Impact of Spontaneous Breathing Trial on Work of Breathing Indices Derived From Esophageal Pressure, Electrical Activity of the Diaphragm, and Oxygen Consumption in Children

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BACKGROUND: The present study aimed to characterize the behavior of 3 components of respiratory muscle function during mechanical ventilation weaning in children to better understand the respective impact of a spontaneous breathing trial on ventilatory mechanical action (esophageal pressure [P_{es}], ventilatory demand (electrical activity of the diaphragm [EA_{di}]), and oxygen consumption. **METHODS:** This was a prospective single-center study. All children > 1 months and <18 y old who were intubated and on mechanical ventilation, and who were hospitalized in the pediatric ICU were eligible. Subjects considered as ready to extubate were included. Simultaneous recordings of oxygen consumption, P_{es} , and EA_{di} were performed during 3 steps: before, during, and after the spontaneous breathing test. **RESULTS:** Twenty subjects (median age, 5.5 mo) were included. Half of them were admitted for a respiratory cause. The increase in P_{es} swings and esophageal pressure-time product during the spontaneous breathing trial was not significant ($P = .33$ and $P = .75$, respectively), and a similar trend was observed with peak EA_{di} ($P = .06$). Oxygen consumption obtained by indirect calorimetry was stable in the 3 conditions ($P = .98$). **CONCLUSIONS:** In these children who were critically ill, a spontaneous breathing trial induced a moderate and nonsignificant increase in work of breathing, as reflected by the respiratory drive with EA_{di} and respiratory mechanics with P_{es} . However, indirect calorimetry did not seem to be a sensitive tool to assess respiratory muscle function during the weaning phase in children who were on mechanical ventilation, especially when work of breathing was slightly increased. *Key words:* mechanical ventilation; indirect calorimetry; work of breathing; weaning; pediatric intensive care unit. [Respir Care 2019;64(5):509–518. © 2019 Daedalus Enterprises]

Introduction

Respiratory failure is the leading cause of admissions in the pediatric ICU and mechanical ventilation is first-line

treatment. Although mechanical ventilation is often life-saving, it can be associated with complications, such as ventilator-induced lung injury,¹ nosocomial infection, airway trauma, and severe diaphragmatic dysfunction.² It, therefore, is important that mechanical ventilation be dis-

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continued as soon as possible, that is, as soon as the patient is capable of spontaneous breathing.

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During the weaning phase of mechanical ventilation, the ability of the respiratory muscles to cope with the imposed load is challenged.³ The assessment of respiratory muscle function during the weaning process could help to predict extubation success and optimize its timing.⁴ Different tools are available to monitor different components of respiratory muscle function during the weaning phase. Esophageal pressure (P_{es}) measurement is the reference method to measure the pressure generated by the patient's inspiratory muscles and has been shown to be a good method to predict weaning outcome.^{5,6}

The electrical activity of the diaphragm (EA_{di}) reflects the patient's ventilatory drive, and it has been used to monitor diaphragm activity during weaning trials.⁷ The neuromechanical or neuroventilatory efficiency of the respiratory system can be estimated by the ratio of the muscle pressure or the ventilatory volume divided by the corresponding EA_{di} .⁸ Moreover, oxygen consumption ($\dot{V}_{O_2}$) has been shown to change on adaptations of mechanical ventilation parameters and modes because the oxygen cost of breathing reflects the output of the respiratory muscles.⁹

Whereas, in normal subjects, the portion of $\dot{V}_{O_2}$ assigned to the respiratory load $\dot{V}_{O_2}$ accounts for 1 to 3% of the whole body $\dot{V}_{O_2}$,¹⁰ this percentage can be considerably higher in patients being weaned from ventilation.^{11,12} Indirect calorimetry, which provides $\dot{V}_{O_2}$ continuously at the bedside, could be an attractive tool to assess the respiratory muscle function because this could be a reliable and less invasive method of estimating the change in the work

QUICK LOOK

Current Knowledge

The assessment of respiratory muscle function during the weaning process could help to predict extubation success and optimize its timing. Different parameters (such as esophageal pressure, electrical activity of the diaphragm, and oxygen consumption measured by indirect calorimetry) are available to monitor various components of respiratory muscle function during the weaning phase.

