



Ventilator-related causes of lung injury: the mechanical power

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Abstract

Purpose: We hypothesized that the ventilator-related causes of lung injury may be unified in a single variable: the mechanical power. We assessed whether the mechanical power measured by the pressure–volume loops can be computed from its components: tidal volume (TV)/driving pressure (ΔP_{aw}), flow, positive end-expiratory pressure (PEEP), and respiratory rate (RR). If so, the relative contributions of each variable to the mechanical power can be estimated.

Methods: We computed the mechanical power by multiplying each component of the equation of motion by the variation of volume and RR:

$$\text{Power}_{rs} = \text{RR} \cdot \left\{ \Delta V^2 \cdot \left[\frac{1}{2} \cdot \text{EL}_{rs} + \text{RR} \cdot \frac{(1 + I : E)}{60 \cdot I : E} \cdot R_{aw} \right] + \Delta V \cdot \text{PEEP} \right\},$$

where ΔV is the tidal volume, EL_{rs} is the elastance of the respiratory system, I:E is the inspiratory-to-expiratory time ratio, and R_{aw} is the airway resistance. In 30 patients with normal lungs and in 50 ARDS patients, mechanical power was computed via the power equation and measured from the dynamic pressure–volume curve at 5 and 15 cmH₂O PEEP and 6, 8, 10, and 12 ml/kg TV. We then computed the effects of the individual component variables on the mechanical power.

Results: Computed and measured mechanical powers were similar at 5 and 15 cmH₂O PEEP both in normal subjects and in ARDS patients (slopes = 0.96, 1.06, 1.01, 1.12 respectively, $R^2 > 0.96$ and $p < 0.0001$ for all). The mechanical power increases exponentially with TV, ΔP_{aw} , and flow (exponent = 2) as well as with RR (exponent = 1.4) and linearly with PEEP.

Conclusions: The mechanical power equation may help estimate the contribution of the different ventilator-related causes of lung injury and of their variations. The equation can be easily implemented in every ventilator's software.

Keywords: ARDS, VILI, Mechanical ventilation, Respiratory mechanics

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Take-home message: Each ventilatory variable found to be associated with lung injury is actually a contributor to the mechanical power delivered to the respiratory system. The equation we propose accurately reflects the measured mechanical power, which increases exponentially with TV, ΔP_{aw} , flow (exponent = 2), and RR (exponent = 1.4) and linearly with PEEP.

Introduction

Ventilator/ventilation-induced lung injuries (VILI) result from the interaction between what the ventilator delivers to the lung parenchyma and how the lung parenchyma accepts it. Over the decades, our understanding of these two realities has progressively increased: from one side, different components of the ventilator load have been differently emphasized; on the other side, the conditions of the lung parenchyma dictating the response to a given ventilator load have been studied and clarified. The ventilator-generated causes of VILI include the pressures [1], volume [2], flow [3], and respiratory rate [4, 5]. On the other hand, the lung conditions favoring VILI primarily depend on the amount of edema, which leads to decreased lung dimensions [6], increased lung inhomogeneity, increased stress risers [7] and cyclic collapse and decollapse [8, 9]. We neglect here, for clarity, “extra-lung” factors such as perfusion, pH, gas tensions and temperature. Obviously, the ventilator and the lung causes of VILI may interact. Positive end-expiratory pressure (PEEP), as an example, on one side increases the ventilator pressure load, and on the other side may decrease lung inhomogeneity and the intratidal lung collapse–decollapse. However, the distinction between the ventilator’s and the lung’s contribution to VILI may help to reach a better VILI-prevention strategy. In fact, it is worth considering that all the ventilator-related causes of VILI, although investigated separately, are components of a unique physical variable (i.e. the mechanical power), while most of the lung-related causes of VILI are primarily consequences of the amount of edema (i.e. the ARDS severity, at least in the early phases). If we consider the ventilatory setting, it is quite clear that tidal volume, pressures and flow are all components of the energy load, which, expressed per unit of time, is the mechanical power. In this paper, we would like to propose a simple model for the quantification of mechanical power at the bedside and to discuss its possible relevance in setting a “safe” mechanical ventilation.

