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Cyclic energy: the transcendental relevance of respiratory rate. A retrospective observational study with Bayesian analysis

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Abstract

Introduction
The calculation of energy transfer in patients with acute respiratory distress syndrome (ARDS), has multiple interpretations and proposals. The parameters described as safe to minimize mechanical ventilator-associated lung injury (VALI) include only static values in their conception, and dynamic variables have been relegated to a secondary role.

Subjects and Methods
Analytical, observational, retrospective study of patients hospitalized in a respiratory intensive care unit, with a diagnosis of severe ARDS due to SARS-CoV-2 in whom mechanical ventilator management was guided by the use of esophageal catheter for the calculation of ventilatory variables. Thirty-four patients were included in this study, 23.5 % were women and the mean body mass index was 34.9 kg/m^2. The primary objective was to quantify the amount of energy (Mechanical Power MP) transmitted by using multiple known equations and the secondary objective was to find the variables best associated with such energy transfer and with the severity of ARDS using Bayesian analysis.

Results
A mean of 22.2 days on invasive mechanical ventilation was recorded. Baseline $MP_{Gattinoni}$ averaged 21.4 J/min, which did not change significantly at 30 minutes (7.5%) or 24 hours (- 0.4%) from baseline, despite esophageal catheter-guided management. The Bayesian analyses used to calculate the a posteriori inclusion probability showed that respiratory rate was the only variable consistently related to energy transfer, regardless of the equation used for its calculation and the chronological time at which these equations were measured [baseline $MP_{Gattinoni}$: (mean, 0.89; 95% Cred Interval: 0.75 to 1.02), at 30 minutes: (mean, 1.09; 95% Cred Interval: 0.68 to 1.49), at 24 hours: (mean, 0.65; 95% Cred Interval: 0.01 to 1.03)] or [baseline $MP_{Modesto}$: (mean, 0.1; 95% Cred Interval: 0.09 to 0.1), at 30 minutes: (mean, 0.1; 95% Cred Interval: 0.09 to 0.1), at 24 hours: (mean, 0.1; 95% Cred Interval: 0.09 to 0.1)].

Conclusions
In severe ARDS, it is essential to minimize VALI. The calculation of energy transfer, regardless of the equation used, should always be a dynamic objective to be measured. Respiratory rate is probably the most relevant dynamic variable in the genesis of VALI.

Keywords: mechanical power, elastic power, respiratory rate, ARDS, COVID-19

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Introduction

From a rheological perspective, [1] cyclicity has absolute implications in the transmission of energy, and the probability of generating injury depends directly on the *resilience* [2] and maximum *strain* (deformation) of a given fluid or material subjected to *stress* (pressure).

So far, the quantification of the energy transmitted from the mechanical ventilator to the lung parenchyma remains the weak point of critical respiratory medicine. Static variables have been proposed as potential genesis of mechanical ventilator-associated lung injury (VALI), and their maximum tolerance ranges have created limits that govern us to this day. Driving pressure (DP), [3] plateau pressure (P_{plat}) [4] and the concept of "*baby lung*" [5] are static variables that have been consolidated as a guide to minimize the risk of VALI. Nevertheless, the dynamic physical properties of fluids and materials underscore the need for an increasingly comprehensive perspective on respiratory pathophysiology. Time-dependent alveolar deformation, [6] and eventual intracyclic shear, inevitably form a fundamental part of the energy transfer equation. Mechanical power, [7] total elastic power [8] and elastic static power (PEEP power) [9] are dynamic variables proposed by different authors to quantify the energy transmitted and potentially injurious to the lung parenchyma.

The main objective of this study was to identify the variables related to greater power transmission as part of the Mechanical Power components. In addition, another objective was to quantify the amount of energy transmitted, using different known equations, and to identify its association with ARDS severity.

Materials and Methods

This is a study with analytical, observational and retrospective design, of 34 patients hospitalized between June and December 2021, in the respiratory intensive care unit (UCIR) of the National Institute of Respiratory Diseases "Ismael Cosío Villegas" (INER), Mexico City, Mexico.

Inclusion criteria were adult patients ≥ 18 years old, with a diagnosis of SARS-CoV-2 viral pneumonia confirmed by PCR test, patients with severe ARDS criteria according to the Berlin classification [10] requiring invasive mechanical ventilation, less than 48 hours since admission to UCIR and ventilated with the volume-controlled ventilation mode. Those patients who met the admission criteria had an esophageal catheter (Cooper Surgical, Trumbull, Connecticut, USA) inserted to monitor esophageal pressure at the end of inspiration ($P_{es}EIO$) and expiration ($P_{es}EEO$), calculating the transpulmonary pressures by subtracting their values from the airway pressure during inspiratory ($PL_{es}EIO$) and expiratory ($PL_{es}EEO$) pauses, respectively. Correct installation was confirmed with Baydur's method [11] and was used as a strategy for individualization of mechanical ventilation management. [12]

Exclusion criteria were patients under 18 years of age, requiring mechanical ventilation for causes other than SARS-CoV-2 viral pneumonia, with more than 48 hours in the ICU and users of ventilatory modes other than volume control.

