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RESEARCH REPORT

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Impact of endotracheal tube shortening on work of breathing in neonatal and pediatric in vitro lung models

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Summary

Background: Work of breathing accounts for a significant proportion of total oxygen consumption in neonates and infants. Endotracheal tube inner diameter and length significantly affect airflow resistance and thus work of breathing. While endotracheal tube shortening reduces endotracheal tube resistance, the impact on work of breathing in mechanically ventilated neonates and infants remains unknown.

Aim: The objective of this in vitro study was to quantify the effect of endotracheal tube shortening on work of breathing in simulated pediatric lung settings. We hypothesized that endotracheal tube shortening significantly reduces work of breathing.

Methods: We used the Active-Servo-Lung 5000 to simulate different clinical scenarios in mechanically ventilated infants and neonates under spontaneous breathing with and without pressure support. Endotracheal tube size, lung resistance, and compliance, as well as respiratory settings such as respiratory rate and tidal volume were weight and age adapted for each lung model. Work of breathing was measured before and after maximal endotracheal tube shortening and the reduction of the daily energy demand calculated.

Results: Tube shortening with and without pressure support decreased work of breathing to a maximum of 10.1% and 8.1%, respectively. As a result, the calculated reduction of total daily energy demand by endotracheal tube shortening was between 0.002% and 0.02%.

Conclusion: In this in vitro lung model, endotracheal tube shortening had minimal effects on work of breathing. Moreover, the calculated percentage reduction of the total daily energy demand after endotracheal tube shortening was minimal.

KEYWORDS
endotracheal tube, in vitro lung model, pediatric, work of breathing

1 | INTRODUCTION

Neonates and infants have an increased risk of respiratory failure due to small airway diameters, high chest wall compliance combined with low lung compliance, low functional residual capacity,[1] high

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relative oxygen consumption, and low breathing mechanical efficiency.[2] Work of breathing (work of breathing) is defined as the sum of the work of resistive and elastic forces to overcome resistance to airflow and volume distension, respectively. This accounts for a significant proportion of oxygen consumption[2] in infants where alveolar ventilation per unit lung volume is twice as high compared to adults.[3] Moreover, the oxygen cost of breathing increases during the weaning process of mechanically ventilated neonates and infants.[4]

Small endotracheal tubes (ETT) increase work of breathing via additional resistance to gas flow. ETT with largest possible inner diameter (ID), removal of secretions, and ETT shortening have been proposed to reduce work of breathing.[5,6] The rational for ETT shortening is based on the Hagen-Poiseuille law describing the relation between tube diameter, length, and flow resistance during laminar flow. Thus, work of breathing increases with smaller diameter and ETT length.[7] However, the impact of ETT length shortening on work of breathing has not been investigated in infants and neonates. The aim of this in vitro study was to quantify the effect of ETT shortening on work of breathing at different pediatric lung settings. We hypothesized that ETT shortening reduces work of breathing significantly during spontaneous breathing in an in vitro lung model mimicking neonatal and pediatric practice.

What's known

- Endotracheal tube (ETT) resistance is dependent on ETT size, length, and design. Reduction of ETT length is postulated to reduce work of breathing; however, this has not yet been investigated in neonates and infants.

What's new

- The results from this in vitro model simulating lung physiology and ETT dimensions for neonates and infants contradicted our hypothesis that shortening of ETT would result in a significantly reduced work of breathing.

2 | MATERIALS AND METHODS

We used the Active-Servo-Lung 5000 test lung monitor (ASL; IngMar Medical, Pittsburgh, PA, USA) to assess the effects of ETT shortening on work of breathing. The ASL can be applied as a test lung monitor or a breathing simulator as in the presented study. It generates inspiratory and expiratory tidal volumes (V_T) with set inspiratory to expiratory ratios and a defined muscle force, which is a device-specific parameter to individually control spontaneous breathing simulated by the ASL. This allows for calculation of work of breathing as appropriate for different age and weight. Individual settings of lung compliance and airway resistances can be simulated by changing the movability of the precisely computer-controlled piston inside the ASL. Furthermore, it can be used as a lung simulator to measure and compare the performance of respirators during different ventilation modes.[8,9] The ASL has also successfully been used for simulating neonatal[9,10] and infant[11] lung parameters.

