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Impact of Positive End-Expiratory Pressure on Partitioned Mechanical Power in Neonates: Predominance of Elastic over Resistive Work

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Author Contributions

Masashi Zuiki designed and performed the experiments and wrote the initial draft of the manuscript. All other authors contributed to interpretation and critically reviewed the manuscript. All the authors approved the final version of the manuscript and shared accountability for all aspects of the work to ensure that questions related to the accuracy or integrity of any part of the work were appropriately investigated and resolved.

Abstract

Purpose: To investigate the impact of positive end-expiratory pressure (PEEP) on partitioned mechanical power (MP) components—elastic (MP_{ELrs}), resistive (MP_{Raw}), and PEEP (MP_{PEEP})—in preterm and term neonates to better characterise energy-related lung stress.

Methods: In this secondary analysis, 21 preterm and 28 term invasively ventilated infants underwent a prospective PEEP protocol across three predefined levels: mild (5 cmH_2O), moderate (7 cmH_2O) and high (10 cmH_2O, or until peak inspiratory pressure reached 25 cmH_2O), followed by decremental reduction back to mild PEEP. Airway pressure and volume data were digitally recorded at each level to calculate mechanical energy (ME) and MP components. Group differences and PEEP-dependent changes were statistically analysed.

Results: At baseline (mild PEEP), single-breath ME did not differ between groups; however, preterm infants exhibited higher respiratory rates, resulting in significantly higher total MP, MP_{ELrs}, and MP_{PEEP}, compared with term infants. Across PEEP levels, MP_{PEEP} increased stepwise in both groups. MP_{ELrs} progressively increased and peaked at high PEEP in preterm infants, showing a significant elevation starting from moderate PEEP. In contrast, term infants exhibited a significant increase in MP_{ELrs} only at high PEEP. MP_{Raw} remained unchanged across all PEEP levels.

Conclusion: High PEEP significantly increases MP in neonates, driven primarily by MP_{ELrs} and MP_{PEEP}, rather than airway resistance. Preterm infants are particularly vulnerable to increased elastic load, even at moderate PEEP. Bedside monitoring of MP_{ELrs} may facilitate individualised PEEP optimisation.

Keywords: positive end-expiratory pressure, mechanical power, lung stress, neonates

List of Abbreviations

EL_{rs}: elastance of the respiratory system

IQR: interquartile range

ME: mechanical energy

ME_{ELrs}: mechanical energy of elastic resistance

ME_{PEEP}: mechanical energy of PEEP

ME_{Raw}: mechanical energy of airway resistance

ME_{Total}: total mechanical energy

$mild_{dec.}$: mild PEEP during the decremental phase

$mild_{inc.}$: mild PEEP during the incremental phase

$moderate_{dec.}$: moderate PEEP during the decremental phase

$moderate_{inc.}$: moderate PEEP during the incremental phase

MP: mechanical power

MP_{ELrs}: mechanical power of elastic resistance

MP_{PEEP}: mechanical power of PEEP

MP_{Raw}: mechanical power of airway resistance

MP_{Total}: total mechanical power

NICU: neonatal intensive care unit

PEEP: positive end-expiratory pressure

RR: respiratory rate

ΔV: tidal volume

VILI: ventilator-induced lung injury

What is Known

- Mechanical power (MP) predicts ventilator-induced lung injury, integrating volume, pressure, flow, and respiratory rate into the delivery of energy.
- Mechanical effects of high levels of positive end-expiratory pressure (PEEP) on lung parenchyma are unclear.

What is New

- High PEEP significantly increases total MP in neonates, driven by its elastic (MP_{ELrs}) and PEEP, rather than airway resistance components.
- Preterm infants show a significant increase in MP_{ELrs} even at moderate PEEP levels, highlighting their heightened susceptibility to elastic load, compared with term infants.

Introduction

Neonates admitted to the neonatal intensive care unit (NICU) often require prolonged mechanical ventilation. Lung-protective strategies are essential to reduce ventilator-induced lung injury (VILI). Although optimal positive end-expiratory pressure (PEEP) prevents alveolar collapse, determining individualised PEEP settings remains difficult. Our previous studies showed that high PEEP can reduce cardiac output and increase dead space [1,2]. These findings highlight the risks of excessive PEEP; however, its mechanical effects on lung parenchyma remain unclear.

