Effect of pediatric ventilation weaning technique on work of breathing

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Research Article

Keywords: pediatrics, mechanical ventilation, work of breathing, weaning, pressure-rate-products, pressure-time-product, phase angle.

Posted Date: March 1st, 2022

DOI: <https://doi.org/10.21203/rs.3.rs-1336451/v1>

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Abstract

Background: Ventilator liberation is one of the most challenging aspects in patients with respiratory failure. Most patients are weaned through a transition from full to partial respiratory support, whereas some advocate using a continuous spontaneous ventilation (CSV). However, there is little scientific evidence supporting the practice of pediatric ventilator liberation, including the timing of onset of and the approach to weaning mode. We sought to explore differences in patient effort between a pressure controlled intermittent mode of ventilation (PC-IMV) with or without pressure support (PS) with a reduced ventilator rate and CSV, and to study changes in patient effort with decreasing PS.

Methods: In this prospective physiology cross-over study, we randomized children <5 years to first PC-IMV $\pm$ PS with a 25% reduction in ventilator rate, or CSV (continuous positive airway pressure [CPAP] + PS). Patients were then crossed over to the other arm. Patient effort was measured by calculating work of breathing (WOB) using the Campbell diagram ($\text{WOB}_{\text{Campbell}}$), and by pressure-rate-product (PRP) and pressure-time-product (PTP). Respiratory inductance plethysmography (RIP) was used to calculate the phase angle. Measurements were obtained at baseline, during PC-IMV $\pm$ PS and CPAP + PS, and during decreasing set PS (maximum -6 cmH₂O).

Results: Thirty-six subjects with a median age of 4.4 (IQR 1.5 – 11.9) months and median ventilation time of 4.9 (IQR 3.4 – 7.0) days were included. Nearly all patients (94.4%) were admitted with primary respiratory failure. $\text{WOB}_{\text{Campbell}}$ during baseline (0.67 (IQR 0.38 – 1.07) Joules/L) did not differ between CSV (0.49 (IQR 0.17 – 0.83) Joules/L) or PC-IMV $\pm$ PS $\pm$ PS $\pm$ PS (0.47 (IQR 0.17 – 1.15) Joules/L). Neither PRP, PTP, ΔPes nor phase angle was different between the two ventilator modes. Reducing pressure support resulted in a statistically significant increase in patient effort, albeit that these differences were clinically negligible.

Conclusions: Patient effort during pediatric ventilation liberation was not increased when patients were in a CSV mode of ventilation compared to a ventilator mode with a ventilator back-up rate. Reducing the level of PS did not lead to clinically relevant increases in patient effort. These data may aid in a better approach to pediatric ventilation liberation.

Trial registration: [clinicaltrials.gov NCT05254691](https://clinicaltrials.gov/ct2/show/study/NCT05254691). Registered 24 February 2022

Background

Mechanical ventilation (MV) is one of the core features of the pediatric intensive care unit (PICU). Despite life-saving, MV is also associated with undesired effects, which may ultimately affect physical functioning and quality of life. These include amongst others the occurrence of ventilator induced lung injury (VILI), nosocomial pneumonia, upper airway trauma, hemodynamic instability and increased need for sedation or even neuromuscular blockade with subsequent risk for withdrawal syndrome or delirium. (1–3) This underscores the need to start ventilation liberation as soon as the clinical condition of the patient allows for this. It is estimated that almost half of the total ventilation time is related to weaning. (4, 5) Unfortunately, there is little scientific evidence supporting the practice of pediatric ventilation liberation, including the

timing of onset of and the approach to weaning. This can be partly explained by the relative short ventilation time and low extubation failure rates observed in the pediatric population. (6–8)

The most common approach to weaning in infants and children is a gradual reduction of ventilatory support through a reduction of the ventilator rate and/or a reduction in inspiratory pressures when the patient is in pressure controlled mode of ventilation (PCV).(9) Alternatively, it has also been proposed to periodically use a continuous spontaneous ventilation (CSV) mode (i.e., pressure support [PS]) in combination with continuous positive airway pressure (CPAP) and alternate this with complete ventilatory support. The rationale for this approach is to (slowly) train and reactivate the respiratory muscles.(9) However, there is no pediatric data that has shown superiority of one approach over the other.(10) Aside from weaning technique, the unanswered question is also how much PS to give. Both over- and undersupport may exert negative effects on respiratory muscle function and patient effort.