In this study, inspiratory work of breathing, defined as the work necessary going from volume A to volume B, was calculated by the ASL based on the following equation:

$$\int_{V_{ei}}^{V_T} \Delta p_{mus} \delta v_L,$$

V_T: tidal volume, V_{ei}: end-inspiratory volume, Δp_{mus}: is the change in the net force produced by the respiratory muscles expressed as an equivalent pressure difference; often called muscle pressure difference, dv_L: differential lunge volume.

The ASL used for these experiments was calibrated according to the manufacturer before starting the experiments. The work of breathing was recorded and calculated by the ASL software.

An EVITA 4 ventilator (Dräger Medical GmbH, Lübeck, Germany), equipped with a small breathing circle and breathing hose for children was used with additional software for neonatal ventilation.

Uncuffed ETT Mallincrodt™ oral/nasal Murphy Eye (Covidien lic, Mansfield, MA, USA) from 2.0 to 3.0 mm internal diameter (ID) were used in lung models for <3 kg body weight. For lung models >3 kg body weight, Microcuff PET (Microcuff, Halyard, Georgia, USA) ID 3.0, 3.5, 4.0, and 4.5 mm were used.

2.1 | Experiments performed

Lung settings using the ASL device were adjusted for three preterm and two full-term neonates, two infants, and four toddlers. Age, weight, respiratory rate, V_T, and lung compliance, as well as resistance for each simulated patient settings were calculated from published data[12] (Table 1). Connection of the Evita 4 ventilator to the ASL was performed with a weight-appropriate ETT (Table 1) inserted through a tight sealing membrane at the ASL-inlet to prevent any air leakage around the ETT. The experimental setting is shown in Figure 1. The automatic tube compensation of the EVITA 4 ventilator was deactivated during all experiments to solely investigate the impact of ETT shortening on work of breathing without additional bias on the measured values. Ventilation through these ETT was performed in original length and after maximal shortening of the ETT depending on the lung model or ETT design, respectively. The maximal shortening for the uncuffed ETT was calculated according to published data for nasotracheal intubation depth[13,14] adding 2.0-2.5 cm to guarantee a sufficient distance of the tube connector from the nares and for safe taping. The maximal shortening in the cuffed ETT was 1.0 cm above the inlet of the cuff-inflation line at the ETT. This resulted in a substantial ETT shortening of 27%-40% from the original ETT length.

The following measurements were performed:

1. Spontaneous breathing at a continuous positive airway pressure (CPAP) of 5 cmH_2O was chosen to investigate the impact of the ETT on the work of breathing during positive end-expiratory pressure only.

TABLE 1 Specifications of the different lung models and the settings for the ASL test lung (lung compliance and resistance) from published data[12] as well as chosen endotracheal tube (ETT) size (uncuffed [*])

Lung model	Gestational weeks†/age in months	Weight (kg)	Respiratory rate (per minute)	Tidal volumes (mL)	Lung compliance (mL/cm$H_2$0)	Lung resistance (cmH_2O L/s)	Tube Size (ID mm)
Preterm 1	24†	0.6	64	5	0.5	177.7	2.0*
Preterm 2	27.5†	1.1	56	11	1.4	126.9	2.5*
Preterm 3	33†	2.2	46	25	3.4	82.6	3.0*
Full-term 1	38†	3.0	41	35	4.8	66.7	3.0
Full-term 2	42†	3.5	40	40	5.4	62.4	3.0
Infant 1	6	7.1	32	75	9.5	43.5	3.0
Infant 2	8	7.9	30	83	10.5	41.1	3.5
Toddler 1	23	12.2	25	130	16.5	32.4	3.5
Toddler 2	24	12.3	25	132	16.8	32.2	4.0
Toddler 3	47	15.6	21	180	23.9	27.6	4.0
Toddler 4	48	16.0	21	184	24.3	27.4	4.5