What This Paper Contributes to Our Knowledge

In children who were critically ill, a spontaneous breathing trial induced a moderate and nonsignificant increase in work of breathing, as reflected by the respiratory drive monitored with electrical activity of the diaphragm and by the respiratory mechanics measured with esophageal pressure. However, indirect calorimetry, which measures oxygen consumption, did not seem to be a sensitive tool to assess respiratory muscle function during the weaning phase in children on mechanical ventilation.

of breathing. However, pediatric data in this field are lacking, especially about the reliability and reproducibility of indirect calorimetry. The present study aimed to characterize the behavior of 3 components of respiratory muscle function during mechanical ventilation weaning in children to better understand the respective impact of a spontaneous breathing trial (SBT) on P_{es} , EA_{di} , and $\dot{V}_{O_2}$.

Methods

This was a prospective study, conducted in the pediatric ICU of Centre Hospitalier Universitaire (CHU) Sainte-Justine, a university affiliated pediatric hospital, from November 2016 to June 2017. The study protocol was approved by the ethics committee of CHU Sainte-Justine, and written informed consent was obtained from the parents or legal tutor.

Subjects

Consecutive children ages between 1 month and 18 y admitted to the pediatric ICU, intubated, and on mechanical ventilation were eligible. The screening was performed by the research assistants Mariana Dumitrascu, Mary-ellen French, and Jouher Nait every working day. Eligible patients were included if they were deemed to be ready for an extubation readiness test as per the attending team, provided the research team and the equipment were available. Patients were excluded if they had one of the fol-

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lowing criteria: contraindications to the placement of a new nasogastric tube, hemodynamic instability, severe respiratory instability, axillary temperature $> 38^{\circ}\text{C}$, cuff leaks $> 10\%$, nitrite oxide therapy, ventilation with high frequency oscillation, or if a limitation of life support treatments was discussed or decided. Detailed inclusion and exclusion criteria are given in the supplementary material (see the supplementary materials at <http://www.rcjournal.com>).

Protocol and Data Recording

P_{es} , EA_{di} , and $\dot{V}_{\text{O}_2}$ data were monitored to characterize respiratory muscle function. P_{es} and EA_{di} were obtained simultaneously by a specific modified 8 French EA_{di} catheter (NeuroVent Research, Toronto, Ontario, Canada) equipped with both microelectrodes (for EA_{di} monitoring) and an esophageal balloon (for P_{es} monitoring) (see the supplementary materials at <http://www.rcjournal.com>), installed 30 min before measurement. The catheter was connected to a Servo-i ventilator (Maquet, Solna, Sweden), to gather the EA_{di} signal. The correct position of the catheter was checked with a specific positioning screen on the Servo-i by following the company recommendation.¹³ In that position, the middle electrodes of the array are very close to the median diaphragm position. The balloon, which is located 1 cm above the upper electrode, therefore, was in the lower esophagus. P_{es} and EA_{di} signals were simultaneously recorded by using an acquisition system (NeuroVent Monitor XIII) and displayed and analyzed by using specific software (NeuroVent Research).

$\dot{V}_{\text{O}_2}$ and resting energy expenditure were measured by a portable indirect calorimeter (Vmax Encore, CareFusion, Yorba Linda, California), which was connected 30 min before measurement. Gas and pressure were calibrated according to the manufacturer's instructions. All data were measured during 3 periods of 30 min each: before, during, and after an SBT in CPAP. The subjects were supine, with the head of bed elevated to 30° , and no or light sedation, according to the attending physician's instructions.

Demographic data and subjects characteristics, including age, sex, weight, time of measurements, admission diagnostic, and comorbidities, and Pediatric Risk of Mortality and Pediatric Logistic Organ Dysfunction scores were collected. Rapid shallow breathing index is defined as the ratio of breathing frequency to tidal volume (V_T). Predicted energy expenditure was calculated according to the Schofield equations (kcal/d) (see the supplementary materials at <http://www.rcjournal.com>). Clinical indices of increased work of breathing and comfort of the subject, assessed with the COMFORT behavior scale, were gathered during the 3 periods. The sedation level was assessed with the sedation score described by Randolph et al,¹⁴ which was adapted to include dexmedetomidine accord-

ing to the study performed by Eren et al.¹⁵ One point was given for morphine or midazolam equivalents of 0.1 mg/kg. Pediatric ICU outcome data included the following: SBT success or failure, extubation success or failure (as defined by the need to re-intubate in the 48 h after extubation), and duration of mechanical ventilation.

