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Lung recruitability determines the impact of PEEP on mechanical power in ARDS

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Abstract

Background Mechanical power increases with positive end-expiratory pressure (PEEP). However, its injurious potential may depend on the available lung gas volume, which can be modified by alveolar recruitment. We investigated how PEEP-induced recruitment affects mechanical power.

Methods We analyzed previously collected data on 20 patients with acute respiratory distress syndrome who underwent a decremental PEEP trial (15–5 cmH_2O). End-expiratory lung volume and respiratory mechanics were measured to quantify recruited volume, functional residual capacity (FRC), and the recruitment-to-inflation (R/I) ratio. Absolute power and power normalized to aerated lung volume (FRC + recruited volume) were calculated at each PEEP level. Patients were classified as having higher or lower recruitability according to the cohort median recruited volume accrued between PEEP 5 and 15 cmH_2O, expressed as a fraction of FRC (median 0.42).

Results Absolute mechanical power increased linearly with rising PEEP (approximately + 1 J/min per cmH_2O), from 20 [16–23] J/min at 5 cmH_2O, to 31 [28–33] J/min at 15 cmH_2O, irrespective of recruitability (low recruitability: + 1.12 J/min per cmH_2O, $p < 0.001$; high recruitability: + 0.96 J/min per cmH_2O, $p < 0.001$, p for interaction = 0.12). Normalized power increased in patients with lower recruitability (+ 0.43 J/min/L per cmH_2O, $p < 0.001$) but decreased in those with higher recruitability (− 0.33 J/min/L per cmH_2O, $p < 0.001$; p for interaction < 0.001). The reduction in normalized power was strongly related to PEEP-induced recruitment, expressed as recruited volume/FRC (− 102% per unit, $R^2 = 0.75$, $p < 0.001$), and to R/I ratio (− 38% per unit, $R^2 = 0.69$, $p < 0.001$). Associations with PEEP-related changes in compliance ($R^2 = 0.40$, $p = 0.003$) and PaO_2/FiO_2 ($R^2 = 0.33$, $p = 0.008$) were weaker. In the multivariate model, PEEP-induced recruitment ($p = 0.002$) and compliance changes ($p = 0.011$) remained independent predictors of normalized power changes.

Conclusions Absolute mechanical power increases with higher PEEP, but power per aerated lung decreases when PEEP produces substantial recruitment. PEEP-induced increases in absolute power do not necessarily imply a higher mechanical load per alveolar unit. Recruited volume and compliance changes are the main physiological determinants of this effect. Among bedside tools, the R/I ratio best identifies whether and to what extent PEEP will reduce or increase mechanical power per alveolar unit.

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Keywords PEEP, ARDS, Recruitability, Mechanical power, End-expiratory lung volume, Functional residual capacity

Background

Mechanical power (MP) integrates the major components of ventilatory workload into a single measure of the energy delivered to the respiratory system each minute, and has been proposed as a key determinant of ventilator-induced lung injury (VILI) [1]. To account for lung volume differences across individuals, MP normalized to resting lung volume (or to compliance) may better represent the power applied to each unit of aerated lung tissue, and it correlates more closely with mortality than absolute MP at constant PEEP [4, 5]. However, when PEEP is titrated, aerated lung volume is not constant: PEEP may increase lung size through recruitment. Therefore, normalizations (e.g., predicted body weight- or compliance-based surrogates) do not capture PEEP-induced changes in aerated lung volume and may misrepresent the mechanical load per ventilated lung unit across PEEP levels. Among the factors contributing to MP, the specific role of PEEP remains debated [2], as PEEP influences not only the elastic load of the respiratory system but also end-expiratory lung volume (EELV) through alveolar recruitment. As a result, although absolute MP may increase with higher PEEP, the specific power delivered per unit of aerated lung volume may fall if PEEP recruits additional alveolar units [3]. Consequently, the overall effect of PEEP on MP per unit of aerated lung volume may depend on the patient's individual recruitability.