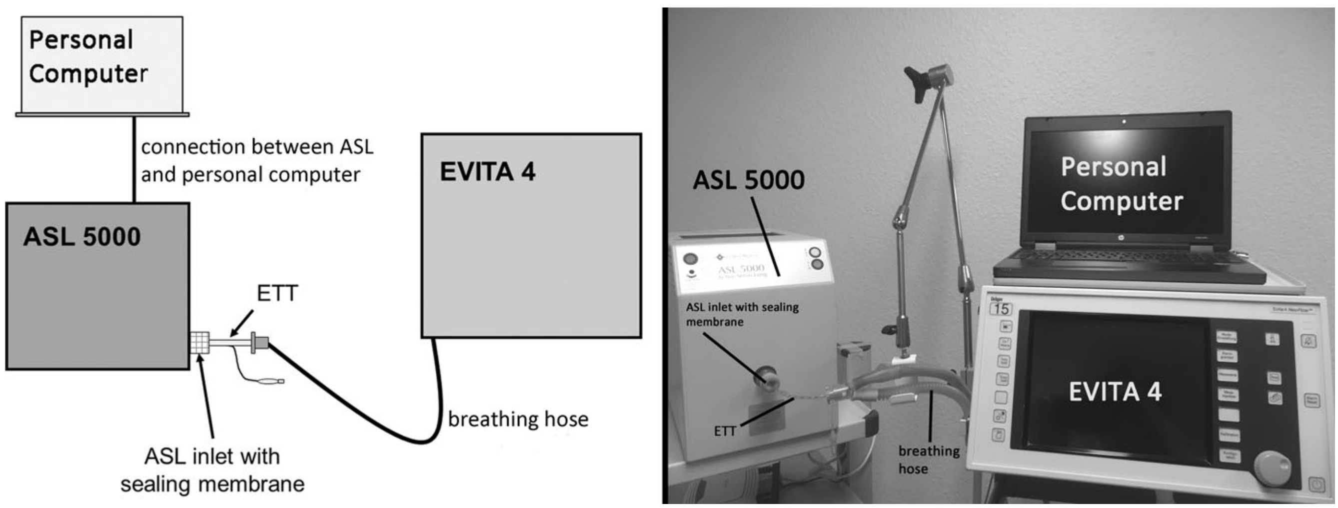

FIGURE 1 Schematic pictogram (left) and black-and-white picture (right) showing the experimental setup with the ASL 5000 intubated with an ETT through the tight sealing membrane and connected to the EVITA 4 ventilator for measurements during spontaneous ventilation. The personal computer was linked to the ASL 5000 and collected data via the specific ASL software

2. Assisted spontaneous breathing (ASB) at a CPAP level of 5 cmH_2O and pressure support ventilation (PSV) of 5 cmH_2O was chosen based on study data indicating the need of 5 cmH_2O PSV to compensate the imposed additional work of breathing by an ETT.[15,16]

These two settings were chosen to simulate clinical conditions encountered both in patients initiating spontaneous breaths and in patients receiving minimal ventilator support before being extubated.

For both spontaneous breathing settings, the inspiratory muscle pressure of the ASL was varied to achieve the intended V_T (Table 1).

In each of the two ventilator setups (A/B) and for each of the 11 lung settings, a new ETT and a new sealing membrane at the ASL were used, resulting in 22 setups. In each setup, measurements were repeated five times (110 measurements). Each measurement lasted 5 minutes. V_T in the age-dependent range was used for further statistical analysis.