Irrespective of the approach chosen by the clinical team, it is imperative to assess work of breathing (WOB) when the patient is weaned from the ventilator. The gold standard for measuring WOB is through the Campbell diagram (WOB_{CAMPBELL}) by making use of an esophageal catheter. This diagram reflects the energy that is needed to expand the lungs and chest wall.(11) Surrogate parameters include esophageal pressure swing (ΔP_{es}), the pressure rate product (PRP) and the pressure time product (PTP), which both can distinguish patient effort from the total effort, and the phase angle calculated from respiratory inductance plethysmography readings. (12–15)

Based on the hypothesis that weaning using CSV would not result in increased WOB, irrespective of the level of PS, we sought to characterize in a randomized cross-over trial patient effort during ventilator weaning by comparing WOB_{CAMPBELL} , PTP, PRP, ΔP_{es} and the phase angle measured during PC-IMV with a reduced ventilator rate and during CSV in ventilated children who were deemed eligible for weaning by the attending physician. We also studied if there was a relationship between patient effort and the level of PS.

Methods

Study design

This study was designed as a prospective, physiological, randomized cross-over study comparing two different weaning strategies and the effect of the level of PS on the work of breathing in mechanically ventilated children admitted to the 20-bed tertiary medical-surgical pediatric intensive care unit (PICU) of the Beatrix Children's Hospital, University Medical Center Groningen (Groningen, The Netherlands). The study was approved by the institutional review board (IRB) (NL38361.042.11), and written informed consent was obtained from parents or legal caretakers.

Patients

Patients were daily assessed for eligibility when the attending physician who identified the patient ability for weaning, which was defined by the ability to maintain adequate oxygenation and ventilation under stable ventilator settings (i.e., no need for increase of inspiratory pressures or positive end-expiratory

pressure, and fraction inspired oxygen (FiO_2) < 0.5 within 6 hours prior to enrolment). Subjects were enrolled if they were younger than 5 years of age, ventilated for at least 24 hours, able to trigger the ventilator and had sufficient respiratory drive and stable hemodynamics (i.e., no need for increase in vaso-active drugs and/or fluid challenges at least 6 hours prior to enrolment). Excluded were subjects born prematurely with a corrected gestational age < 40 weeks, congenital or acquired neuromuscular disorders, congenital or acquired paralysis of the diaphragm, severe traumatic brain injury (i.e., Glasgow Coma Score < 8), uncorrected congenital heart disorder, chronic lung disease and severe pulmonary hypertension. Patients with endotracheal tube (ETT) leakage > 18% were also excluded.

Ventilator protocol

Prior to enrolment, subjects were ventilated with the AVEA® ventilator (Vyaire, Mettawa, Ill, USA) in supine position using a time-cycled, pressure limited ventilation mode (either in assist/control [A/C] or in the synchronized intermittent mandatory ventilation [SIMV]) or CPAP/PS, targeting expiratory Vt 5–7 ml/kg actual bodyweight (as there was no obesity in the patient cohort). VTe was measured at the Y-piece of the patient circuit (VarFlex™, Vyaire, Mettawa, Ill, USA). Peak inspiratory pressures (PIP) were aimed at < 28 cmH₂O (< 32 cmH₂O when there was an increased chest wall elastance). Fraction inspired oxygen was targeted at SpO_2 of 92–97%. Flow trigger was set between 0.5 and 1.0 L/min. A heat moisture exchanger (Gibeck, Teleflex Medical, Vianen, The Netherlands) was in situ between the patient circuit and the endotracheal tube (ETT) (KimVent, Microcuff Endotracheal Tube, Paediatrics, Roswell, USA).

All patients are routinely instrumented with a catheter to measure the esophageal pressure (Pes) (Avea SmartCath 6 or 8 Fr, Vyaire, Mettawa, Ill, USA). Correct positioning was visually confirmed by checking for pressure deflections during spontaneous breathing and/or by a chest radiograph that was done for other indications.⁽¹⁶⁾

Randomization protocol

Baseline defined the ventilator mode and settings that the subject was on before randomization. Subjects were randomized to one of two groups (A and B), defining the order of the weaning approaches tested. Subjects randomized to group A were on CPAP + PS with the level of PS equal to the set pressure above PEEP (PAP) that the subject was on before randomization first, and subsequently to PCV with the ventilator rate set at 25% of baseline. Subjects randomized to group B were on PCV with the ventilator rate set at 25% of baseline first, and subsequently to CPAP + PS.