This study aims to determine whether the extent of recruited lung volume determines the effect of PEEP on absolute MP and on MP normalized to aerated lung size.

Methods

This is a reanalysis of data from a previously published study involving 20 patients with COVID-19 acute respiratory distress syndrome, enrolled between April and July 2021. The protocol was approved by the local ethics committee (ID UCSC915920/20) and written informed consent was obtained by all patients in accordance with committee recommendations.

All patients were studied in the semirecumbent position under neuromuscular blockade while receiving volume-controlled ventilation with a ventilator capable of EELV measurement (Carescape R860, GE healthcare, Chicago, IL, USA). Tidal volume was set at 6 ml/kg of predicted body weight, inspiratory flow at 60 L/min. Respiratory rate and FiO_2 were adjusted according to clinical needs. After a 40-min stabilization period at PEEP 15 cmH_2O, a 5-step decremental PEEP trial was performed (15, 13, 10, 8, 5 cmH_2O), with each step lasting 8 min. All other ventilator settings remained unchanged. Patients with airway closure were excluded, defined as the presence of a positive airway opening pressure (airway opening pressure above the applied end-expiratory pressure), indicating closed airways at end-expiration and unreliable estimation of recruited volume with PEEP changes [1]. Static respiratory mechanics and EELV (using modified nitrogen washout-washin) were measured [2]. Functional residual capacity (FRC), defined as the EELV at PEEP 0 cmH_2O, was estimated by measuring exhaled tidal volume during a one-breath derecruitment maneuver, in which PEEP was transiently lowered from 5 to 0 cmH_2O with prolonged exhalation. Recruited volume and (over)inflation, total aerated lung volume (FRC + recruited volume) were calculated as previously described [3–5]. The recruitment-to-inflation (R/I) ratio was derived from EELV measurements [3, 4]. MP (J/min) was calculated for each PEEP level using a validated equation [6]:

$$\begin{aligned} MP =& 0.098 \times respiratoryrate \times tidalvolume \\ & \times [Peakinspiratorypressure \\ & - \frac{1}{2}(PlateauPressure - PEEP) \end{aligned}$$

Normalized MP (J/min/L) was defined as MP divided by total aerated lung volume.

Statistical analysis

Data were expressed as median [interquartile range] and compared using the Mann–Whitney test. We classified recruitability using the recruited volume accrued between PEEP 5 and 15 cmH_2O, expressed as a fraction of estimated FRC (dimensionless). This is a cohort-specific operational definition to separate lower vs higher recruitability within the studied population [5, 7]. The relationship between change in PEEP and absolute and normalized MP was evaluated using linear mixed-effects models including random intercepts for repeated measures. Slopes and 95% CIs were derived from fixed-effects estimates.

Because recruited volume/FRC is not routinely measurable, we assessed the R/I ratio [3], PaO2/FiO2, and respiratory system compliance as potential surrogates using univariate and multivariable linear regression. The multivariable model included candidate predictors simultaneously; non-linearity was explored using second-order terms, without fitting additional interaction terms beyond those implied by the polynomial specification. Model performance was evaluated using R^2. A two-sided $p < 0.05$ was considered significant. All analyses were performed using MATLAB R2024b (MathWorks, Natick, MA, USA).

Results

Twenty patients with COVID-19 ARDS were enrolled within 24 h after intubation. At PEEP 5 cmH_2O, median [interquartile range] PaO_2/FiO_2 was 107 [90–130] mmHg, respiratory system compliance was 45 [30–53] ml/cmH_2O, driving pressure was 9 [8–11] cmH_2O, and FRC was 1,344 [953–1,682] ml. Full patients' clinical characteristics are reported in the original manuscript [3].

Patients were classified as having higher (n = 10) or lower (n = 10) recruitability according to whether their recruited volume between 5 and 15 cmH2O of PEEP was above or below 42% of FRC, which was the median value of the cohort.