2.2 | Calculations of work of breathing and daily energy demand and statistical analysis

For interpretation of the impact of ETT shortening on the reduction in work of breathing, we additionally calculated the resulting daily energy reduction and related this to the weight-dependent total daily energy demand of each model. This daily energy demand was calculated by multiplying the simulated body weight of the patient model with the energy demand in kilocalories (kcal) per kilogram body weight. The feeding standard procedures of the University Children's Hospital Zurich and published data were used as a basis.[17-19]

1. Preterm neonates <1250 g of weight: 100 kcal/kg day (parenteral route)
2. Preterm neonates >2000 g of weight: 120 kcal/kg day (enteral route)

TABLE 2 Means of tidal volumes (V_T), work of breathing (WOB J/L), and difference in WOB (%) for the lung settings without pressure support. ETT shortening in percent (%) from the original length

Lung model	% ETT shortening	Mean (95% CI) for original ETT length			Mean (95% CI) for shortened ETT length			δ-percent WOB (%)	Reduction in % daily kcal demand
		n	V_T (mL)	WOB (J/L)	n	V_T (mL)	WOB (J/L)		
Preterm 1	37	1093	5.27 (5.26-5.28)	1.36 (1.35-1.37)	1456	5.28 (5.27-5.29)†	1.28 (1.27-1.28)*	−5.9	0.015
Preterm 2	35	1311	11.08 (11.07-11.09)	1.26 (1.26-1.26)	1308	10.97 (10.95-10.98)*	1.23 (1.23-1.23)*	−2.8	0.009
Preterm 3	30	1016	25.15 (25.10-25.21)	1.36 (1.36-1.37)	818	25.44 (25.38-25.51)*	1.31 (1.30-1.32)*	−4.0	0.006
Full-term 1	27	986	35.12 (35.01-35.14)	1.37 (1.37-1.37)	1015	35.17 (35.16-35.19)*	1.30 (1.30-1.30)*	−3.0	0.012
Full-term 2	27	998	40.03 (40.01-40.05)	1.47 (1.47-1.47)	997	40.05 (40.03-40.07)‡	1.40 (1.40-1.40)*	−4.8	0.012
Infant 1	27	683	75.22 (75.19-75.25)	1.95 (1.95-1.95)	644	75.07 (75.03-75.10)*	1.81 (1.80-1.81)*	−7.2	0.019
Infant 2	32	745	83.13 (83.09-83.18)	1.61 (1.61-1.61)	746	83.07 (83.05-83.10)§	1.50 (1.50-1.50)*	−6.8	0.013
Toddler 1	32	620	130.33 (130.30-130.37)	1.98 (1.97-1.97)	618	130.29 (130.25-130.33)¶	1.82 (1.82-1.83)*	−8.1	0.016
Toddler 2	33	618	132.48 (132.44-132.51)	1.65 (1.64-1.65)	617	132.24 (132.20-132.27)*	1.54 (1.54-1.54)*	−6.7	0.011
Toddler 3	33	519	180.59 (180.56-180.63)	1.83 (1.82-1.83)	505	180.41 (180.34-180.49)*	1.70 (1.70-1.70)*	−7.1	0.012
Toddler 4	40	520	184.20 (184.16-184.24)	1.64 (1.64-1.64)	519	184.04 (184.00-184.09)¶	1.55 (1.55-1.55)*	−5.5	0.009

n=number of valid measurements, *P*-values: **P*<.001; †*P*=.179; ‡*P*=.227; §*P*=.01; ¶*P*=.114

TABLE 3 Means of tidal volumes (V_T), work of breathing (WOB J/L), and difference in WOB (%) for the lung settings with pressure support. ETT shortening in percent (%) from the original length