VILI involves volutrauma, barotrauma, biotrauma, and atelectrauma. More recently, mechanical power (MP) has emerged in adult critical care as a predictor of VILI, integrating factors such as respiratory rate (RR) and flow into a measure of energy transfer over time [3]. MP can also be partitioned into respiratory system elastance (EL_{rs}), airway resistance (R_{aw}), and PEEP components (MP_{ELrs}, MP_{Raw}, and MP_{PEEP}, respectively). A recent prospective NICU study demonstrated that neonates with respiratory disorders exhibit significantly higher MP, and dynamic/static strain components than healthy controls do, with MP correlating with impaired oxygenation and lung aeration [4].

In this study, we aimed to investigate the effects of PEEP variation on individual MP components and their cumulative total (MP_{Total}) in neonates to better characterise energy-related lung stress in this vulnerable population.

Materials and Methods

This study is a secondary analysis of a prospective PEEP protocol dataset [1,2]. While previous reports addressed

hemodynamics [1] and volumetric capnography [2], this study uniquely investigates partitioned MP, which was not evaluated in prior publications. Newborns with birth weights ≥1000 g admitted to the neonatal intensive care unit between April 2022 and August 2024 were included. The study focused on patients receiving invasive mechanical ventilation in synchronous intermittent mandatory ventilation mode. The study protocol was reviewed and approved by the Institutional Review Board of Kyoto Prefectural University of Medicine (ERB-C-2145-1). All procedures were performed in accordance with the Declaration of Helsinki. Informed consent for the original study was obtained from the parent or legal guardian as approved by the ethics committee. Prior consent was also obtained for secondary data analysis.

Study Protocol

As previously described in detail [2], all included patients were clinically stable and received target ventilation settings (tidal volume [ΔV] 5–7 mL/kg via volume guarantee) with fixed fraction of inspired oxygen, inspiratory time, and RR. Infants with air leaks (>10%), pneumothorax, ventilator fighting, or structural airway anomalies were excluded. PEEP was incrementally increased from 5 to 7 and 10 cmH_2O (or until peak inspiratory pressure reached 25 cmH_2O) every 10–20 min, followed by a decremental reduction back to 5 cmH_2O. A physiological monitor was interfaced with the ventilator (Dräger VN500; Dräger Medical, Lübeck, Germany), and airway pressure and volume data were digitally acquired on a computer at a sampling interval of 8 ms at each stabilised PEEP level.

Calculation of Mechanical Energy and Power

From the constructed pressure–volume loops, individual mechanical energy (ME) components were calculated as follows. The total ME (ME_{Total}) was calculated from the ventilator pressure–volume (P-V) loop, where the delivered energy per breath is defined as the area between the inspiratory airway pressure curve and volume axis [3]. The ME of EL_{rs} (ME_{ELrs}) and the ME of PEEP (ME_{PEEP}) were calculated using Gattinoni's equations, as follows [3].

$$\mathrm{ME_{ELrs}} = 0.098 \cdot \frac{1}{2} \cdot \mathrm{EL_{rs}} \cdot \Delta \mathrm{V}^2$$

$$\mathrm{ME_{PEEP}} = 0.098 \cdot \Delta \mathrm{V} \cdot \mathrm{PEEP}$$

E_{Lrs} was calculated as $\Delta P/\Delta V$, where ΔP was the difference between end-inspiratory pressure and PEEP obtained from the ventilator. To avoid overestimating the ME of Raw (ME_{Raw}) under pressure controlled ventilation with Gattinoni's formulas [3,5], we calculated ME_{Raw} by subtracting ME_{ELrs} and ME_{PEEP} from $ME_{Total.}$ $MP_{Total,}$ $MP_{ELrs,}$ MP_{Raw}, and MP_{PEEP} represent the $ME_{Total,}$ $ME_{ELrs,}$ ME_{Raw}, ME_{PEEP}, respectively, delivered during a single breath, multiplied by the RR. Median values were calculated from at least 10 consecutive breaths and normalized to body weight at the time of measurement.

Statistical Analysis

ME and MP during the mild incremental phase ($mild_{inc.}$), were compared between preterm and term infants using the Mann–Whitney U test. Furthermore, ventilator settings and MP metrics were compared across the five PEEP levels—$mild_{inc.}$, moderate incremental phase ($moderate_{inc.}$), high PEEP, moderate decremental phase

(moderate$_{dec.}$), and mild decremental phase (mild$_{dec.}$)—using Friedman's analysis followed by Bonferroni post hoc comparisons. All statistical analyses were performed using EZR software version 1.54 (Saitama Medical Centre, Jichi Medical University, Saitama, Japan).