Absolute MP at PEEP 5 cmH_2O, was similar between patients with lower and higher recruitability (20 [16–23] vs. 21 [18–23] J/min; p = 0.97). However, normalized MP was higher in patients with greater recruitability (21 [16–25] vs. 14 [10–17] J/min/L; p = 0.017), consistent with their smaller aerated lung volume at PEEP = 5 cmH_2O (1,011 [847–1,420] vs. 1,626 [1,282–2,267] mL; p = 0.016). At PEEP 15 cmH_2O, both absolute and normalized MP were similar between groups (31 [28–33] vs 31 [27–35] J/min; 16 [12–20] vs. 16 [12–20] J/min/L; p = 0.76 and 0.57, respectively), reflecting convergence of total aerated lung volumes (1,614 [1,408–2,081] vs. 1,832 [1,540–2,391] mL; p = 0.36).

In the overall cohort, absolute MP increased linearly with PEEP (+ 1.04 J/min per cmH_2O, p < 0.001). This increase was similar across recruitability strata (low recruitability: + 1.12 J/min per cmH_2O, p < 0.001; high recruitability: + 0.96 J/min per cmH_2O, p < 0.001), with no evidence of effect modification by recruitability (PEEP × group interaction p = 0.12). In contrast, MP normalized to aerated lung volume did not change overall (p = 0.50), as it reflected opposing trends: an increase in patients with lower recruitability (+ 0.43 J/min/L per cmH_2O, p < 0.001), and a decrease in patients with higher recruitability (– 0.33 J/min/L per cmH_2O, p < 0.001), with a significant PEEP × group interaction (p < 0.001) (Fig. 1).

In univariate analysis, recruited volume (slope – 102% per 1.0 increase in recruited volume/FRC; i.e., ≈ – 10% for each 0.1 increase, p < 0.001, $R^2 = 0.75$) and the R/I ratio (slope – 38% per 1.0 increase in R/I; i.e., ≈ – 3.8% for each 0.1 increase, p < 0.001, $R^2 = 0.69$) explained a large proportion of the variance in the PEEP-induced change in normalized MP. Changes in compliance and PaO_2/FiO_2 were also significantly but less strongly correlated with normalized MP changes induced by PEEP (– 1% per compliance increase = 1%, p = 0.003, $R^2 = 0.40$; -50% per PaO2/FiO2 increase = 100%, p = 0.008, $R^2 = 0.33$, respectively). In the multivariate model (second-order polynomial $R^2 = 0.89$), both the recruited volume (p = 0.002) and changes in compliance (p = 0.011) remained independently associated with changes in normalized MP (Fig. 2).

Discussion

In this physiological study, absolute MP increased with PEEP by approximately 1 J/min per cmH_2O, consistent with the mathematical formulation of MP. However, once MP was normalized to aerated lung volume, the response diverged markedly according to recruitability. At low PEEP, patients with higher recruitability showed substantially higher normalized MP, despite having absolute