Data Analysis

For P_{es} and EA_{di} recordings, after elimination of the cycles with artifacts, such as coughing or esophageal spasms, at least 20 consecutive breath cycles in the 3 different respiratory conditions were used for subsequent analysis. P_{es} -time product (PTP_{es}) was obtained by measuring the area under the P_{es} signal between the onset of inspiration and the end of inspiration as determined on EA_{di} tracing. PTP_{es} was also expressed per minute by multiplying the PTPs per breath by the breathing frequency ($\text{PTP}_{\text{es}}/\text{min}$). Neuro-mechanical and neuroventilatory efficiencies were assessed by the ratio of swing P_{es} to peak EA_{di} , and V_T to peak EA_{di} , respectively.

The mean $\dot{V}_{\text{O}_2}$ and resting energy expenditure were calculated during the 3 periods. Data from the first 10 min and from periods of documented physical movement or nursing care, such as endotracheal suctioning, were excluded. The steady state was defined as 10 consecutive minutes during which $\dot{V}_{\text{O}_2}$ and carbon dioxide production vary less than $\pm 10\%$, as previously described.¹⁶ The respiratory load $\dot{V}_{\text{O}_2}$ was defined as the difference between $\dot{V}_{\text{O}_2}$ during SBT and $\dot{V}_{\text{O}_2}$ under conventional mechanical ventilation.

Statistical Analysis

Data were expressed as median values (interquartile range [IQR]) for continuous variables and as number and/or frequency (%) for categorical data. Differences for categorical variables were tested by using the chi-square or the Fisher exact test (when expected frequencies were < 5). Differences in continuous variables were assessed by using the non-parametric Mann-Whitney test or the paired t test, depending on the variable distribution. Repeated measures analysis of variance was used to compare the different conditions (before, during, and after SBT in CPAP) on the different variables. Pearson correlation coefficient (R) and determination coefficient (R^2) were used to evaluate the correlation between changes in swing P_{es} , PTP_{es} , EA_{di} , and $\dot{V}_{\text{O}_2}$. All P values were 2-tailed and considered significant if $P < .05$. Statistical analyses were performed by using SPSS 24.0 (SPSS, Chicago, Illinois). Details regarding the sample size are given in the supplementary material (see the supplementary materials at <http://www.rcjournal.com>).

Results

Study Population

During the study period, 568 patients were admitted to the pediatric ICU, and 280 were mechanically ventilated. Thirty-one patients were eligible and approached by the study team. Five parents or guardians did not consent to the study, whereas 4 patients were extubated before inclusion. In 2 subjects, measurements were not performed due to clinical deterioration. In total, 20 subjects were enrolled (10 boys), with a median age of 5.5 (IQR, 2–64) months. The subjects' characteristics are presented in Table 1. They were studied 7 (IQR, 3–11) d after initiation of mechanical ventilation. The main reason for admission to the pediatric ICU was respiratory failure ($n = 10$ [50%]), and 3 subjects (15%) were admitted after surgery. Before SBT, the median COMFORT score was 14 (IQR, 12–16). Five subjects (25%) received intermittent analgesic treatments only, whereas 5 (25%) received both sedative and analgesics agents with a continuous infusion. In 2 subjects, EA_{di} could not be measured due to technical problems and, for another subject, the measurements from indirect calorimetry were inaccurate due to air leaks of >10% that occurred after inclusion. All the subjects were on the same settings after SBT as before SBT.

Breathing Pattern and Work of Breathing During SBT

As detailed in the Table 2, the breathing frequency tended to increase during the SBT, although this did not reach significance ($P = .23$). No clear changes in V_T , minute ventilation, and the rapid shallow breathing index were observed. Unexpectedly, the increase in P_{es} swings and PTP_{es}/min during the SBT was not significant ($P = .33$ and $P = .75$, respectively) (Fig. 1). P_{es} swings increased by at least 10% during SBT in 14 subjects (70%). A similar trend was observed with peak EA_{di} ($P = .059$). Neuromechanical and neuroventilatory efficiency did not change significantly before, during, or after SBT. We did not observe any association between P_{es} and EA_{di} changes and the level of comfort or the sedation score.