Lung model	% ETT shortening	Mean (95% CI) for original ETT length			Mean (95% CI) for shortened ETT length			δ-percent WOB (%)	Reduction in % daily kcal demand
		n	V_T (mL)	WOB (J/L)	n	V_T (mL)	WOB (J/L)		
Preterm 1	37	528	5.25 (5.23-5.26)	1.29 (1.28-1.30)	645	5.34 (5.32-5.36)*	1.28 (1.28-1.29)†	−0.6	0.002
Preterm 2	35	757	10.52 (10.48-10.55)	1.12 (1.12-1.12)	794	10.43 (10.39-10.46)*	1.08 (1.08-1.08)*	−3.7	0.009
Preterm 3	30	510	24.91 (24.79-25.03)	1.02 (1.01-1.02)	487	24.95 (24.83-25.07)‡	0.97 (0.97-0.97)*	−4.8	0.007
Full-term 1	27	420	35.04 (34.99-35.10)	1.03 (1.03-1.03)	435	34.92 (34.92-35.03)§	0.94 (0.93-0.94)*	−8.7	0.006
Full-term 2	27	643	39.68 (39.61-39.74)	1.09 (1.08-1.09)	599	39.61 (39.55-39.68)¶	1.02 (1.01-1.02)*	−6.4	0.012
Infant 1	27	499	75.03 (74.97-75.09)	1.51 (1.51-1.51)	464	75.16 (75.10-75.21)**	1.36 (1.36-1.37)*	−9.9	0.020
Infant 2	32	618	83.40 (83.31-83.49)	1.17 (1.17-1.18)	611	83.58 (83.50-83.66)**	1.07 (1.06-1.07)*	−8.6	0.012
Toldder 1	32	569	130.59 (130.52-130.67)	1.49 (1.49-1.50)	597	130.41 (130.35-130.48)*	1.34 (1.33-1.34)*	−10.1	0.016
Toddler 2	33	545	132.58 (132.51-132.65)	1.17 (1.17-1.17)	523	132.18 (132.10-132.26)*	1.07 (1.07-1.07)*	−8.6	0.011
Toddler 3	33	491	180.02 (179.42-180.12)	1.32 (1.31-1.32)	493	180.26 (180.17-180.34)††	1.19 (1.19-1.19)*	−9.9	0.011
Toddler 4	40	444	184.44 (184.34-184.55)	1.14 (1.14-1.14)	499	184.10 (184.01-184.18)*	1.05 (1.05-1.05)*	−7.9	0.008

n=number of valid measurements, *P*-values: **P*<.001; †*P*=.03; ‡*P*=.627; §*P*=.102; ¶*P*=.167; ***P*=.003; ††*P*=.001.

3. Full-term neonates, infants, and toddlers: 90 kcal/kg day (enteral route)

The difference of the total daily work of breathing in kcal/day for each studied experimental setup between the shortened ETT and the original ETT was calculated as follows:

$$[\text{WOB shortened ETT (Joule/Liter)} - \text{WOB original ETT (J/L)}] \times \text{respiratory rate (age-dependent)} \times V_T(\text{mL}) \times 60(\text{for per hour}) \times 24(\text{for per day}) \text{ for each lung model.}$$

Respiratory data (V_T and work of breathing) from the ASL were analyzed by device-specific software on a personal computer. Data were compiled in Microsoft Excel 2013 (Microsoft Corporation, Redmond, WA, USA) and processed using SPPS Statistics 22.0 (IBM, Armonk, NY, USA). Data are presented as mean (95% confidence interval [95% CI]). *P*-values <.05 were considered statistically significant.