Methods

Derivation of mechanical power equation

Equation of motion

According to the classical equation of motion [10] (with the addition of PEEP [11]), at any given time, the pressure (P) in the whole respiratory system is equal to:

$$P = EL_{rs} \cdot \Delta V + R_{aw} \cdot F + PEEP. \quad (1)$$

Every component of the equation of motion is a pressure, in fact:

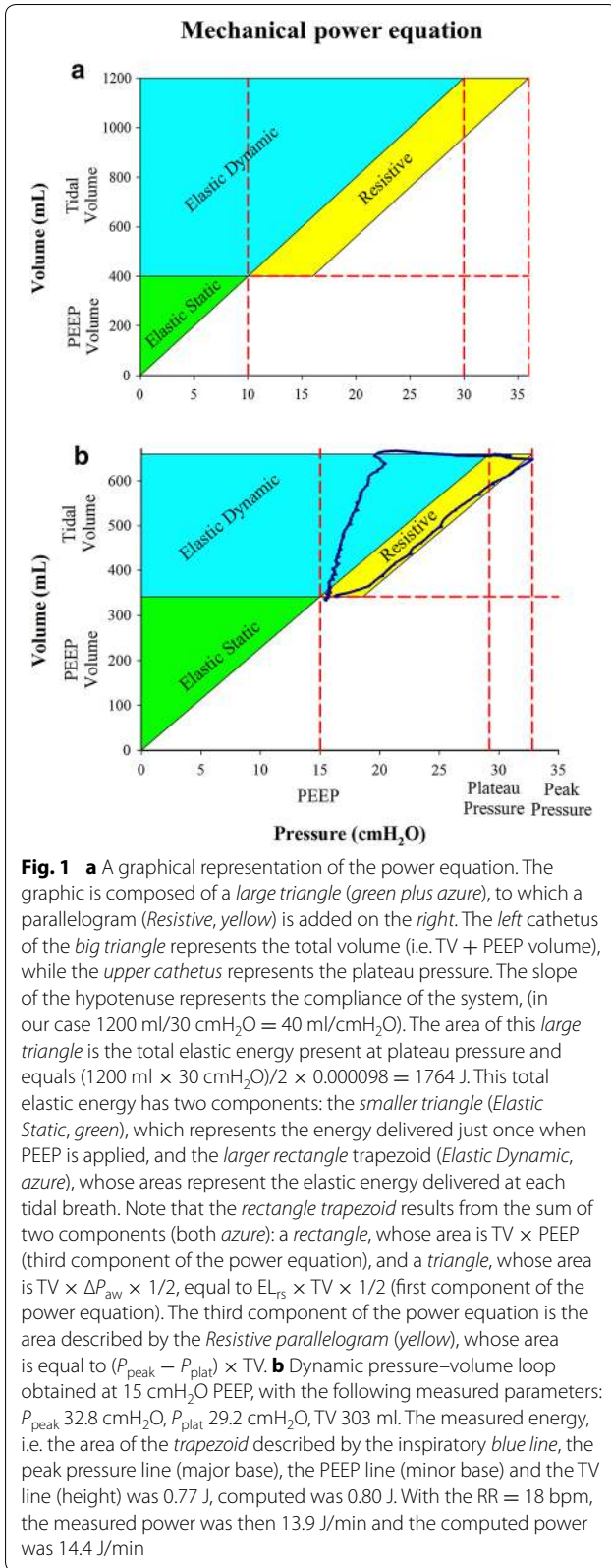
- $EL_{rs} \times \Delta V = \Delta P$ (pressure component due to the elastic recoil), being $EL_{rs} = (P_{plat} - PEEP)/\Delta V$ (i.e. respiratory system elastance).
- $R_{aw} \times F = P_{peak} - P_{plat}$ (pressure component due to the motion), being $R_{aw} = (P_{peak} - P_{plat})/F$,
- $PEEP = P_{end-expiration}$ it is not per se linked to motion, but it represents the baseline tension of the lung, as it is the pressure present in the respiratory system when ΔV and flow are equal to zero.

Energy per breath

In Fig. 1, we represent the energy that must be applied to the respiratory system in order to increase its volume (ΔV) above its resting volume. For sake of clarity, we assume that the pressure–volume curve of the respiratory system (or of the lung) is linear in the range of volumes considered, i.e. up to the beginning of the total lung capacity (TLC) region.

- Energy per breath at ZEEP. The energy (i.e. the area between the inflation line and the y axis) is the product of the absolute value of pressure (P) times the variation of volume (ΔV), i.e. $P \times \Delta V$. Therefore, when the PEEP is zero, the energy applied to compensate the elastic recoil will be the area of the triangle, i.e. $1/2 \times P_{plat} \times \Delta V$.
- Energy per breath with PEEP. When PEEP is applied, the energy to reach the PEEP volume (ΔV_{PEEP}) would be equal to $1/2 \times PEEP \times \Delta V_{PEEP}$, but it will be needed only once (as long as the PEEP will be maintained), since during the tidal ventilation the ΔV_{PEEP} equals zero and consequently the term $1/2 \times P \times \Delta V$ also equals zero. However, in the presence of PEEP, more energy is required to inflate the lung. Accordingly, the energy needed for the TV to reach the P_{plat} is $\Delta P + PEEP$ (i.e. the P_{plat}) multiplied by the volume displaced from the PEEP volume up to the plateau volume. This energy equals the area of the trapezoid having P_{plat} and PEEP as bases and TV as height (see Fig. 1). For a more detailed discussion on the role of PEEP, see the Electronic Supplement, section E-1.
- Energy per breath for gas motion. This energy is nearly equal to the area of the parallelogram on the right side of Fig. 1, in which one side is the $(P_{peak} - P_{plat})$ and the other side is the ΔV . This representation is actually a simplification of the reality, since it may change during volume-controlled or pressure-controlled ventilation.