Measurement protocol

After obtaining informed consent and enrolment, age appropriate respiratory inductance plethysmography (RIP) bands (Viasys, Healthcare, Respiband Plus, Hoechberg, Germany) were placed circumferentially around the patient's chest and abdomen. For calibration, the ETT was occluded at the end of an exhalation during a stable breathing for 3–5 consecutive breaths. (12, 17) The esophageal catheter was connected to a BiCore II pulmonary monitor (CareFusion, Houten, The Netherlands) with a sampling frequency of 200 Hz. Then, the esophageal balloon volume was titrated up to a maximum of 1.25ml H₂O (pediatric balloon) or

2.5ml H₂O (adult balloon). Optimal balloon volume was achieved by titrating volume and graphically depicting the maximum amplitude of the Pes curve (Δ Pes).

Baseline recordings were obtained during 5 minutes of stable breathing with the ventilator settings the subject was on before randomization. Subsequently, the subject was placed on the ventilator mode and settings according to the randomization outcome. After 5 minutes of stabilisation, data was then recorded for 5 minutes. Thereafter, the subject was placed on the baseline ventilator mode and settings for 10 minutes and then on the ventilator mode and settings according to the randomization outcome. After 5 minutes of stabilisation, data was then recorded for 5 minutes. In a second series of measurements, each patient had the level of PS reduced by 2 cmH₂O on three consecutive steps. Each step consisted of 5 minutes of stabilization followed by 5 minutes of recordings. (Fig. 1)

Data collection included respiratory rate (RR), heart rate (HR), central venous pressure (CVP), mean arterial blood pressure (ABP), transcutaneous measured oxygen saturation (SpO₂), minute volume (AMV), expired tidal volume (VTe), end-tidal CO₂ (EtCO₂), inspiratory pressures, PEEP, FiO₂, inspiratory time (T_{insp}), mean airway pressure (P_{mean}) and set flow trigger. Patient comfort was assessed by calculating the Comfort B score. (18) If patients had an indwelling arterial line, blood samples were drawn to determine arterial partial pressure of CO₂ (PaCO₂) and O₂ (PaO₂). For characterization of the cohort, gender, age, weight, 24-hr Pediatric RISK of Mortality (PRISM) III score, admission diagnosis, ETT-size were collected in the database. (19) Respiratory terminology was used based on the Chatburn classification.(20)

Data analysis

Patient breathing effort was primary assessed by WOB_{CAMPBELL}. Secondary outcomes included PRP, PTP, Δ Pes and the RIP phase angle. Pes and RIP data was analyzed using a custom-build software program (Polybench, Applied Biosignals, Weener, Germany). Pes and RIP signals were first offline reviewed for artifacts (i.e., pressure swings due to esophageal spasms, coughing or body movement) and signal quality. We then selected 30 consecutive, stable breaths and manually placed markers in the RIP and Pes signal to indicate the onset and end of inspiration. WOB_{CAMPBELL} was calculated as the integral of the Pes over the volume displaced (21). Δ Pes represented the amplitude of inspiratory tidal Pes swings. PTP was calculated by the integral of the Pes signal over time during inspiration multiplied by respiratory rate, and PRP by Δ Pes multiplied by the respiratory rate. The phase angle was calculated from the RIP tracings as described previously. (22) The rapid shallow breathing index (RSBI) was calculated by dividing Vte-exp by the respiratory rate.

Statistical analysis

Data was assessed for normality using the Kolmogorov-Smirnov test. Descriptive data were expressed as median (interquartile range), percentage (%) or mean ($\pm$ SD) of total. The Wilcoxon signed rank test was used to detect differences between study time points. By using a generalized, linear mixed model the correlation between WOB_{CAMPBELL} and multiple parameters was studied. Statistical analysis was performed using SPSS v23 (IBM, Armon, NY, USA). *P* values < 0.05 were considered statistically significant.

