons for not extubating a child despite their passing an ERT were physician preference and excessive secretions. Children who were not extubated were younger. This is consistent with our findings in children who failed extubation and may have played a role in physician preference not to extubate. A survey of pediatric critical care practitioners reported that most clinicians assess the highly subjective character of tracheal secretions when determining a child's readiness for extubation.(13) The association between secretion volume and successful extubation is unclear.(14) Also unclear is whether pulmonary secretions are better removed by endotracheal suctioning or by spontaneous effective coughing without an artificial airway. Objective measures of inadequate secretion management may facilitate future clinical decision-making.

Future modifications in the *RESTORE* ERT may also improve its predictive value. Specifically, with the common use of high flow, high humidity nasal cannula and other forms of NIV, children may be successfully extubated despite tachypnea, the most common reason for failing the *RESTORE* ERT.(1, 15) Additional tests and monitoring, such as respiratory inductance plethysmography and esophageal manometry, may better predict upper airway obstruction post-extubation.(16)

Given that so few patients were extubated after failing the *RESTORE* ERT, we are only confident in our reporting of the test's PPV with and without NIV included in the definition of extubation failure. Passing the *RESTORE* ERT can identify, with good accuracy, children who can be successfully extubated, but the test can say little about those who fail the ERT. Our reported PPV is similar to other pediatric ERTs,(14, 17–19) but these studies may have overestimated their PPV by including children without respiratory disease. The *RESTORE* ERT slightly improved on the 87% PPV reported by Randolph *et al.*(4)

Although the *RESTORE* ERT was designed to identify children who are ready for extubation in the setting of a clinical trial, benefits can be applied in practice. When the ERT was performed per protocol, children were extubated earlier in the day which may improve PICU workflow.

Our study has several limitations. First, a third of children who passed their first ERT were not extubated within 10 hours of the test and this could have affected the estimates of the diagnostic accuracy. Second, the *RESTORE* ERT may overestimate extubation success due to the level of pressure support used during the test.(2) Unfortunately, we were unable to determine the association between level of pressure support and extubation success because these data were not collected during the trial. Third, we included the use of NIV in our secondary definition of extubation failure; however, we did not standardize its use or collect data on the level or rationale for the NIV support provided. Finally, the decision to reintubate a child was not standardized in *RESTORE*.

CONCLUSION

In this secondary analysis of data from a multicenter trial, we described the accuracy of an ERT when applied to children with acute respiratory failure from lower respiratory tract disease who are spontaneously breathing with an oxygenation or oxygen saturation index

6. Passing the *RESTORE* ERT can identify, with reasonable accuracy, children who will be successfully extubated. Performance of this test is associated with extubation earlier during the day.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Figure 1.
Flow diagram for patients in the primary cohort
Legend: ERT, extubation readiness test.

Table 1**Daily Test for Patient Readiness for Extubation**

Every morning at 06:00 ± 2 hours the child is assessed for the following:

- ☐ Spontaneous breathing
- ☐ Oxygenation or oxygen saturation index ≥ 6 (MAP/PF ratio $\times 100$; If an arterial blood gas is unavailable, then estimate the PaO_2 from the SpO_2)

If the child meets these ERT criteria, then the child is tested for extubation readiness.

RESTORE Extubation Readiness Test (ERT):

1. Temporarily stop enteral feedings
2. If FiO_2 not at 0.50, then titrate FiO_2 to 0.50 as tolerated and assess; if tolerated, then
3. If PEEP not at 5 cm H_2O , then titrate PEEP to 5 cm H_2O as tolerated and reassess
4. Evaluate SpO_2 after each ventilator change
 - a. If $\text{SpO}_2 \geq 95\%$, change mode to straight PS with set PS minimum level based upon the size of the ETT
 - ☐ 10 cm H_2O if ETT 3–3.5 mm
 - ☐ 8 cm H_2O if ETT 4–4.5 mm
 - ☐ 6 cm H_2O if ETT ≥ 5 mm
 - b. Monitor SpO_2 , exhaled tidal volume, and respiratory rate

The child is ready for extubation (from a pulmonary perspective) if all 3 of the following are present for ≥ 2 hours:

- ☐ $\text{SpO}_2 \geq 95\%$
- ☐ Exhaled tidal volume ≥ 5 mL/kg (ideal weight)
- ☐ Respiratory rate within respiratory rate goal of age:
 - <6 months 20–60; 6 months–2 years 15–45; 2–5 years 15–40; >5 years 10–35

If the child does not pass the ERT, s/he is returned to their pre-test ventilator settings and re-tested the next morning. If the clinical team judges that the *child failed the ERT because of sedation-related hypoventilation, then a modified daily arousal assessment is completed and an ERT is repeated before 16:00* as per *RESTORE* study protocol. If the child does not meet the criteria at 16:00, s/he is returned to their pre-test ventilator settings and re-tested the following morning.