Accordingly, we can compute the energy per breath multiplying each pressure in the motion equation by the volume variation, as follows:



$$E_{\text{breath}} = \Delta V \cdot \Delta V \cdot EL_{rs} \cdot \frac{1}{2} + \Delta V \cdot R_{aw} \cdot F + \Delta V \cdot PEEP. \quad (2)$$

The first term of the Eq. (2), which is equal to $\Delta V \times \Delta P$, has been divided by 2 (area of a triangle) in order to approximate the integral of their product (see Fig. 1a), while the second and the third terms do not require any correction, as they represent a parallel translation along the axis.

From Eq. (2):

$$E_{\text{breath}} = \Delta V^2 \cdot EL_{rs} \cdot \frac{1}{2} + \Delta V \cdot \left(R_{aw} \cdot \frac{\Delta V}{T_{\text{insp}}} \right) + \Delta V \cdot PEEP. \quad (3)$$

Therefore:

$$E_{\text{breath}} = \Delta V^2 \cdot \left(EL_{rs} \cdot \frac{1}{2} + \frac{1}{T_{\text{insp}}} \cdot R_{aw} \right) + \Delta V \cdot PEEP. \quad (4)$$

In order to express the T_{insp} as a function of respiratory rate (RR) and inspiratory-to-expiratory ratio ($I:E$), both readily available in every ventilator's settings, the following derivation may be applied:

• Premises:

- $T_{\text{insp}}/T_{\text{exp}} = I/E$,
- $T_{\text{insp}} + T_{\text{exp}} = T_{\text{tot}}$,
- $T_{\text{tot}} = 60/RR$.

- It follows that: $T_{\text{insp}} = T_{\text{tot}} \times (I/E/(1 + I:E))$
- Thus, substituting T_{insp} in the Eq. (4):

$$E_{\text{breath}} = \Delta V^2 \cdot \left(EL_{rs} \cdot \frac{1}{2} + RR \cdot \frac{(1 + I : E)}{60 \cdot I : E} \cdot R_{aw} \right) + \Delta V \cdot PEEP \quad (5)$$

If we express the volumes in liters and the pressures in cmH₂O, their product multiplied by 0.098 will be expressed in Joules.

Mechanical power

According to Eq. (5), the mechanical power expressed in J/min will be:

$$\text{Power}_{rs} = 0.098 \cdot RR \cdot \left\{ \Delta V^2 \cdot \left[\frac{1}{2} \cdot EL_{rs} + RR \cdot \frac{(1 + I : E)}{60 \cdot I : E} \cdot R_{aw} \right] + \Delta V \cdot PEEP \right\}. \quad (6)$$

Table 1 Patients' characteristics

Characteristics	Surgical control subjects (n = 19)	Medical control subjects (n = 11)	Mild ARDS patients (n = 26)	Moderate and severe ARDS patients (n = 24)	p value
Age, years	56 ± 14	51 ± 18	64 ± 15	57 ± 16	0.11
Female sex, no. of patients	12	5	12	6	0.09
Body mass index, kg/m ²	24 ± 2	23 ± 2	23 ± 3	25 ± 5	0.58
Height, cm	168 ± 7	169 ± 8	172 ± 10	172 ± 9	0.35
TV/IBW, mL/kg	9.9 ± 2.0	8.7 ± 1.7	9.0 ± 2.2	8.8 ± 2.3	0.29
Minute ventilation, l/min	6.3 ± 1.0	7.5 ± 1.5	7.3 ± 1.5	9.1 ± 2.5	<0.0001
Respiratory rate, bpm	10.7 ± 2.6	13.0 ± 4.9	12 ± 4	16 ± 4	0.0002
Respiratory system elastance, cmH ₂ O/l	19 ± 6	24 ± 6	24 ± 9	26 ± 8	0.02
FRC, ml	1715 ± 734	1166 ± 392	1088 ± 391	1013 ± 593	0.002
PaO ₂ /FiO ₂	443 ± 101	314 ± 77	249 ± 30	126 ± 43	<0.0001

From the above formula, it is possible to calculate the effects of changing whatever variable (tidal volume, driving pressure, respiratory rate, resistance) on the mechanical power applied to the respiratory system.