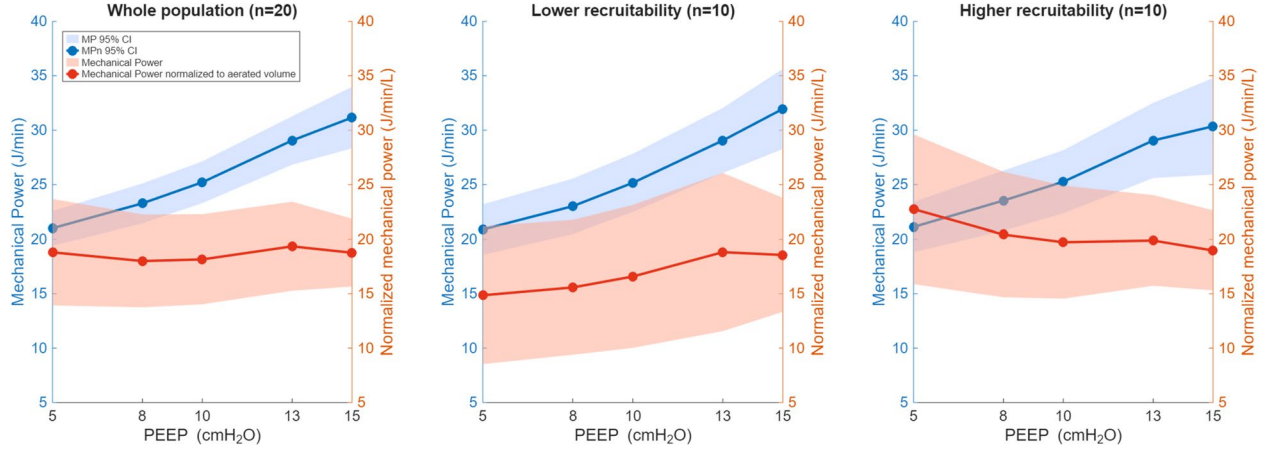

Fig. 1 Effect of PEEP on absolute and normalized mechanical power in the overall population and according to lung recruitability. The left panel shows mechanical power (blue circles; J/min) and mechanical power normalized to aerated lung volume (red circles; J/min/L) across PEEP levels in the entire cohort (n = 20). Normalized mechanical power was calculated as mechanical power divided by total aerated lung volume (FRC + recruited volume, in liters). (n = 20). Shaded areas represent 95% confidence intervals. In the overall population, absolute mechanical power increased linearly with PEEP, while normalized mechanical power remained stable. The other panels display subgroup analyses according to lung recruitability. In patients with low potential for recruitment (n = 10), normalized mechanical power tended to increase with PEEP, indicating a rising energy load per unit of ventilated lung. In contrast, in patients with high potential for lung recruitment, normalized mechanical power decreased with PEEP, suggesting that alveolar recruitment redistributed the applied energy over a larger aerated volume, thereby homogenizing mechanical load