Results

This study included 28 term (median gestational age, 38 [interquartile range {IQR}, 38–40] weeks; median birth weight, 2,924 [IQR, 2,725–3,109] g) and 21 preterm (median gestational age, 33 [IQR, 31–34] weeks; weight, 1,918 [IQR, 1,356–2,186] g) newborns. Further details of the patient characteristics are provided in a previous study [2].

Table 1 shows the parameters for each ME and MP component during mild$_{inc.}$. No significant difference in ME was observed between preterm and term infants. However, the preterm group showed a higher RR (50 [40–50] /min vs. 39 [35–44] /min, $p = 0.0012$) and higher MP_{Total}, MP_{ELrs}, and MP_{PEEP} values, compared with the term group (MP_{Total}: 0.29 [0.25–0.39] J/kg/min vs. 0.24 [0.20–0.29] J/kg/min, $p = 0.011$; MP_{ELrs}: 0.09 [0.07–0.12] J/kg/min vs. 0.06 [0.04–0.09] J/kg/min, $p = 0.003$; MP_{PEEP}: 0.14 [0.11–0.16] J/kg/min vs. 0.10 [0.09–0.12] J/kg/min, $p = 0.0014$, respectively).

Regarding the response to PEEP changes (relative to baseline mild$_{inc.}$), MP_{PEEP} increased stepwise with increasing PEEP levels in both groups ($p < 0.01$ at moderate and high PEEP). In preterm infants, MP_{ELrs} progressively increased, showing a significant elevation from moderate$_{inc.}$ ($p < 0.05$) and reaching a peak at high PEEP ($p < 0.01$); however, during the decremental phase at moderate PEEP (moderate$_{dec.}$), MP_{ELrs}

returned to a level comparable to baseline ($mild_{inc.}$). In contrast, term infants exhibited a significant increase in MP_{ELrs} compared with $mild_{inc.}$ only at high PEEP level ($p < 0.01$), with no significant changes observed at moderate PEEP (Fig. 1). The relative change MP_{ELrs}, calculated as $(moderate_{inc.} - mild_{inc.})/mild_{inc.}$, was significantly higher in preterm than term infants (0.25 [0.15-0.70] vs 0.11 [0.00-0.29], p = 0.0293).

Discussion

This study demonstrates that ME did not differ between term and preterm infants under mild PEEP, whereas MP was significantly higher in preterm infants due to their higher RR. In addition, high PEEP significantly increased MP in preterm and term neonates, driven by MP_{ELrs} and MP_{PEEP}.

Infants born before 36 weeks of gestation are in the canalicular and saccular stages of lung development, whereas alveolar proliferation and maturation occur primarily during the alveolar phase after 36 weeks [6,7]. Consequently, preterm infants often require higher RR to maintain adequate ventilation. In the present study, the energy per breath delivered to the respiratory system, referred to as ME, did not differ significantly between preterm and term infants under mild PEEP. However, in preterm infants with relatively higher RR, MP was elevated, suggesting an increased risk of ventilator-induced lung injury.

To our knowledge, this study is the first to evaluate PEEP effects on partitioned MP in neonates. At high PEEP levels, both MP_{PEEP} and MP_{ELrs} increased, whereas MP_{Raw} remained unchanged. Because ΔV and RR were fixed by protocol, the stepwise increase in MP_{PEEP} is mathematically deterministic. Thus, the key physiological finding is the elevation of MP_{ELrs} relative to stable MP_{Raw}, indicating that high PEEP primarily increases elastic

stress rather than resistive load. Although high PEEP may dilate airways [2], this did not offset the overall increase in MP. Furthermore, preterm infants exhibited a significant MP_{ELrs} increase from moderate PEEP unlike term infants. As full maturation and stabilisation of the extracellular matrix (particularly elastin and collagen cross-linking) occur predominantly during late gestation, preterm infants possess structurally immature, stiffer lungs with reduced compliance [8-10]. Consequently, even moderate increases in PEEP can disproportionately increase MP_{ELrs} and induce alveolar overdistension in these vulnerable infants. Notably, the increase in MP_{ELrs} observed at $moderate_{inc.}$ was not apparent at $moderate_{dec.}$ in preterm infants. This attenuation suggests a hysteresis effect, where temporary exposure to high PEEP recruited collapsed alveoli and improved lung elastance at subsequent moderate PEEP.