Variables Measured By Indirect Calorimeter

$\dot{V}O_2$ obtained by indirect calorimetry was stable in the 3 conditions ($P = .98$). In 10 subjects (50%), $\dot{V}O_2$ decreased during SBT. Resting energy expenditure and the respiratory load $\dot{V}O_2$ patterns did not differ according to the COMFORT and sedation score. Predicted resting energy expenditure was overestimated compared with the measured resting energy expenditure (47 [40–54] kcal/kg/d vs 23 [21–29] kcal/kg/d, $P < .001$) and the median (IQR)

Table 1. Characteristics of the Study Population

Characteristic	Results
Age, median (IQR) mo	5.5 (2–64)
Weight, median (IQR) kg	6.4 (4.1–17.6)
Boys, n (%)	10 (50)
Predicted REE, median (IQR) kcal/kg	47 (40–54)
Days between admission and inclusion, median (IQR)	7 (3–12)
Days between mechanical ventilation initiation and inclusion, median (IQR)	7 (3–11)
Main reasons for pediatric ICU admission, n (%)	
Respiratory failure	10 (50)
Hemodynamic failure	4 (20)
Neurologic disorder	3 (15)
Postoperative admission	3 (15)
Chronic condition, n (%)	
Respiratory disease	7 (35)
Cardiac disease	4 (20)
Neurologic disease	3 (15)
Clinical status at baseline, median (IQR)	
PIM–2 score (on admission day)	2.8 (0.6–18.8)
PELOD score	7 (1–19)
Temperature, °C	36.9 (36.5–37.2)
pH	7.38 (7.35–7.40)
P_{aCO_2} , mm Hg	47.4 (44.2–53.3)
HCO_3^- , mm Hg	28.0 (26.0–30.8)
Lactate, mmol/L	1.4 (0.9–1.8)
Hemoglobin, g/L	10.3 (9.6–11.1)
Ventilator modes and settings	
NAVA, n	7
NAVA level, median (IQR) cm $H_2O/\mu V$	0.5 (0.3–0.5)
PSV, n	9
PSV, median (IQR) cm H_2O	9 (6–11)
PC, n	4
IPAP, median (IQR) cm H_2O	14 (11–15)
PEEP, median (IQR) cm H_2O	5 (5–6)
F_{IO_2} , median (IQR)	30 (25–40)
ETT	
ETT size, median (IQR) mm ID	3.5 (3.5–4.5)
Cuffed ETT, n (%)	18 (90)
Air leakage around ETT, median (IQR) %	5 (2–7)
Sedation status	
COMFORT score, median (IQR)	14 (12–16)
Sedation score, median (IQR)	12 (5–26)
Continuous intravenous sedation, n (%)	14 (70)
Analgesic bolus only, n (%)	5 (25)
Outcome	
SBT failure, n (%)	0 (0)
Time between SBT and first extubation, median (IQR) h	18 (1.5–43.5)
Re-intubation in the 48 h after extubation, n (%)	2 (10)

$N = 20$.

IQR = interquartile range

REE = resting energy expenditure

PIM = pediatric index of mortality

PELOD = pediatric logistic organ dysfunction

NAVA = neurally adjusted ventilatory assist

PSV = pressure support ventilation

PC = pressure control

IPAP = Inspiratory positive airway pressure

ETT = endotracheal tube

ID = internal diameter

SBT = spontaneous breathing trial

Table 2. Clinical Status and Respiratory Muscle Assessment Before, During, and After SBT