Results

Thirty-six subjects were included (66.7% male) with an overall median age of 4.4 (IQR 1.5–11.9) months and weight 6.5 (IQR 4.6–9.9) kg. Forty-two out of 252 data samples were excluded due to poor quality (Supplemental Fig. 1). Patient characteristics were comparable between group A and B (Table 1). Almost all patients were admitted with primary respiratory failure (94.4%). Twenty-seven subjects (75%) had received neuromuscular blockage (NMBA) for a median time of 33.8 (IQR 15.1–41.5) hours. They were discontinued 43.5 (IQR 26.7–71.4) hours before randomization (Table 1, extra supplemental material). Baseline ventilator settings before enrolment for the whole cohort was PEEP 6 (IQR 5–6) cmH₂O, PS 14 (IQR 12–16) cmH₂O and FiO₂ 0.30 (IQR 0.26–0.39) (Table 2). Subjects were ventilated for 4.92 (IQR 3.4–7.0) days before enrolment; median time to extubation after enrolment was 23.0 (17.8–44.6) hours. Extubation failure (reintubation < 48 hours) occurred in 3 patients (8.3%) due to upper airway obstruction (n = 2) or clinically judged excessive work of breathing (n = 1).

Patient effort during CSV and PC-IMV ± PS

Median WOB_{CAMPBELL} during baseline recording was 0.67 (IQR 0.38–1.07) Joules/L and decreased to 0.49 (IQR 0.17–0.83) for CPAP/PS and 0.47 (IQR 0.17–1.15) Joules/L for PC-IMV ± PS (Fig. 2A). Except for respiratory rate which was significantly higher when patients were in CPAP + PS, no other differences in clinical parameters were observed (Table 2). The Comfort B score was similar between CPAP + PS and PC-IMV ± PS.

Similar observations regarding comparable patient effort were found in PRP (baseline 296 (IQR 181–445), CPAP + PS 212 (IQR 119–417) and PC-IMV ± PS 213 (IQR 140–320) cmH₂O/min) and PTP (baseline 138 (IQR 68–195), CPAP + PS 105 (IQR 54–170), and PC-IMV ± PS 114 (IQR 61–155) cmH₂O*s/sec) (Fig. 3). ΔPes decreased from baseline 8.37 (IQR 4.36–12.56) cmH₂O to 7.28 (IQR 3.39–10.25) cmH₂O during CPAP + PS and 6.33 (IQR 4.08–11.89) cmH₂O during PC-IMV ± PS. The phase angle was higher during PC-IMV ± PS (28.7 (IQR 12.7–42.3), although this did not reach statistical significance when compared to baseline (21.1 (IQR 8.1–42.3)) or during CPAP + PS (25.8 (IQR 1.7–38.6)).

Patient effort during PS titration

We observed a significant increase in WOB_{CAMPBELL} from baseline (0.28 (IQR 0.11–0.76)) to 0.71 (IQR 0.40–1.22) Joules/L when PS was decreased by 6 cmH₂O (Fig. 2B). EtCO₂ significantly increased, whereas respiratory rate, expiratory Vt (mL/kg) and the RSBI index did not change during the downwards PS titration (Table 2). Similarly, PRP and PTP significantly increased during the downwards PS titration, with PRP increasing to 390 (IQR 231–608) cmH₂O/min and PTP to 173 (IQR 112–289) cmH₂O*s/min at PS -6 cmH₂O. ΔPes increased by 4.84 cmH₂O at PS -6 cmH₂O. (Fig. 3) The phase angle did not change.

In a correlation analysis, we did not find a significant association between WOB_{CAMPBELL} and duration of MV prior to enrollment, use of high-frequency oscillatory ventilation, ETT size, extubation outcome, or

NMBA use or time between discontinuation and study measurements.

Discussion

We have demonstrated in this physiology study that using a continuous spontaneous ventilation mode in pediatric patients resolving from respiratory failure did not lead to increased patient effort compared with an IMV mode. Decreasing PS resulted in a statistically significant, but clinically acceptable increase in patient effort. These data may contribute to a better understanding of the patient effort during pediatric ventilation liberation.

To our best of knowledge, this is one of the first studies that compared two different ventilation liberation approaches in children recovering from acute respiratory failure by evaluating patient effort according to the golden standard (i.e., Campbell diagram).(21) We did not detect clinical relevant differences in patient effort between CPAP/PS and PC-IMV $\pm$ PS. Observed values for WOB_{CAMPBELL} and PRP and phase angle were in line with previous reported values in children (15, 23–25). This means that weaning patients in a CSV mode does not lead to increased patient effort. In fact, the PRP values in our study were lower compared with the PRP values reported by Khemani et al in extubated, spontaneously breathing children. (15) This may suggest that even lower levels of support can be used.