For a simplified version of Eq. (6) and for the computation of the mechanical power applied to the lung instead of to the whole respiratory system, see the Electronic Supplement, sections E-2 and E-3.

Measurements of applied energy/power

We used data from a previous study, which included 30 patients with normal lungs (19 surgical and 11 medical control subjects) without ARDS and 50 ARDS patients (mild = 26, moderate = 16, severe = 8). The characteristics of the population are summarized in Table 1 (further details can be found in tables 1–3 of the original study) [12]. Each patient with and without ARDS was tested with four tidal volumes (6, 8, 10 and 12 ml/kg) and two PEEP levels (5 and 15 cmH₂O). Flow and airway (P_{aw}) pressures were recorded at 100 Hz and processed on a dedicated data acquisition system (Colligo; Elekton, Milan, Italy). The energy applied per breath has been measured using the dynamic pressure–volume curve recorded during tidal ventilation. The delivered energy per breath (airways + respiratory system) was defined as the area between the inspiratory limb of the airway pressure and the volume axis (see Fig. 1b). Note that pressure is expressed in absolute values (i.e. PEEP is included) while volumes are expressed as delta-volume above the EELV. The integral of the volume–pressure area, measured as liters × cmH₂O, was then expressed in Joules (1 l × cmH₂O = 0.000098 J). The mechanical power was obtained by multiplying the energy per breath by the respiratory rate.

Statistical methods

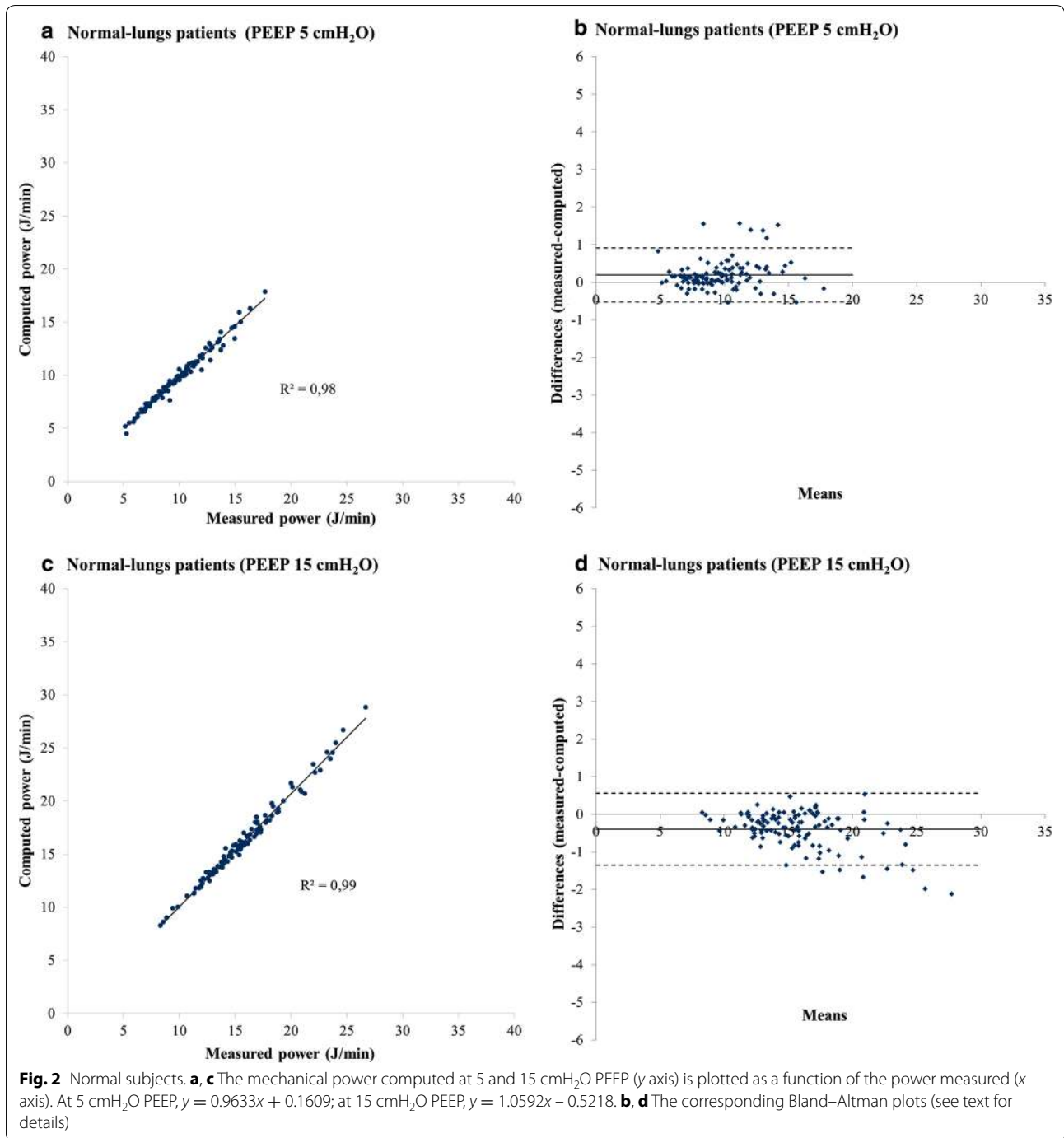
Univariable logistic regression was used for the assessment of the association between measured and computed mechanical power. In order to further assess the agreement between measured and computed mechanical power values, Bland–Altman analysis was used. Analysis was performed using SAS software, v.9.2 (SAS Institute, Cary, NC, USA).