Variables were collected in an anonymized electronic database. For each patient, demographic variables corresponding to gender, age, weight, height, BMI, and severity scales (SOFA and APACHE II) were collected. In addition, ventilatory variables were collected sequentially at three time points (at admission and prior to esophageal catheter installation, 30 minutes and 24 hours after admission and esophageal catheter installation).

The primary objective was to quantify the amount of energy transmitted, using different equations for each of the variable measurement times. The secondary objectives were to identify the most important variables for each of the equations used in the calculation of energy transfer and to evaluate the association of these variables with the severity of ARDS.

This study has the corresponding Informed consent for each participant and was approved by the Ethics and Research Committee of the aforementioned Institute (#C44-21). The design of this study complies with the rigor standards recommended by international regulations (STROBE).

Equations for the calculation of energy transfer

To measure the amount of transmitted power, we use the following equations:

Mechanical power Gattinoni

$$0.098 \times RR \times (V_T) \times (P_{peak} - [DP/2])$$ [7]

Mechanical power Modesto

$$0.098 \times RR \times \text{Strain surrogate} \times \text{Strain-rate surrogate} \times PEEP$$ [13]

Total elastic power

$$0.098 \times V_T \times RR \times ([P_{plat} + PEEP]/2)$$ [8]

Elastic static power

$$0.098 \times V_T \times RR \times PEEP$$ [8]

Where, V_T is the tidal volume (liters), RR is the respiratory rate (breaths per minute), P_{plat} is the plateau pressure (cmH_2O), PEEP is the positive end-expiratory pressure (cmH_2O), P_{peak} is the peak pressure (cmH_2O), DP is the driving pressure (cmH_2O), Strain surrogate is DP or P_{plat} - PEEP (cmH_2O), and Strain-rate surrogate is the subrogate of strain rate: Flow/PEEP ($L/s/cmH_2O$). All energy transfer (or power) measurement equations are expressed in J/min.

Statistical analysis

STATA v.18 (StatsCorp, College Station, TX, USA) was used for data analysis. In the descriptive analysis of the sample, continuous quantitative variables are presented as means and their respective standard deviations. Categorical variables are presented as proportions and their respective standard errors. For the comparison between the different chronological times (admission or baseline, 30 minutes and 24 hours), the Bayesian T-contrast for independent samples was used. The comparison of frequencies was established through contingency tables, being expressed by Bayes Factor (BF) obtained by Bayesian linear regression with Metropolis-Hastings (MH) adaptive algorithm, using *a priori* non-informative Jeffreys distribution for the calculation of the covariance of a multivariate normal distribution using the Laplace-Metropolis approximation.

For each chronological time and for each equation of the energy transfer calculation, the choice of the final model components was made through the computation of the a posteriori inclusions probability (PIP) for each variable obtained by robust Bayesian regressions (Bayesian Model Average).

To obtain the final models, multiple Bayesian linear regressions were performed, using a non-informative a priori beta-binomial model (MCMC sample size=10,000, 22 models, g=64), [14] for a sampling correlation of 0.98. Comparative testing was then performed by diagnostic confirmation of parsimonious convergence of the models to the respective *a posteriori* distribution.

The results of the *a posteriori* distributions are presented as means with their respective 95% credible intervals (Cred Interval), [14] both in summary tables and graphically.

Results

A total of 34 patients were included. The mean age was 43.3 years (± 12.5), female gender corresponded to 23.5%. The mean weight was 100.6 kg (± 24.8), height was 169.6 (± 8.7), and body mass index was 34.9 kg/m2 (± 8).
Regarding the variables predicting mortality, the mean SOFA score was 5.4 (± 2.3) points and 18.7 (± 3.9) points for APACHE II. There was a mortality rate of 20% and a rate of 22.2 days (± 14) on invasive mechanical ventilation.