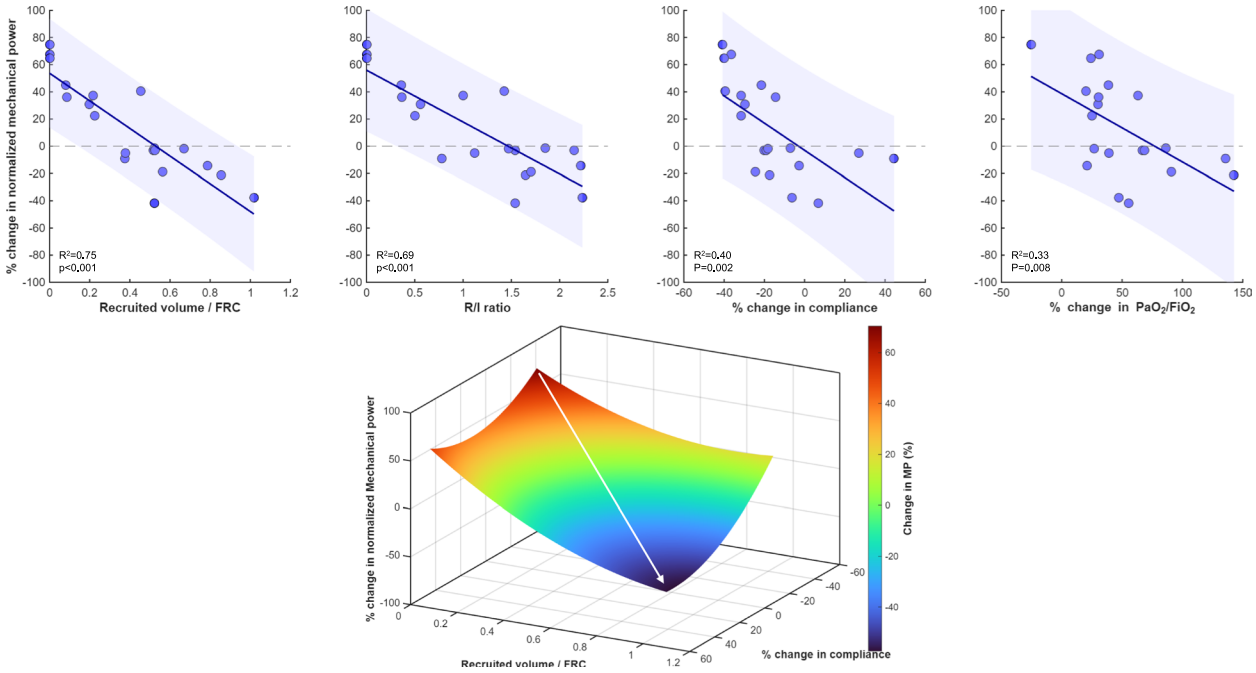

Fig. 2 (Top) Univariate relationships between PEEP-induced % changes in normalized mechanical power and recruited volume/FRC, recruitment-to-inflation (R/I) ratio, % change in respiratory system compliance, and % change in PaO_2/FiO_2 from PEEP 5 to PEEP 15 cmH_2O. The PEEP-induced reduction in normalized mechanical power was strongly associated with recruited volume and the R/I ratio, and to a lesser extent with compliance and oxygenation changes. (Bottom) Three-dimensional surface illustrating the joint relationship between recruited volume, compliance change, and normalized mechanical power. Both compliance and recruitment were independently associated with PEEP-induced variations in normalized mechanical power, consistent with their direct mechanistic role in determining how PEEP redistributes the energy applied to the lung. A second-order polynomial model best described the relationship between PEEP-induced changes in normalized MP, recruited volume/FRC, and compliance change ($R^2 = 0.89$). This suggests a non-linear interaction between the extent of recruitment and the mechanical effects of PEEP, with diminishing returns at higher levels of recruitment or compliance improvement. The white arrow indicates the 'ideal' effect of higher recruitability in the model. The R/I ratio, although strongly correlated with these parameters, was not significant at the multivariable model because of collinearity, yet it remains the most reliable bedside index to anticipate the direction and magnitude of these physiological effects.

MP similar to those with lower recruitability. As PEEP increased, normalized MP rose in patients with lower recruitability but decreased in those with higher recruitability, reflecting their increase in total aerated volume.

The divergent behavior of normalized MP is explained by the relationship between alveolar recruitment and energy distribution. Because tidal volume, inspiratory flow, and respiratory rate were kept constant across PEEP steps, the divergent changes in normalized MP primarily reflect the PEEP-related elastic components and their redistribution over the aerated lung volume. When previously collapsed alveoli are opened, the same total energy is redistributed across a larger aerated volume, thus reducing mechanical stress on individual alveolar units [8]. Accordingly, differences in normalized MP observed at low PEEP disappeared at higher PEEP, as recruitment mitigates the initial imbalance between lung volume and energy distribution per alveolar unit [9]. Conversely, under low-PEEP conditions, highly recruitable lungs are exposed to higher mechanical stress per aerated unit, because a smaller ventilated volume receives a comparable total energy load, creating conditions that favor ventilation-induced lung injury through excessive strain [10, 11].

The multivariate model showed that recruited volume normalized to FRC and changes in compliance are independent mechanistic determinants of how PEEP modulates normalized MP. This implies that assessing MP at different PEEP levels would require direct measurement of absolute lung volume, which is not feasible at the bedside. Alternative normalizations (e.g., predicted body weight or compliance-based indices) were not compared because they do not capture PEEP-induced changes in aerated lung volume, which is central when PEEP is titrated. For bedside translation, recruitability assessment with the R/I ratio was robustly associated with whether PEEP reduced or increased normalized MP. By contrast, changes in compliance and PaO_2/FiO_2, although significant, explained only a modest fraction of the effect. Moreover, compliance often decreased as PEEP increased, reflecting loss of tidal recruitment [12]. This decrease was only attenuated in patients with higher recruitability, limiting its utility as a reliable predictor of individual PEEP response [13]. Overall, oxygenation and

compliance capture beneficial population-level effects of PEEP on energy distribution, but they do not provide sufficient precision for individualized care.