If the child passes the ERT, s/he is placed on comfortable ventilator settings and the medical team is notified that the child is ready (from a pulmonary perspective) for unassisted breathing. Extubation may be delayed for non-pulmonary reasons.

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Table 2

Characteristics of Children According to First Extubation Readiness Test Result

Characteristic	Passed ERT (<i>n</i> = 444)	Failed ERT (<i>n</i> = 598)	<i>p</i> ^a
Age at PICU admission (IQR), y	1.8 (0.6–7.7)	0.6 (0.2–4.4)	<0.001
Female, <i>n</i> (%)	205 (46)	265 (44)	0.61
Non-Hispanic white, <i>n</i> /total (%)	221/438 (50)	304/596 (51)	0.65
Cognitive impairment (baseline PCPC score >1), <i>n</i> (%) ^b	107 (24)	118 (20)	0.049
Functional impairment (baseline POPC score >1), <i>n</i> (%) ^b	125 (28)	141 (24)	0.08
PRISM III-12 score	7 (3–12)	5.5 (2–11)	0.03
Risk of mortality based on PRISM III-12 score, %	2.9 (1.0–10.2)	2.2 (0.9–7.7)	0.12
Primary diagnosis category, <i>n</i> (%) ^c			<0.001
Restrictive lung disease	264 (59)	295 (49)	
Obstructive lung disease	180 (41)	303 (51)	
Neuromuscular blockade for the entire duration of days 0 to 2, <i>n</i> (%)	37 (8)	25 (4)	0.007
Days of mechanical ventilation prior to day of first ERT	3 (1–6)	2 (1–5)	0.009
Sedative exposure on day before first ERT ^d			
Opioid exposure, mg/kg	2.5 (1.2–4.7)	1.8 (0.8–3.5)	<0.001
Benzodiazepine exposure, mg/kg	2.3 (1.1–4.5)	1.8 (0.9–3.6)	0.005
Number of sedative classes, mean ± SD ^e	2.3 ± 0.7	2.1 ± 0.5	0.006
PARDS on day of first ERT, <i>n</i> (%) ^f			<0.001
At risk (OI <4.0 or OSI <5.0)	361 (81)	422 (71)	
Mild (OI 4.0–7.9 or OSI 5.0–7.4)	78 (18)	163 (27)	
Moderate (OI 8.0–15.9 or OSI 7.5–12.2)	5 (1)	12 (2)	
Severe (OI ≥16.0 or OSI ≥12.3)	0	1 (<1)	
SBS score at start of first ERT, <i>n</i> (%)			0.23
–3/–2	15 (3)	42 (7)	
–1/0	389 (89)	492 (84)	
+1/+2	33 (8)	50 (9)	
Missing	7	14	

ARF, acute respiratory failure; ERT, extubation readiness test; IQR, interquartile range; OI, oxygenation index; OSI, oxygen saturation index; PARDS, pediatric acute respiratory syndrome; PCPC, Pediatric Cerebral Performance Category; PICU, pediatric intensive care unit; POPC, Pediatric Overall Performance Category; PRISM III-12, Pediatric Risk of Mortality III score from first 12 hours in the PICU; SBS, State Behavioral Scale; SD, standard deviation.

Values are median (IQR) unless otherwise specified.

^a*P* values for the comparison between groups were calculated using linear, logistic, and cumulative logit regression accounting for PICU as a cluster variable using generalized estimating equations for log-transformed continuous, binary, and ordinal variables, respectively.

^bPCPC and POPC range from 1 to 6, with higher categories indicating greater impairment.

^cDiagnoses for restrictive lung disease: pneumonia, sepsis, aspiration pneumonia, pulmonary edema, thoracic trauma, pulmonary hemorrhage, ARF post bone marrow transplant, acute chest syndrome/sickle cell disease, pertussis, pneumothorax (non-trauma), ARF related to multiple blood

transfusions, lymphangiectasia, pulmonary embolism. Diagnoses for obstructive lung disease: bronchiolitis, asthma, laryngotracheobronchitis, acute exacerbation of lung disease (cystic fibrosis or bronchopulmonary dysplasia).

^dTwo children passed first ERT on day 0, so no data available for day before first ERT.

^eDifferent sedative classes include opioids, benzodiazepines, α 2-adrenergic agonists (dexmedetomidine or clonidine), propofol, barbiturates (pentobarbital or phenobarbital), ketamine, and chloral hydrate.

^fOxygenation index was calculated as $([\text{FIO}_2 \times \text{mean airway pressure}]/\text{PaO}_2 \times 100)$. When an arterial blood gas measurement was not available, SpO₂ was used to estimate PaO₂ in order to calculate OSI $([\text{FIO}_2 \times \text{mean airway pressure}]/\text{SpO}_2 \times 100)$. Lower scores reflect better oxygenation.