We did observe higher baseline values in WOB_{CAMPBELL} , PTP, PRP and ΔP_{es} than during stable, quiet breathing in CPAP/PS or PC-IMV $\pm$ PS. This may be explained by the fact that subjects had to be instrumented prior to study measurement which may have caused patient discomfort leading to a temporarily increase in respiratory rate and larger esophageal pressure swings rather than reflecting true increased patient effort, especially since at baseline there was no reduction in ventilator rate or inspiratory pressures. Increases in respiratory rate are easily picked up by PTP and PRP, thus potentially explaining our observations.(26)

In our study, we found that patient effort increased when PS was decreased, although the clinical relevance of this increase can be questioned. PRP increased, but reached levels that are comparable with the PRP values reported by Khemani et al.(15) It is common practice in pediatrics to add a minimum amount of PS because of the presumed increased resistances of especially smaller endotracheal tubes and thus the fear of increasing the imposed work of breathing (WOB_{imp}). (9, 27, 28). The findings from our present study however support previous work from us and others, in which we showed both in a bench and in a clinical study that there was no difference in WOB_{imp} between smaller and larger bigger ETT sizes. (29, 30) Therefore, during pediatric ventilation liberation it appears to be appropriate to use a lower level of PS when assessing patient effort and that spontaneous breathing trials can be performed without added PS. Setting more PS than actually needed has been shown to overestimate extubation readiness in children.(31) Importantly, our study was not designed to test superiority or inferiority of CPAP + PS versus PC-IMV $\pm$ PS with reduced ventilator breath rate. Nonetheless, our data confirms that neither approach do lead to increased patient effort, hence the next step would be to design a randomized controlled trial exploring if weaning and ventilation time can be shortened by one approach or the other.

Some limitations of this study need to be addressed. First, it was a single-center study, albeit that it included a homogenous study population, thereby potentially limiting the generalizability although we think this is of no concern for a physiology study such as ours. Second, the 10 minutes duration for the measurements was arbitrarily chosen as others also have done (13, 15). Nevertheless, this does not rule out that the period was too short to detect clinically meaningful changes. It may be surmised that a longer duration on each approach could have led to increasing fatigue and different results. Third, the decision to start weaning was at the discretion of the attending physician and not protocolized, making it subject to practice variability and that subjects may have difference in baseline efforts of breathing. Reassuringly, we did not find a significant correlation between duration of ventilation prior to enrolment and indices of patient effort of breathing.

Conclusion

In children recovering from acute respiratory failure and who are ready to be weaned from the ventilator, effort of breathing was comparable between CPAP + PS and PC-IMV ± PS with a reduced ventilator breath rate. Reducing PS did not lead to clinically unacceptable effort of breathing. Our study findings provide helpful insights into optimizing the weaning strategy in ventilated children.

Abbreviations

ABP	-	Mean arterial blood pressure
A/C	-	Assist/control
AMV	-	Minute volume
CPAP	-	Continuous positive airway pressure
CSV	-	Continuous spontaneous ventilation
CVP	-	Central venous pressure
ETT	-	Endotracheal tube
EtCO ₂	-	End-tidal CO ₂
FiO ₂	-	Fraction inspired oxygen
HR	-	Heart rate
IMV	-	Intermittent mode of ventilation
IQR	-	Interquartile range
IRB	-	Institutional review board

MV	-	Mechanical ventilation
NMBA	-	Neuromuscular blockage
PaO ₂	-	Arterial partial pressure of O ₂
PaCO ₂	-	Arterial partial pressure of CO ₂
PAP	-	Pressure above PEEP
PC-IMV	-	Pressure controlled intermittent mode of ventilation
PCV	-	Pressure controlled mode of ventilation
PEEP	-	Positive end expiratory pressure
Pes	-	Esophageal pressure
PICU	-	Pediatric intensive care unit
PIP	-	Peak inspiratory pressure
Pmean	-	Mean airway pressure
PRISM	-	Pediatric risk of mortality
PRP	-	Pressure-rate-product
PS	-	Pressure support
PTP	-	Pressure-time-product
RIP	-	Respiratory inductance plethysmography
RR	-	Respiratory rate
RSBI	-	Rapid shallow breathing index
SD	-	Standard deviation
SpO ₂	-	Transcutaneous measured oxygen saturation
SIMV	-	Synchronized intermittent mandatory ventilation
T _{insp}	-	Inspiratory time
USA	-	United states of america