Taken together, these findings support the concept that recruitability assessment should complement MP evaluation when manipulating PEEP. The R/I ratio is a useful bedside marker to predict the direction and magnitude of PEEP-induced changes in normalized MP. The loss of statistical significance of the R/I ratio in the multivariable model is best explained by collinearity with recruited volume/FRC and compliance change, reflecting both shared physiology and (in this dataset) a partially shared EELV-derived measurement basis. This does not diminish the clinical usefulness of R/I as a bedside tool, as it can be obtained without full lung-volume monitoring and provides a robust estimate of recruitability to predict the direction and magnitude of the normalized power response to PEEP. Failure to account for recruitability may partly explain why, in large clinical studies applying PEEP across heterogeneous patients, absolute MP alone has shown inconsistent associations with outcomes [14].

Several limitations must be acknowledged. First, this was a small physiological cohort studied under controlled conditions and was not designed or powered to evaluate clinical outcomes; therefore, the results should not be interpreted as evidence that changes in normalized MP translate into differences in VILI or patient-centered outcomes. Second, normalized MP requires EELV measurement, which is not routinely obtainable at the bedside; the strong association with the R/I ratio indicates a feasible surrogate. However, in this study R/I was derived from EELV rather than from the simplified bedside maneuver. Although the two approaches show excellent correlation [15], EELV-derived R/I yields higher absolute values, warranting caution in interpreting absolute R/I values displayed in this study. Third, this cohort included only early COVID-19 ARDS, which may limit generalizability. However, the mechanism tested is etiology-agnostic (PEEP changes aerated lung size through recruitment), and differences across etiologies are expected to affect the effect size rather than the direction of the relationship.

Conclusion

Absolute MP increases with PEEP, but power per aerated alveolar unit decreases when PEEP produces substantial recruitment. Therefore, an increase in absolute MP with higher PEEP does not necessarily imply a higher mechanical load per ventilated lung unit. Bedside assessment of recruitability, most consistently captured by the R/I ratio, may help identify patients in whom increasing PEEP is more likely to reduce (vs increase) normalized MP, providing physiological context for PEEP titration.

Abbreviations

PEEP	Positive end-expiratory pressure
MP	Mechanical power
EELV	End-expiratory lung volume
R/I	Recruitment-to-inflation ratio
FRC	Functional residual capacity

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Author contributions

DLG, TT, FC and IS designed the study. DLG, AMDA and GP collected the data. DLG conducted statistical analysis. DLG and TT interpreted the data and wrote the first draft of the manuscript. All authors critically revised the manuscript. All the authors reviewed the final draft of the manuscript and agreed on submitting it to Critical Care.

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Data availability

DLG takes responsibility for (is the guarantor of) the content of the manuscript, including the data and analysis. The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Declarations

Human ethics and consent to participate

The institutional review board of the coordinator center (Catholic University of The Sacred Heart, Fondazione Policlinico Universitario A. Gemelli IRCCS, Rome, Italy) reviewed and approved the study protocol before trial initiation (ID UCSC915920/20). All enrolled patients provided written informed consent in accordance with committee recommendations.

Consent for publication

Not applicable.

Competing interests

DLG has received payments for travel expenses by Getinge, Draeger and Hamilton, research grants by Fisher and Paykel and GE, speaking fees by Fisher and Paykel, GE and Draeger, and non-financial support for research by Intersurgical, Dimar and Harol. LC has received payments for travel expenses by Getinge, Draeger and Hamilton, EuroSet research grants by Fisher and Paykel and Drager, speaking fees by Fisher and Paykel, EuroSet and Draeger and Hamilton. MA has received payments for Board participation from Menarini, and Shionogi, and a research grant by General Electric Healthcare.

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