In adult medicine, bedside PEEP titration methods, such as volumetric capnography and electrical impedance tomography, are well established, whereas evidence-based neonatal approaches remain limited [11]. Jimenez et al. demonstrated the utility of MP for assessing PEEP titration in adult acute respiratory distress syndrome [12]. Our findings suggest that MP_{ELrs} may help identify the optimal PEEP threshold before alveolar overdistension occurs. Given its accessibility and feasibility for routine clinical use, MP_{ELrs} represents a practical tool for individualised respiratory management with potential for NICU adoption.

This study has a few limitations. The association between MP and pulmonary or developmental outcomes in neonates remains unclear. Future studies in extremely preterm infants are needed to correlate these energetic changes with long-term outcomes such as bronchopulmonary dysplasia. In addition, the relatively small sample size may have limited the statistical power to detect subtle changes in MP_{Raw}, potentially leading to a Type II

error. Furthermore, excluding unstable infants may have introduced selection bias.

In conclusion, high PEEP significantly increases MP in neonates, primarily by elevating its elastic and PEEP components, rather than airway resistance. Partitioning MP may provide an objective, bedside approach for identifying optimal PEEP levels and advancing individualised lung-protective ventilation in the NICU.

Declarations:

Funding

No funding was received for conducting this study.

Competing Interests

The authors have no relevant financial or non-financial interests to disclose.

Ethics Approval

This study was performed in line with the principles of the Declaration of Helsinki. Approval was granted by the Kyoto Prefectural University of Medicine Clinical Ethics Committee in Kyoto, Japan (Date, 4 October 2021; No. ERB-C-2145-1).

Consent to Participate

Informed consent was obtained from legal guardians.

Consent to Publish

Written informed consent was obtained from the patient's parent or legal guardian for publication of this research.

Data Availability

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

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Figure Legends

Fig. 1 Impact of PEEP on mechanical power components

Mechanical power components in **(a)** preterm and **(b)** term infants. Data are presented as medians with error bars representing the standard error of the mean (SEM). Differences across PEEP levels were analysed using Friedman's test followed by Bonferroni post hoc adjustment.

Abbreviations: $mild_{dec.}$, mild PEEP during the decremental phase; $mild_{inc.}$, mild PEEP during the incremental phase; $moderate_{dec.}$, moderate PEEP during the decremental phase; $moderate_{inc.}$, moderate PEEP during the incremental phase; MP, mechanical power; MP_{ELrs}, mechanical power of elastic resistance; MP_{Raw}, mechanical power of airway resistance; PEEP, positive end-expiratory pressure; SEM, standard error of the mean