VILI	-	Ventilator induced lung injury
VT _e	-	Tidal volume
WOB	-	Work of breathing
WOB _{imp}	-	Imposed work of breathing
ΔPes	-	Esophageal pressure swing

Declarations

Ethics approval and consent to participate

The study was approved by the institutional review board (IRB), and written informed consent was obtained from parents or legal caretakers. (NL38361.042.11)

Consent for publication

Available if requested.

Availability of data and material

The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.

Competing interest

MK received lecture fees from Vyaire, Mettawa, Ill, USA and has received technical support from Vyaire, Mettawa, Ill, USA and Applied Biosignals, Weener, Germany. The remaining authors declare that they have no competing interests.

Funding

Not applicable.

Author's contributions

JvD - Data collection, analysis and interpretation, and drafting the manuscript.

A.K - Data collection and interpretation, and provided intellectual content to the manuscript.

R.G.T.B - Data collection and interpretation, and provided intellectual content

to the manuscript.

L.B.L - Data collection

S.D. - Data collection

J.G.M.B. - Statistical analysis and provided intellectual content
to the manuscript.

M.C.J.K. - Principal investigator, supervision of the project, data analysis and
interpretation, and provided intellectual content to the manuscript.

All authors have significantly contributed to the manuscript and approve its final version.

Acknowledgements

The authors want to thank R.E. Stewart of the University of Groningen, Groningen, the Netherlands, for statistical support.

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Tables

Table 1. Characteristics of the cohort. Data are shown as number (% of total) or median (interquartile range)

	Randomisation group		<i>p</i> - value
	A	B	
Number of patients	18	18	
Male (%)	61.1	72.2	0.584
Age (yrs)	0.56 (0.23 – 1.34)	0.23 (0.11 – 0.56)	0.091
0 – 3 months (%)	27.8	55.6	
3 – 6 months (%)	22.2	11.1	
6 – 12 months (%)	11.1	22.2	
1 – 2 years (%)	27.8	5.6	
2 – 5 years (%)	11.1	5.6	
Weight (kg)	9.05 (5.15 – 10.50)	5.40 (4.08 – 7.07)	0.075
PRISM III (24 h) score	3.00 (2.00 - 6.00)	3.00 (0.75 – 4.00)	0.161
PIM II (24 h) score	-4.55 (-4.67 - -4.08)	-4.24 (-4.74 - -3.83)	0.584
Admission diagnosis (<i>n</i>)			1.000
Respiratory	17	17	
Postoperative	1	1	
Respiratory disease (%)			0.539
Healthy lungs	5.6	5.6	
Obstructive disease	11.1	16.7	
Restrictive disease	22.2	5.6	
Obstructive+ restrictive disease	61.1	72.2	
Duration of mechanical ventilation (days)	3.88 (2.66 – 6.46)	5.94 (3.92 – 7.83)	0.054
HFO ventilation (%)	44.4	50.0	0.791
HFO ventilation duration (days)	2.15 (1.05 – 2.94)	2.67 (1.98 – 4.06)	0.139
Length of PICU stay (days)	5.83 (3.46 – 8.53)	7.31 (5.11 – 10.44)	0.085
Extubation outcome			
Reintubation < 48hrs (%)	5.6	11.1	0.791
UAO (<i>n</i>)	1	1	
Excessive WOB (<i>n</i>)	-	1	

Table 2. Patient vital parameters. Data is compared to the baseline or the previous step in the stepwise reduction of the amount of pressure support. No blood samples were withdrawn during the downgrading of pressure support. Data is shown as median (IQR). Statistic test used is the Wilcoxon signed rank test.
*p<0.05