Parameter	SBT, Median (IQR)			P
	Before	During	After	
Respiratory status				
S _{pO₂}	99 (96–100)	99 (95–100)	97 (95–100)	.79
Measured frequency, breaths/min	29 (22–31)	35 (26–40)	30 (25–37)	.23
V _T , mL/kg	7.1 (5.4–7.8)	6.4 (4.4–7.8)	7.8 (5.1–8.1)	.89
V̇ _E , L/min	1.5 (0.9–2.8)	1.7 (1.1–2.8)	1.6 (0.9–3.2)	.76
RSBI (f/V _T), breaths/min/mL/kg	4.1 (3.1–6.3)	5.4 (4.0–7.3)	5.0 (3.9–6.1)	.76
COMFORT score	14 (12–16)	14 (12–16)	13 (12–16)	.86
Hemodynamic status				
Heart rate, beats/min	115 (97–135)	121 (99–143)	120 (101–141)	.76
Mean arterial pressure, mm Hg	69 (59–85)	72 (62–80)	72 (62–83)	.96
WOB indices				
P _{es} derived data				
Swing P _{es} , cm H ₂ O	3.9 (1.7–6.2)	5.5 (2.7–8.5)	3.1 (1.1–5.5)	.33
PTP _{es} /min, cm H ₂ O × s/min	23 (5–89)	83 (24–110)	31 (10–69)	.75
EA _{di} derived data				
Peak EA _{DI} , μV	7.5 (3.2–16.3)	15.9 (5.2–22.1)	9.1 (3.0–14.4)	.059
Neuromechanical efficiency (ΔP _{es} /ΔEA _{di})	0.6 (0.4–1.1)	0.8 (0.3–1.0)	0.6 (0.2–1.5)	.56
Neuroventilatory efficiency (V̇ _T /ΔEA _{di})	5.1 (2.2–21.4)	3.3 (1.4–6.7)	5.2 (1.8–26.2)	.30
Indirect calorimeter derived data				
V̇ _{O₂} /kg, mL/kg/min	3.6 (3.1–4.6)	3.8 (3.0–5.2)	3.8 (3.2–5.2)	.98
Respiratory load V̇ _{O₂} /kg, mL/kg/min	NA	−0.2 (−0.5 to 0.44)	NA	
V̇ _{CO₂} /kg, mL/kg/min	2.8 (2.3–3.3)	2.5 (2.1–3.6)	2.5 (2.3–3.3)	.57
Resting energy expenditure, kcal/kg	23 (21–29)	24 (19–33)	23 (21–33)	.96
Respiratory quotient	0.71 (0.69–0.78)	0.72 (0.68–0.78)	0.70 (0.65–0.77)	.70

SBT = spontaneous breathing trial
IQR = interquartile range
V_T = tidal volume
V̇_E = minute volume
RSBI = rapid shallow breathing index
WOB = work of breathing
P_{es} = esophageal pressure
PTP_{es} = esophageal pressure–pressure-time product
EA_{di} = electrical activity of the diaphragm
V̇_{O₂} = oxygen consumption
NA = not applicable
V̇_{CO₂} = carbon dioxide production

respiratory quotient measured by indirect calorimetry was 0.71 (0.69–0.78).

Correlations Between P_{es}, EA_{di}, and V̇_{O₂}

Overall, changes in V̇_{O₂} were not correlated with the changes observed with PTP_{es} and peak EA_{di} (R² = 0.05 and R² = 0.01, respectively). Similarly, only a poor correlation was observed between changes in P_{es} and changes in EA_{di} (R² = 0.3) (Fig. 2).

Outcome

SBT was considered a success in 20 subjects (100%), and extubation was successful in 17 subjects (89%). One subject was not extubated and died after limitation of life

support treatment. Median (IQR) duration of mechanical ventilation and stay in the pediatric ICU were 10 (4–14) d and 18 (7–42) d, respectively. After extubation, 9 subjects (45%) required no respiratory support, whereas 2 (10%) were reintubated, and 8 (40%) were on noninvasive respiratory support within 1 h of extubation. The pattern of PTP_{es}, EA_{di}, and V̇_{O₂} during the SBT were not associated with extubation failure, although the number of subjects was limited.

Discussion

In this series of 20 children who were critically ill, we observed that SBT in CPAP was associated with a nonsignificant increase in P_{es} derived indices of effort of breathing and of EA_{di}. However, the respiratory load V̇_{O₂} measure-

Fig. 1. Work of breathing before, during and after SBT, assessed by breathing frequency (A), swing peak esophageal pressure (P_{es} , B), peak electrical activity of the diaphragm (EA_{di} , C), and oxygen consumption ($\dot{V}_{O_2}$, D). SBT = spontaneous breathing trial.

ments were stable during the maneuver. In children, the benefit of weaning protocols, including SBT, to shorten the duration of ventilation has been demonstrated,¹⁷ and the recent consensus conference on pediatric ARDS recommends that SBT and/or extubation readiness tests should be performed.¹⁸ For monitoring patient-ventilator interactions during SBT, clinicians mostly rely on patient breathing patterns and waveforms that are available on most ventilators.