$* p < 0.05, ** p < 0.01$ vs. $mild_{inc.}$

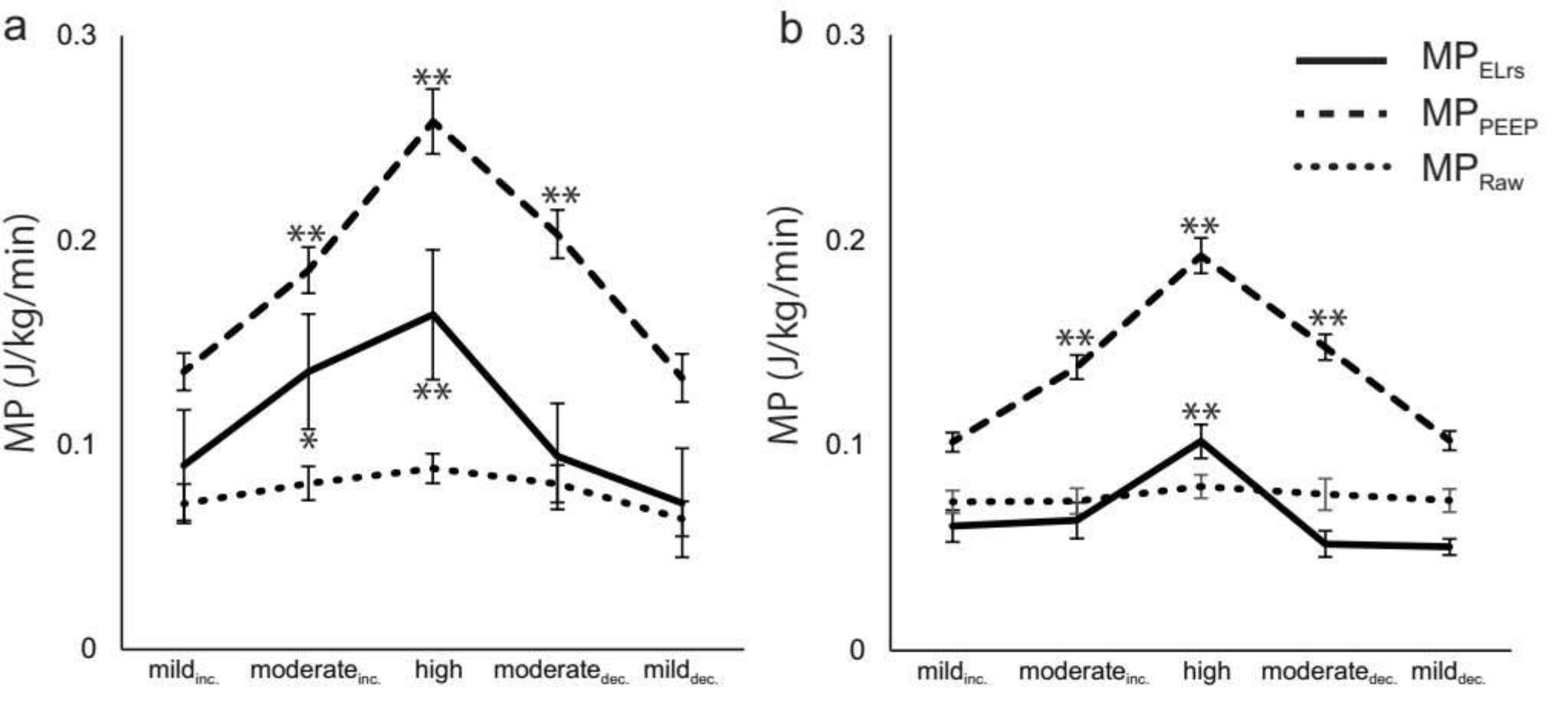

a
b
0.3
0.2
0.1
0
MP (J/kg/min)
MP (J/kg/min)
MP ELrs
MP PEEP
MP Raw
mild inc.
moderate inc.
high
moderate dec.
mild dec.
**
*

Table 1. Mechanical energy and power components at mild PEEP during the incremental phase

	Preterm infants	Term infants	*p*
PEEP,cmH_2O	5.0 (5.0-5.1)	5.0 (5.0-5.1)	0.250
EIP, cmH_2O	12.5 (10.9-14.5)	11.0 (9.9-13.6)	0.109
RR, /min	50 (40-50)	39 (35-44)	0.0012
ΔV, ml/kg	5.4 (5.1–5.8)	5.1 (4.7–5.8)	0.210
ME_{Total}, mJ/kg	6.3 (5.2-8.3)	6.2 (5.7-7.2)	0.741
ME_{ELrs}, mJ/kg	1.8 (1.5-2.5)	1.7 (1.1-2.2)	0.080
ME_{Raw}, mJ/kg	1.6 (1.1-2.0)	1.9 (1.2-2.3)	0.953
ME_{PEEP}, mJ/kg	2.8 (2.6-2.9)	2.6 (2.4-2.9)	0.241
MP_{Total}, J/kg/min	0.29 (0.25-0.39)	0.24 (0.20-0.29)	0.011
MP_{ELrs}, J/kg/min	0.09 (0.07-0.12)	0.06 (0.04-0.09)	0.003
MP_{Raw}, J/kg/min	0.07 (0.05-0.10)	0.07 (0.05-0.10)	0.095
MP_{PEEP}, J/kg/min	0.14 (0.11-0.16)	0.10 (0.09-0.12)	0.0014

Values are represented as median (interquartile range). ME_{Total}, total mechanical energy; ME_{ELrs}, mechanical energy of elastic component; ME_{Raw}, mechanical energy of resistive component; ME_{PEEP}, mechanical energy of PEEP component; MP_{Total}, total mechanical power; MP_{ELrs}, mechanical power of elastic component; MP_{Raw}, mechanical power of resistive component; MP_{PEEP}, mechanical power of PEEP component; PEEP, positive end-expiratory pressure; EIP, end inspiratory pressure; RR, respiratory rate; ΔV, tidal volume. We used the Mann–Whitney U test to investigate the differences in the measurements of preterm and term infants.