Results

Computed versus measured mechanical power

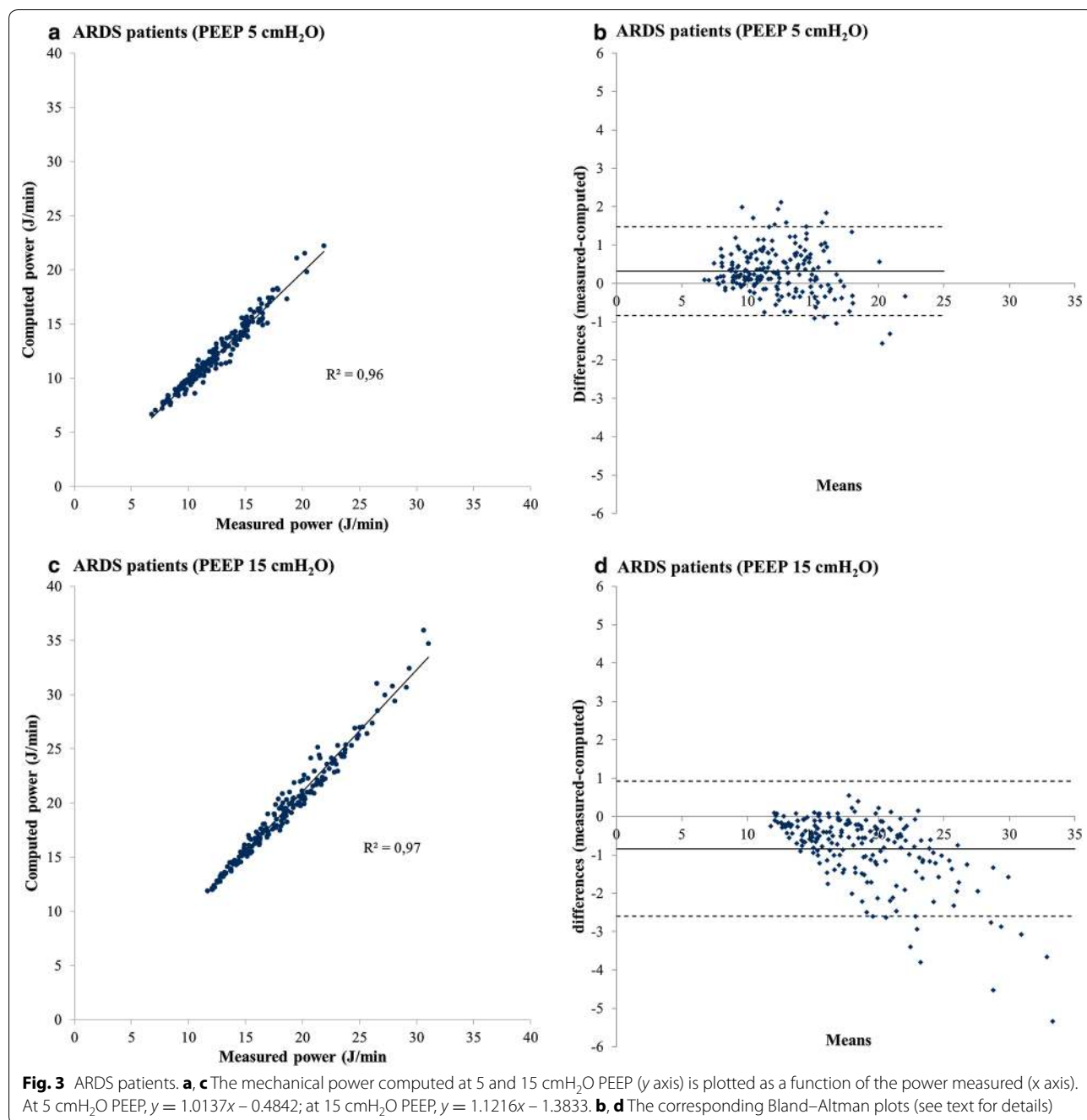
The regression between the mechanical power measured and computed in 30 patients mechanically ventilated for pathologies unrelated to the lung (i.e. “normal” lungs) are reported in Fig. 2a (5 cmH₂O PEEP) and panel C (15 cmH₂O PEEP). The mechanical powers were measured at 6, 8, 10, 12 ml/kg TV, accounting for 120 measurements for each PEEP level. The measured mechanical power (x axis) was strictly correlated with the one computed via the power equation, according to the following regressions: computed = 0.96 × measured + 0.16, $R^2 = 0.98$, $p < 0.0001$ (at 5 cmH₂O PEEP) and computed = 1.05 × measured – 0.52, $R^2 = 0.99$, $p < 0.0001$ (at 15 cmH₂O PEEP). The correspondent Bland–Altman analyses are reported in Fig. 2b, d. As shown, at PEEP 5 cmH₂O, the mean of the differences was 0.196 J/min, the upper limit of agreement was 0.916 J/min, the lower limit of agreement was –0.525 J/min. At PEEP 15 cmH₂O, the mean of the differences was –0.396 J/min, the upper limit of agreement was 0.560 J/min, and the lower limit of agreement was –1.353 J/min.