However, several difficulties remain to assess the patient's contribution to the work of breathing with usual clinical monitoring during mechanical ventilation.¹⁹ Measurements of P_{es} and EA_{di} provide the clinicians with a

bedside evaluation of respiratory effort from 2 different points of view. Assessment of P_{es} is the reference method to measure the pressure generated by the patient's inspiratory muscles. The direct monitoring of respiratory muscle function by P_{es} has been shown to be helpful in titrating ventilator support in different pathologies²⁰ and, as Jubran and Tobin⁵ showed in adults, the P_{es} trend during an SBT can provide an accurate prediction of weaning outcome.

However, EA_{di} gives the clinician a bedside evaluation of diaphragm activity.²¹ EA_{di} can be considered as a parameter that reflects patient ventilatory drive, and it provides a continuous indirect reflection of the evolution in work of breathing.²² Because adequate diaphragmatic function is paramount for weaning success, the relevance of monitoring EA_{di} during the weaning process has also been described.²³ Wolf et al⁷ observed that the ability to generate a higher diaphragmatic activity for the same V_T in pressure-support ventilation was a predictor of successful extubation. Combining EA_{di} and V_T in the neuroventilatory index is an interesting concept because the comparison of ventilatory demand with mechanical output provides information on diaphragmatic efficiency.

Our initial hypothesis was that $\dot{V}_{O_2}$ provided at the bedside of children who are critically ill by indirect calorimetry could provide a reliable and less-invasive method to estimate the change in the work of breathing during weaning from conventional ventilation. We reasonably assumed that no confounding factor except increasing the work of breathing could induce an increase in $\dot{V}_{O_2}$ during SBT. We, therefore, chose to record 3 periods of 30 min, during which time, the underlying metabolic condition could not change, as suggested in a previous study.¹²

Many investigators, rather than focusing on mechanical muscle function, evaluated the role of the respiratory load $\dot{V}_{O_2}$ as a predictor of weaning success,^{9,24} and other investigators reported that the respiratory load $\dot{V}_{O_2}$ was closely correlated to PTP.²⁵ In children, the use of indirect calorimetry for respiratory purposes is scarcely reported.²⁶ In a few studies, $\dot{V}_{O_2}$ has been measured in children on mechanical ventilation in different clinical conditions to assess the effects of therapeutics such as neuromuscular blockers²⁷ or inhaled salbutamol.²⁸ To our knowledge, $\dot{V}_{O_2}$ measurement during weaning from pediatric mechanical ventilation has never been studied.

Compared with measurements from P_{es} and EA_{di} , the respiratory load $\dot{V}_{O_2}$ did not tend to accurately reflect changes in work of breathing. We could expect a respiratory load $\dot{V}_{O_2}$ of ~10% of $\dot{V}_{O_2}$ according to the study by Hoher et al²⁹ who found that subjects on assisted ventilation spent 11% more energy than those on controlled ventilation, as supported by another study.¹² Yet, we found, in the present study, that the respiratory load $\dot{V}_{O_2}$ was not influenced by ventilator mode, in agree-

Fig. 2. Relationship between the changes of swing ventilatory mechanical action (esophageal pressure [P_{es}]) vs peak ventilatory demand (electrical activity of the diaphragm [EA_{di}]) (A) and swing P_{es} vs oxygen consumption ($\dot{V}_{O_2}$) (B) from conventional settings to spontaneous breathing trial (SBT) (▲) and from SBT to previous settings (●).

ment with the study published by Briassoulis et al³⁰ in a population of 11 children who were critically ill and on mechanical ventilation.

We suggested several hypotheses to analyze this finding. First, the subjects were relatively stable and had a low level of support before SBT. In that context, the respira-

tory load $\dot{V}_{O_2}$ may not be as sensitive as P_{es} or EA_{di} to detect a small change in the work of breathing. According to the study performed by Frankenfield and Ashcraft,³¹ measurements from the Vmax Encore Calorimeter can be biased by 5% in the same subject. One may speculate that, in patients with worse respiratory function, the results might have been different. Second, this finding could be explained by the great heterogeneity of our population, in terms of pathologies, mode of ventilation, ventilator settings, duration of ventilation, time of inclusion, and degree of sedation.³⁰ Third, SBT may induce changes in functional residual capacity, which results in changes in spirometer volume unassociated with $\dot{V}_{O_2}$.