In the descriptive analysis, we found an average baseline V_T of 6.3 ml/kg PBW (± 0.6), 25.5 (± 2.3) breaths per minute, 10.4 cmH_2O (± 2.3) PEEP, 12.5 cmH_2O (± 2.2) driving pressure and 112.5 mmHg (± 28.4) for PaO_2:FiO_2. Likewise, the average $P_{es}EEO$ was 11.9 cmH_2O (± 2.6) and -1.3 cmH_2O (± 2.3) for $PL_{es}EEO$. Regarding the energy transfer measurement equations, we found a basal $MP_{Gattinoni}$ of 21.4 J/min (± 3.9) and a $MP_{Modesto}$ of 5 J/min (± 0.3); in addition, we found a basal average of 16.6 J/min (± 3.1) for total elastic power and 10.3 J/min (± 2.4) for elastic static power. The rest of the variables are shown in Table 1.

When the variables were compared sequentially at the three chronological times, only FiO_2 showed a significant positive change, both at 30 minutes (BF: 27.4) and 24 hours (BF: 40.5), with respect to baseline. Likewise, the only variable that presented a significant negative modification was the elastic static power, both at 30 minutes (BF: -12.2) and 24 hours (BF: -11.5), with respect to baseline. The rest of the comparative analysis is shown in Table 1.

In the *a posteriori* probability of inclusion (PIP) analysis, multivariate models for the analysis of $MP_{Gattinoni}$, showed respiratory rate as the only variable of relevance, both for baseline (mean, 0.89; 95% Cred Interval: 0.75 to 1.02), as well as at 30 minutes (mean, 1.09; 95% Cred Interval: 0.68 to 1.49), and at 24 hours (mean, 0.65; 95% Cred Interval: 0.01 - 1.03) (Table 2 and Figure 1).

Similarly, in the multivariate models for the analysis of $MP_{Modesto}$, we found that respiratory rate was the only variable of relevance for the three sequential times (mean, 0.1; 95% Cred Interval: 0.09 - 0.1) (Table 2 and Figure 2).

Likewise, when total elastic power was analyzed, respiratory rate was again the most relevant variable, both at baseline (mean, 0.65; 95% Cred Interval: 0.53 - 0.77), at 30 minutes (mean, 0.81; 95% Cred Interval: 0.67 - 0.94) and also at 24 hours (mean, 0.77; 95% Cred Interval 95%: 0.67 - 0.87) (Table 2 and Figure 3).

Finally, in the *a posteriori* inclusion probability analysis, the multivariate models for the analysis of elastic static power, respiratory rate repeated as the only variable of relevance, both at baseline (mean, 0.39; 95% Cred Interval: 0.31 - 0.48), at 30 minutes (mean, 0.6; 95% Cred Interval: 0.47 - 0.72), and at 24 hours (mean, 0.57; 95% Cred Interval: 0.48 - 0.67) (Table 2 and Figure 4).

Table 1 Descriptive analysis of the study variables

Variable	Baseline	30 min	BF	24 hours	BF
V_T (ml)	404.4 (58.4)	385.9 (63.8)	- 2.8	392.3 (60.6)	- 1.1
V_T ml/kgPBW	6.3 (0.6)	5.9 (0.5)	8.9	6.1 (0.5)	9.1
RR (rpm)	25.5 (2.3)	24.5 (2.3)	- 0.9	24.4 (2.8)	- 6.5
Flow (L/min)	26.9 (3.9)	25.7 (4.3)	- 2.9	26.2 (4)	- 1.2
R_{aw} (cmH_2O/L/s)	17.4 (5.3)	18.7 (5.8)	- 3.1	15.9 (6.1)	- 4.6
PEEP (cmH_2O)	10.4 (2.3)	14.2 (2.5)	- 2.7	13.2 (2.7)	- 6.4
P_{peak} (cmH_2O)	27.5 (3.1)	30.7 (2.8)	4.1	28.2 (3.4)	- 2.4
P_{plat} (cmH_2O)	22.8 (3)	25.9 (2.6)	5.4	24 (2.7)	3.2
P_{es}EIO (cmH_2O)	13.4 (2.6)	14.2 (2.9)	- 3.5	14.3 (3.4)	- 8.4
P_{es}EEO (cmH_2O)	11.9 (2.6)	12.5 (2.8)	- 2.5	12.3 (3.3)	- 7.9
C_{stat} (ml/cmH_2O)	34.3 (8.1)	34.9 (8.3)	- 0.5	38.1 (9.1)	- 3.8
PL_{es}EIO (cmH_2O)	9.4 (3.1)	11.7 (2.5)	6.4	9.3 (2.7)	4.4
PL_{es}EEO (cmH_2O)	-1.3 (2.3)	1.9 (1.5)	7.8	1.2 (1.2)	15.2
DP (cmH_2O)	12.5 (2.2)	11.7 (2.1)	0.7	10.9 (2.1)	0.7
DPL_{es} (cmH_2O)	10.7 (1.9)	9.9 (2.2)	- 3.4	8.7 (2.2)	- 3
Strainrate sr (L/s/cmH_2O)	2.7 (0.8)	1.9 (0.4)	21	2.1 (0.5)	15.2
FiO_2 (%)	67.5 (17.9)	44.6 (7.9)	27.4	41 (5.3)	40.5
PaO_2 (mmHg)	71.5 (7.2)	73.4 (9.6)	- 9.5	73.1 (6.4)	3.8
$PaCO_2$ (mmHg)	44.2 (6.1)	43.2 (6.8)	- 3.8	42.5 (7.1)	- 5.2
$ETCO_2$ (mmHg)	36.4 (5.9)	35.8 (5.1)	5	36.5 (5.7)	1.8
P/F	112.5 (28.4)	168.6 (31.5)	- 3.8	180.9 (28.2)	- 0.3
VD (%)	17.9 (7.4)	16.7 (8.2)	- 3.1	15.9 (8.8)	- 5.5
MP (J/min) [Gattinoni]	21.4 (3.9)	23 (5.1)	- 9	21.3 (5.1)	- 8.9
MP (J/min) [Modesto]	5 (0.3)	5.1 (0.3)	1.9	4.9 (0.3)	1.3
TEPower (J/min)	16.6 (3.1)	18.6 (4.1)	- 9.1	17.3 (3.7)	- 6.1
EEP (J/min)	10.3 (2.4)	13.2 (3.4)	- 12.1	12.3 (3.4)	- 11.5