3 | RESULTS

In total, 42 761 valid breaths were recorded and analyzed. All results measured during each experimental setting were normally distributed. work of breathing was reduced between 0.03 and 0.16 J/L (P<.001) in the experimental lung setting for spontaneous breathing without pressure support and between 0.01 and 0.15 J/L (P<.03) for spontaneous breathing at 5 cmH_2O pressure support. Overall, ETT shortening during spontaneous breathing without pressure support decreased work of breathing between 2.8% and 8.1% (P<.001) (Table 2) and from 0.6% to 10.1% (P<.03) during spontaneous breathing at 5 cmH_2O pressure support (Table 3). Figure 2 displays work of breathing before and after ETT shortening for spontaneous breathing without pressure support as well as the reduction of work of breathing in percent. Figure 3 shows work of breathing during spontaneous breathing with a pressure support of

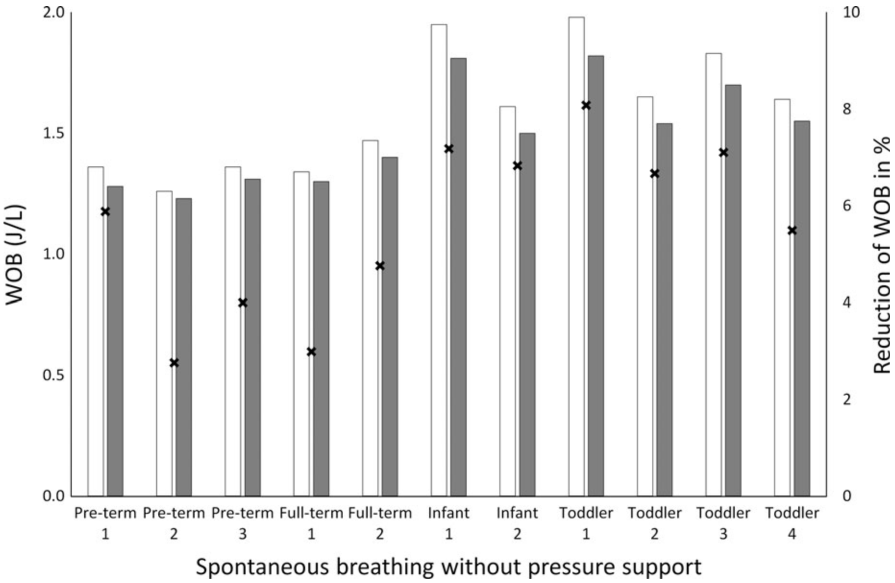

FIGURE 2 Mean work of breathing (WOB [J/L]) during spontaneous breathing without pressure support for the different lung settings. Unshortened ETT: white bar, shortened ETT: gray bar, and reduction of WOB in percent as cross

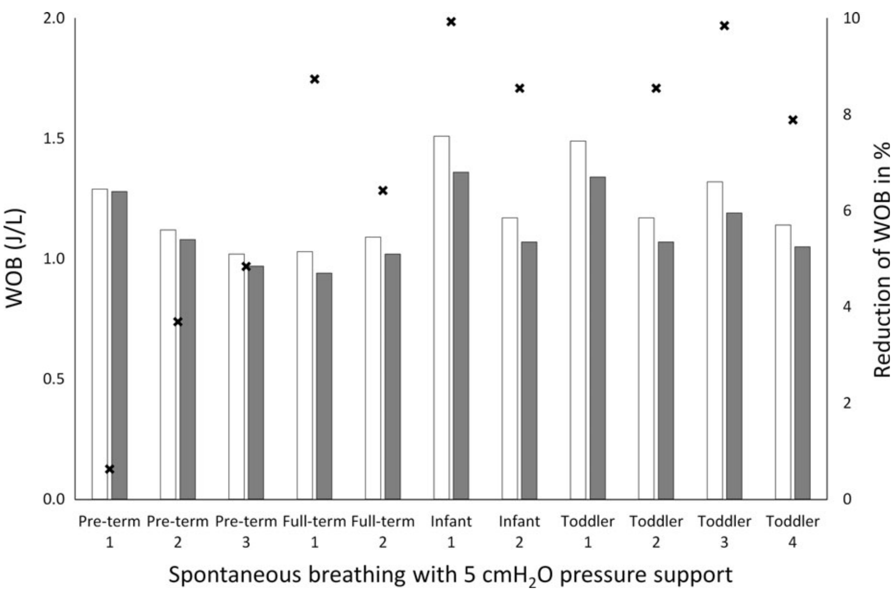

FIGURE 3 Mean work of breathing (WOB [J/L]) during spontaneous breathing with 5 cmH_2O pressure support for the different lung settings. Unshortened ETT: white bar, shortened ETT: gray bar, and reduction of WOB in percent as cross

5 cmH_2O before and after ETT shortening as well as the reduction of work of breathing in percent.