Also, it is important to note that agitation or distress that may accompany a difficult SBT can also contribute to the $\dot{V}_{O_2}$ increase. In our study, the changes in $\dot{V}_{O_2}$ were small, and similar values of COMFORT behavior scores were observed during the 3 periods of the protocol (before, during, and after SBT), which made it difficult to assess this potential relationship. Further work is clearly needed to assess the value of indirect calorimetry during the weaning phase in other contexts and, in particular, earlier in the course of ventilation and in patients with a worse respiratory condition and a higher rate of SBT failure.

Besides the main study goal, we, interestingly, observed absolute $\dot{V}_{O_2}$ values that were lower than previously reported.^{26,32} Most of these studies were performed at the early stage of the disease.³³ Moreover, most of the subjects in those studies were admitted after trauma, and some of them received nutritional therapy, which could explain such difference. In our study, because we performed indirect calorimetry measurements during the weaning phase, we hypothesized that the metabolic rate was low in the recovery period. Although we consider observed $\dot{V}_{O_2}$ values as true, we cannot exclude that confounding factors could explain such results. First, although we excluded patients with $F_{IO_2} > 0.6$ or cuff leaks $> 10\%$, values could be less accurate in subjects with $F_{IO_2} > 0.4$ or cuff leaks $> 5\%$.³⁴ In addition, even though we used a standardized and validated approach for indirect calorimetry measurements, we could not rule out the possibility of inaccurate measurements or technical problems.³⁵

Both EA_{di} and P_{es} are well-known parameters that indirectly reflect respiratory muscle function. Previous studies show a tight correlation between EA_{di} and P_{es} .^{22,36} However, there is high inter-individual variability.³⁶ In our study, the changes observed between the 3 periods for these 2 variables were relatively small, and the data were limited, which likely explained the poor correlation observed, due to limited statistical power. This can also reveal that the effort needed to breathe before SBT was not significantly increased over normal physiologic conditions, which would not have been the case if measurements had been performed earlier in the course of mechanical ventilation.

Of note, the relationship between EA_{di} and P_{es} can also be affected by sedation³⁷ or by the level of assistance.³⁸ These factors, in addition to the great heterogeneity in our population, could also explain the moderate correlation between EA_{di} and PTP. An impaired neuromuscular coupling³⁹ seemed unlikely in these subjects with a near-normal respiratory condition. Also, our findings regarding the difference between predicted and measured resting energy expenditure were in agreement with those reported elsewhere. Indeed, several studies showed that predictive equations overestimated resting energy expenditure in children who were critically ill and with various clinical situations.^{32,40} Our results tended to confirm that such equations could not substitute for indirect calorimetry measurement of resting energy expenditure.

There were several limitations in the present study. This was a single-center study, which tends to limit its generalizability. The sample size was small and, therefore, this study may have been underpowered to demonstrate the correlation between the variables and to show any significant impact of SBT on the indices that reflected the effort of breathing. The sample size had been estimated when we hypothesized a greater impact of SBT and a high correlation between the 3 methods of work of breathing assessment. We performed measurements during daytime and weekdays only, which could lead to a selection bias. The study population was heterogeneous in terms of reasons for admission, duration of mechanical ventilation, age, and degree of sedation of the patients. This may lead to different respiratory behavior during weaning from mechanical ventilation. However, the population reflected a usual pediatric ICU population.

In addition, work of breathing indices were assessed during a 30-min SBT, whereas some investigators have suggested a longer extubation readiness test.²⁰ Nevertheless, significant changes in respiratory mechanics occur rapidly after modification of ventilator settings. Regarding the P_{es} measurement, due to the unique catheter used to monitor both EA_{di} and P_{es} , it was not possible to independently adjust the position specifically for P_{es} , although the position in the lower esophagus was relatively guaranteed by the probe design. It was possible that this induced a suboptimal P_{es} signal in some subjects. Noteworthy, the impact of the position was likely the same during the 3 ventilation periods. Finally, we did not assess respiratory muscle function after extubation.

Conclusions

In these children who were critically ill, an SBT on CPAP induced a moderate and nonsignificant increase in the work of breathing, as reflected by the respiratory drive with EA_{di} and by respiratory mechanics with P_{es} . In this specific population with relatively stable respiratory sta-

tus, the $\dot{V}_{O_2}$ measurement was not a sensitive parameter to detect an increase in respiratory muscle activity during the SBT. The interest of this monitoring technology should be further evaluated, in particular, in patients with a higher work of breathing.

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