The regression between the mechanical power measured and computed in 50 ARDS patients are reported in Fig. 3a (5 cmH₂O PEEP) and Fig. 3c (15 cmH₂O PEEP). The mechanical powers were measured at 6, 8, 10, 12 ml/kg TV,



accounting for 200 measurements for each PEEP level. The measured mechanical power (x axis) was strictly correlated with the one computed via the power equation, according to the following regressions: computed = $1.01 \times$ measured $- 0.48$, $R^2 = 0.96$, $p < 0.0001$ (at 5 cmH₂O PEEP) and computed = $1.12 \times$ measured $- 1.38$, $R^2 = 0.97$, $p < 0.0001$ (at 15 cmH₂O PEEP). The correspondent Bland–Altman

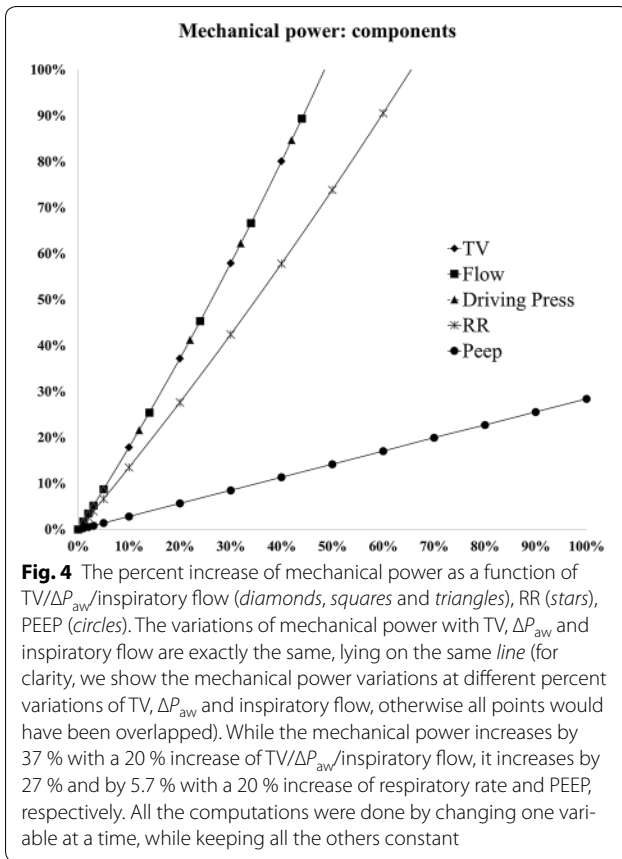
analyses are reported in Fig. 3b, d. As shown, at PEEP 5 cmH₂O the mean of the differences was 0.316 J/min, the upper limit of agreement was 1.471 J/min, the lower limit of agreement was -0.840 J/min. At PEEP 15 cmH₂O, the mean of the differences was -0.840 J/min, the upper limit of agreement was 0.924 J/min, and the lower limit of agreement was -2.604 J/min.



Effects of ventilatory parameters on mechanical power

In Fig. 4, starting from a normal condition (EL_{TS} 10 cmH₂O/l, R_{aw} 8 cmH₂O/l/s), we show the changes of mechanical power as a function of the increase of one of its components (TV, ΔP_{aw} , inspiratory flow, RR and PEEP) in 10 % steps, while the other components are maintained constant. As shown, the same percentage change of TV, driving pressure and inspiratory flow produce an identical exponential increase of mechanical power (exponent = 2),

i.e. doubling the TV (as an example, from 6 to 12 ml/kg), produce a fourfold increase in mechanical power. For the same percentage increase of frequency, mechanical power increases exponentially, but with an exponent of 1.4, while an increase of PEEP causes a linear increase in mechanical power. The effects on mechanical power of changes in airway resistance and respiratory system elastance are reported in Fig. 5. The effects of different combinations of ventilator variables on the mechanical power may be



seen on ad hoc computer program, which can be downloaded from the following link: <http://www.ains.med.uni-goettingen.de/de/abteilung-anaesthesiologie/forschung/energy-calculator-software>.