The calculated reduction of total daily energy demand by ETT shortening was between 0.002% and 0.02%.

4 | DISCUSSION

It has been demonstrated that ETT impose additional work of breathing of more than 50% of the total work of breathing in adults.[20,21] Hence, ETT shortening has the potential to alleviate breathing efforts in mechanically ventilated patients via lower resistance to flow. Based on this assumption a reduction of work of breathing has been postulated in both pediatric and adult studies.[22-24] In this in vitro study, we quantified the impact of ETT shortening on the work of breathing in eleven different neonatal and pediatric lung settings. Our main finding was that substantial tube shortening decreased work of breathing to a maximum of 10%.

Given the beneficial effects on oxygen consumption, minimizing respiratory efforts in infants and neonates remains an important goal during mechanical ventilation. Bell et al.[25] investigated the clinical impact of additional work of breathing in children and stated that a median increase by 15.5% was not clinically significant. The absolute values regarding work of breathing measured by the ASL in the present in vitro study are similar to those published in clinical studies investigating work of breathing in intubated patients.[25,26] Furthermore, the change in V_T is only 0.01-0.71 mL and the change in work of breathing was only 0.03-0.16 J/L. Moreover, the calculated percentage reduction of the total daily energy demand after ETT shortening is minimal.

work of breathing is used to predict extubation readiness in children[27] as increased work of breathing correlates with a higher extubation failure rate during the weaning process.[28] Clinical studies investigating extubation outcome found a difference of about 40% in work of breathing (defined as the transdiaphragmatic pressure-time product) between failed and successful extubation in infants.[29] When comparing these clinical findings with our in vitro study, we question whether a maximum difference of 10% in work of breathing has the potential to influence extubation outcomes in infants and children.

To achieve sufficient minute ventilation high ventilation rates with short inspiratory times are frequently applied in neonatal ventilation. This results in an increased flow acceleration leading to high airway resistance, as demonstrated by Hentschel et al.[30] In vitro models allow for simulating these age-specific clinical conditions as found in infants. To include the relevance of a high minute ventilation on work of breathing, we simulated the upper limit for age-dependent respiratory rate and V_T. The fact that there was only a small difference under this high minute ventilation allows for the assumption that bigger differences are very unlikely under lower minute volume conditions.

An important limitation of our study is the in vitro setting of the presented lung models, in which gas composition and temperature (including oxygen fraction and humidity) are not comparable with in vivo setting. In vitro settings have the advantage of precision and reproducibility, but the small variability does not reflect clinical reality. Hence, there is a risk that even very small differences in V_T (eg, 0.1 mL) and work of breathing (eg, 0.03 J/L) result in statistically significant numbers. Furthermore, the two spontaneous breathing settings of this in vitro study aim at patients during weaning process. Patients being fully ventilated or with little respiratory effort were not investigated in the present settings. Therefore, the impact of ETT shortening on these two scenarios cannot be estimated.

In conclusion, ETT shortening in this in vitro study mimicking neonates, infants, and toddlers has minimal effects on work of breathing and the calculated percentage reduction of the total daily energy demand after ETT shortening was minimal. Clinical trials are needed to investigate the impact of endotracheal tube shortening in mechanically ventilated neonates and infants.

CONFLICT OF INTEREST

No conflicts of interest declared.

ETHICAL APPROVAL

No ethics approval needed for this in vitro study

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