	Baseline	CPAP/PS	PC - (S)IMV ± PS	Baseline	PSV -2cmH ₂ O	PSV -4cmH ₂ O	PSV -6cmH ₂ O
Clinical parameters							
Comfort score	12 (11 – 15)	11 (11 – 14)	12 (11 – 13)	11 (11 – 14)	11 (11 – 14)	11 (11 – 14)	11 (11 – 14)
Heart rate (beats/min)	138 (123 – 149)	135 (122 – 149)	138 (116 – 150)	134 (117 – 144)	134 (119 – 142)	130 (114 – 149)	133 (117 – 150)
Peripheral saturation (%)	98 (95 – 99)	97 (95 – 98)	98 (96 – 98)	97 (95 – 98)	97 (95 – 98)	96 (94 – 98)	97 (96 – 100)
Respiratory rate (/min)	37 (26 – 48)	35 (22 – 48)	32 (23 – 43)*	37 (21 – 48)	36 (23 – 53)*	37 (30 – 53)*	35 (27 – 53)
Respiratory parameters							
Expired tidal volume (ml)	41.1 (27.9 – 82.9)	41.9 (26.2 – 85.7)	43.8 (26.1 – 88.2)	41.1 (24.8 – 79.9)	38.2 (22.2 – 69.6)*	34.6 (23.7 – 74.8)*	36.5 (28.2 – 73.4)
End tidal CO ₂ (mmHg)	49.4 (45.9 – 54.5)	49.05 (43.7 – 54.9)	48.8 (45.1 – 53.4)	49.7 (44.8 – 52.5)	49.3 (45.6 – 53.5)	49.4 (44.7 – 56.3)	53.0 (46.7 – 55.8)*
T _{insp}	0.50 (0.43 – 0.67)	0.52 (0.39 – 0.69)	0.63 (0.44 – 0.73)*	0.52 (0.40 – 0.76)	0.49 (0.38 – 0.68)*	0.51 (0.41 – 0.63)	0.53 (0.43 – 0.69)
RSBI	0.88 (0.33 – 1.64)	0.78 (0.31 – 1.70)	0.61 (0.29 – 1.50)*	0.80 (0.28 – 1.74)	1.00 (0.33 – 2.09)*	1.10 (0.40 – 2.09)	0.88 (0.36 – 2.07)*
Ventilator settings							
Fraction inspired oxygen (%)	30 (26 – 39)	30 (26 – 39)	30 (26 – 39)	30 (25 – 40)	30 (27 – 40)	30 (27 – 40)	30 (27 – 40)
PEEP (cmH ₂ O)	6 (5 -6)	6 (5 -6)	6 (5 -6)	6 (5 -6)	6 (5 -6)	6 (5 -6)	6 (5 -6)
PS (cmH ₂ O) ¹	14 (12 – 16)	14 (12 – 16)	14 (12 – 16)	14 (12 – 16)	12 (10 – 14)	10 (8 – 12)	8 (6 – 10)
Metrics of oxygenation and ventilation							
	76.51	74.93	76.51 (67.21				

PaO ₂ (mmHg)	(66.68 – 87.76)	(66.54 – 85.89)	– 86.26)	No blood samples withdrawn
PaCO ₂ (mmHg)	50.10 (56.25 – 46.50)	50.18 (45.00 – 5.28)	51.75 (47.25 – 54.98)	
Oxygenation index	4.92 (3.79 – 6.03)	4.33 (3.72 – 5.82)	4.63 (3.79 – 5.74)	
PF Ratio	257 (181 – 295)	228 (185 – 278)	249 (192 – 287)	

1) Set pressure support or the applied pressure above PEEP when on pressure regulated ventilation

Figures

Figure 1

Study design of the different data collection moments during the two different weaning strategies (*top figure*) and the three step downgrading of pressure support (*bottom figure*). CRF = case record file, Pes= esophageal pressure, RIP= respiratory inductance plethysmography

Figure 2

The work of breathing calculated through the gold standard, the Campbell diagram (Joules/L). Figure 2a shows the work of breathing during the different weaning strategies. Figure 2b shows the work of breathing during downtapering of pressure support. *p<0.05

Figure 3

The work of breathing calculated through the pressure-rate-product (PRP) and pressure-time-product (PTP). Figure 3a shows the work of breathing during the different weaning strategies. Figure 3b shows the work of breathing during downtapering of pressure support. *p<0.05

Supplementary Files

This is a list of supplementary files associated with this preprint. Click to download.

- [Figure1ESM.jpg](#)
- [Table1ESM.docx](#)