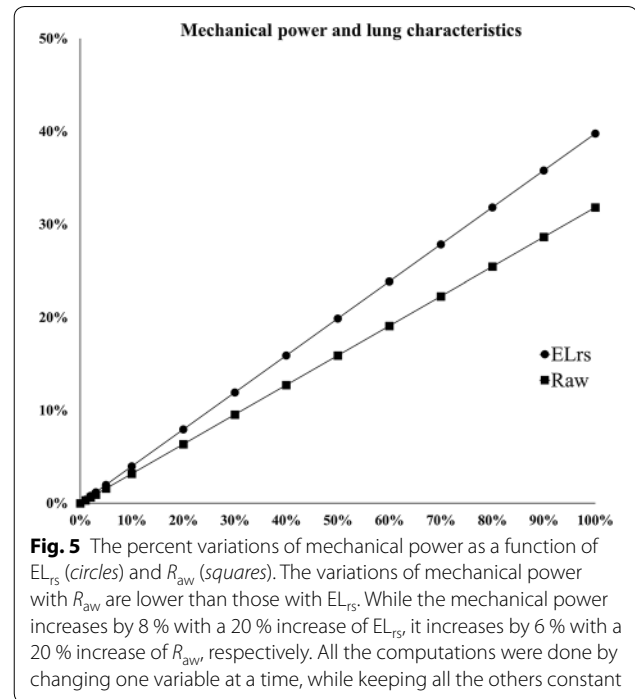
Discussion

Considering the time factor together with at least some components of the mechanical power in the genesis of VILI is obviously not new [13–15]. What we found in this study is that the “power equation”, as derived from the classical equation of motion [10, 16] (to which PEEP has been added, while the inertial forces have been neglected), provides results very similar to those obtained experimentally through the pressure–volume curve analysis. The advantage of a mathematical description of the mechanical power is that it enables the quantification of the relative contribution of its different components (TV, RR, ΔP_{aw} , PEEP, $I:E$, flow) and anticipate the effects of their changes.

Components of mechanical power

Respiratory system elastance

The first component of the power equation (i.e. the power associated with the tidal volume/driving pressure) assumes a linear pressure–volume curve. If the



elastance increases near the total lung capacity, due to overdistension, the computed energy will be underestimated. In contrast, the energy computed will be overestimated if the elastance decreases, as an example, due to recruitment. It must be noted, however, that the two phenomena (overdistension and recruitment) may occur simultaneously in different lung regions, resulting in an unchanged total elastance. In addition, a 10–20 % of change in elastance (either increasing or decreasing) should correspond to a 5–10 % change (either increasing or decreasing) in computed mechanical power (see Fig. 5). An automated system measuring the derivative of the pressure–volume at each P–V pair would avoid any possible over- or underestimation.

Airway resistance

The second component of the equation of power is the energy associated to the gas movement. As shown in Fig. 1a, in our model we assumed that both the resistance and the flow are constant during inflation. Accordingly, the difference $P_{peak} - P_{plat}$ immediately reaches its working level, which is then maintained until the end of inspiration. This assumption is obviously an oversimplification. Actually, during mechanical ventilation, the airway resistances do decrease when the end-expiratory lung volume (EELV) increases [17, 18]. Both in normal subjects and in ARDS patients, when the ventilation started from 15 cmH₂O PEEP, we found that computed mechanical power was higher than the measured one.

The systematic overestimation is evident in the Bland–Altman plots related to the ventilation at 15 cmH₂O PEEP (Figs. 2, 3d). Also in this case, an automated system measuring the airway resistances and flow would increase the accuracy of the computed power estimated.

Positive end-expiratory pressure

The third component of the equation of power equals the energy needed to overcome, throughout the whole inspiratory phase, the fibers' tension due to PEEP.

In the work-of-breathing computations implemented in the ventilators, the PEEP is not considered, as the P–V loop starts from point (0, 0), regardless of PEEP and of end-expiratory lung volume. However, although the PEEP does not contribute to the cyclic energy load associated with the ventilation, its presence increases the energy load delivered to the respiratory system by a factor equal to $PEEP \times \Delta V$ (see also the Electronic Supplement, section E-1). This effect of PEEP has been often neglected, although an increase in PEEP of 10–20 % increases the mechanical power to a similar extent.