Table 3

Characteristics of Children with Planned Extubations Within 10 Hours of Passing First Extubation Readiness Test According to Extubation Result

Characteristic	Successful Extubation (n = 272)	Reintubated within 24 h (n = 23)	p ^a
Age at PICU admission (IQR), y	2.5 (0.6–10.3)	1.3 (0.2–3.3)	<0.001
Female, n (%)	123 (45)	8 (35)	0.41
Non-Hispanic white, n/total (%)	140/271 (52)	14/23 (61)	0.29
Cognitive impairment (baseline PCPC score >1), n (%) ^b	65 (24)	8 (35)	0.27
Functional impairment (baseline POPC score >1), n (%) ^b	77 (28)	8 (35)	0.56
PRISM III-12 score	7 (3–12)	4 (0–7)	<0.001
Risk of mortality based on PRISM III-12 score, %	2.9 (1.0–9.8)	1.3 (0.5–4.3)	<0.001
Primary diagnosis category, n (%)			0.21
Restrictive lung disease	162 (60)	10 (43)	
Obstructive lung disease	110 (40)	13 (57)	
Days of mechanical ventilation prior to day of first ERT	3 (1–6)	3 (1–7)	0.77
Sedative exposure on day before first ERT ^c			
Opioid exposure, mg/kg	2.5 (1.1–4.7)	2.5 (0.5–4.2)	0.57
Benzodiazepine exposure, mg/kg	2.4 (1.1–4.4)	2.1 (0.6–5.0)	0.69
Number of sedative classes ^d	2 (2–3)	2 (2–2)	0.84
PARDS on day of first ERT, n (%) ^e			0.86
At risk (OI <4.0 or OSI <5.0)	230 (85)	20 (87)	
Mild (OI 4.0–7.9 or OSI 5.0–7.4)	40 (15)	1 (4)	
Moderate (OI 8.0–15.9 or OSI 7.5–12.2)	2 (<1)	2 (9)	
Severe (OI ≥16.0 or OSI ≥12.3)	0	0	
SBS score at start of first ERT, n (%)			0.002
–3/–2	9 (3)	0	
–1/0	239 (90)	17 (74)	
+1/+2	17 (6)	6 (26)	
Missing	7	0	
Non-invasive ventilation immediately post-extubation, n (%) ^f	37 (14)	7 (30)	0.053

ERT, extubation readiness test; IQR, interquartile range; OI, oxygenation index; OSI, oxygen saturation index; PARDS, pediatric acute respiratory syndrome; PCPC, Pediatric Cerebral Performance Category; PICU, pediatric intensive care unit; POPC, Pediatric Overall Performance Category; PRISM III-12, Pediatric Risk of Mortality III score from first 12 hours in the PICU; SBS, State Behavioral Scale.

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^aP-values for the comparison between groups were calculated using linear, logistic, and cumulative logit regression accounting for PICU as a cluster variable using generalized estimating equations for log-transformed continuous, binary, and ordinal variables, respectively.

^bPCPC and POPC range from 1 to 6, with higher categories indicating greater impairment.

^cOne child passed ERT on day 0, so no data available for day before first ERT.

^d Different sedative classes include opioids, benzodiazepines, α_2 -adrenergic agonists (dexmedetomidine or clonidine), propofol, barbiturates (pentobarbital or phenobarbital), ketamine, and chloral hydrate.

^e Oxygenation index was calculated as $([\text{FIO}_2 \times \text{mean airway pressure}]/\text{PaO}_2 \times 100)$. When an arterial blood gas measurement was not available, SpO₂ was used to estimate PaO₂ in order to calculate OSI $([\text{FIO}_2 \times \text{mean airway pressure}]/\text{SpO}_2 \times 100)$. Lower scores reflect better oxygenation.

^f Non-invasive ventilation includes biphasic positive airway pressure or continuous positive airway pressure ≥ 5 cm H₂O.

Table 4

Accuracy of the Extubation Readiness Test

	Positive Predictive Value	Negative Predictive Value	Sensitivity	Specificity
Primary cohort (first ERT, <i>n</i> = 325)				
Successful extubation vs Reintubated within 24 h	92% (89–95%)	3% (0–17%)	90% (86–93%)	4% (0–21%)
Successful extubation vs Reintubated within 24 h or non-invasive ventilation immediately post-extubation	80% (75–84%)	20% (8–39%)	91% (87–94%)	9% (3–19%)
Secondary cohort (first planned extubation, <i>n</i> = 861)				
Successful extubation vs Reintubated within 24 h	93% (91–95%)	8% (3–17%)	92% (90–93%)	10% (4–21%)
Successful extubation vs Reintubated within 24 h or non-invasive ventilation immediately post-extubation	81% (78–83%)	21% (12–32%)	92% (89–94%)	9% (5–14%)

ERT, extubation readiness test.

Data presented as value (exact 95% confidence interval).