Mechanical power and VILI

The VILI originates from the interaction between the mechanical power transferred to the ventilable lung parenchyma and the anatomic-pathological characteristics of the latter. Actually, $TV/\Delta P_{aw}$, RR, flow, and PEEP are all components of a unique physical dimension, although each of them has been studied separately from the others and, likely, may contribute differently to the mechanical power. If the mechanical damage to the lung parenchyma is a function of the mechanical power, it is possible that different combinations of its components, resulting in a mechanical power greater than a given threshold, may produce similar damage, as recently suggested by animal experiments [5]. Obviously, as the mechanical power is influenced by the capacitive properties of the system, it should be standardized for a unit of lung gas volume or grams of lung tissue exposed to the ventilation.

Healthy lungs

Most of the literature on VILI in healthy lungs implies the use of different combinations of TV and PEEP, while the RR is usually set in order to maintain a given range of PaCO₂. To induce injury in healthy lungs at “normal” frequency, TV greater than 30–40 ml/kg or even more, are required. These values, if referred to the lung size, correspond to a strain needed to reach the total lung capacity (2–3 times the FRC volume) [15]. To understand the relationship between mechanical power and healthy lungs in different species, we believe that two factors must be taken into account: the first are the

lung dimensions and the second is the lung-specific elastance, which reflects the intrinsic elasticity of the lung parenchyma (12 cmH₂O in humans, 6 cmH₂O pigs and 4 cmH₂O in rats) [19]. In healthy pigs weighing on average 21 kg, with an average FRC of 295 ml, we prospectively found a threshold value for VILI, as assessed by edema in CT scans, of 12 J/min [5], corresponding to approximately 40 mJ/min/ml.

Diseased lungs

The considerations about the lung dimensions and specific lung elastance also apply to the acutely diseased lung. The smaller the “baby lung”, the lower the mechanical power needed to induce damage should be, being the specific lung elastance similar to normal [20]. It is difficult for a mechanical power, such as to increase the “baby lung” near to its total capacity, would be applied in clinical practice. The diseased lung, however, is characterized by the presence of several interfaces between regions of different elasticity which may by doubling them concentrate the applied forces [7]. Indeed, the inhomogeneity of the lung, which dictates an inhomogeneous distribution of forces and obviously of mechanical power, is likely the main lung-dependent cause for the occurrence of VILI.

Limitations of the study

The energy delivered per breath is in part stored as elastic energy and in part dissipated, through various mechanism, into the lung. This fraction, represented by the hysteresis area of the P–V loop, is the one potentially harmful. However, as the hysteresis area is a near-constant fraction of the delivered energy (at least in the physiological range of tidal volumes) [21, 22], for simplicity we referred to the last one, which may be more easily computable and understandable.

The energy/power computation assumes a linear relationship between lung volume and elastance and resistance. As previously discussed, these linearities are likely lost at higher volume (15 cmH₂O PEEP), leading to a possible over-/underestimation of mechanical power. However, if the mechanical power concept will prove to be useful, both elastance and resistance and could be automatically computed at each volume point on the P–V loop, overcoming the linearity bias.

To understand the relative weight of the different variables introduced in the equation of power, we investigated them individually, while keeping the other variables constant. This approach is obviously questionable, as increasing the TV—as an example—may be associated in normal practice with a decreased of respiratory rate, change of flow, etc. However, we provide an easy tool to compute whatever combination of variable is thought appropriate.

It must be stressed that the mechanical power is just one part of the problem. The other part is represented by the lung's conditions. The same mechanical power may have different effects depending on dimensions of the lung, the presence of inhomogeneity, the extent of the stress risers, and the vessels' filling state, all factors which condition an uneven distribution of the delivered energy. Therefore, to be clinically meaningful, the mechanical power must be normalized, at least to the lung volume [23].

Conclusions

The mechanical power analysis underlines concepts which may be of clinical relevance. First, it accounts for the extreme importance of $TV/\Delta P_{aw}$ in inducing VILI [24], as widely recognized in the scientific community. Secondly, it may account for the ambiguous effect of PEEP. In fact, the mechanical power increases linearly with PEEP, and may contribute to VILI. On the other hand, PEEP may decrease the lung-dependent causes of VILI (lung inhomogeneity and intratidal collapse–decollapse). The final effect (positive or negative) will depend on which of the two actions prevails and in which patients. Thirdly, the mechanical power underlines the usually neglected, but potentially relevant effect of respiratory rate, as the power increases exponentially when the RR increases. In summary, considering the mechanical power as a whole may provide better insights than considering its components separately.

Electronic supplementary material

The online version of this article (doi:10.1007/s00134-016-4505-2) contains supplementary material, which is available to authorized users.

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Compliance with ethical standards

Conflicts of interest

On behalf of all authors, the corresponding author states that there is no conflict of interest.

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