Values are expressed as means and their respective standard deviations (SD). Recording is sequential, at three time points, starting from esophageal catheter installation.
BF, Bayes factor. V_T, tidal volume. PBW, predicted weight. RR, respiratory rate. R_{aw}, airway resistance. PEEP, positive end-expiratory pressure. P_{peak}, peak pressure. P_{plat}, plateau pressure. P_{es}EIO, end-inspiratory esophageal pressure. P_{es}EEO, esophageal end-expiratory pressure. C_{stat}, static compliance. PL_{es}EIO, end-inspiratory transpulmonary pressure. PL_{es}EEO, end-expiratory transpulmonary pressure. DP, driving pressure. DPL_{ES}, transpulmonary driving pressure. Strain-rate sr, strain rate surrogate. FiO_2, fraction inspired oxygen. PaO_2, arterial oxygen pressure. $PaCO_2$, arterial carbon dioxide pressure. $ETCO_2$, exhaled carbon dioxide. P/F, PaO_2/FiO_2 ratio. VD, dead space. MP, mechanical power. TEPower, total elastic power. EEP, elastic static power.

Table 2 Bayesian analysis of the multivariate models with the estimated *a posteriori* probabilities for each energy transfer calculation equation and each variable

	Baseline		30 min		24 hours	
	mean	95% Cred Interval	mean	95% Cred Interval	mean	95% Cred Interval
$MP_{Gattinoni}$						
RR (rpm)	0.89	0.75 to 1.02	1.09	0.68 to 1.49	0.65	0.01 to 1.03
P_{es}EIO (cmH_2O)	9.62	0 to 17.69	-	-	-	-
PL_{es}EIO (cmH_2O)	9.52	- 0.08 to 17.57	-	-	-	-
P_{peak} (cmH_2O)	0.9	0.74 to 1.06	0.05	- 0.12 to 0.42	0.04	- 0.09 to 0.36
PEEP (cmH_2O)	- 4.8	- 16.81 to 0.5	-	-	-	-
P_{plat} (cmH_2O)	- 4.75	- 16.81 to 0.63	-	-	-	-
DP (cmH_2O)	- 5.22	- 16.99 to 0	- 0.01	- 0.33 to 0.29	- 0.05	- 0.5 to 0.19
V_T (ml)	- 0.05	0.05 to 0.06	0.04	0.02 to 0.05	0.04	- 0.02 to 0.06
$MP_{Modesto}$						
RR (rpm)	0.1	0.09 to 0.1	0.1	0.09 to 0.1	0.1	0.09 to 0.1
Strain-rate (L/s/cmH_2O)	0.1	0.07 to 0.13	0.1	0.04 to 0.15	0.1	0.05 to 0.14
P_{plat} (cmH_2O)	0.1	0.09 to 0.1	0.1	0.09 to 0.1	0.1	0.09 to 0.1
Total Elastic Power						
RR (rpm)	0.65	0.53 to 0.77	0.81	0.67 to 0.94	0.77	0,67 to 0.87
PEEP (cmH_2O)	-	-	0.43	0 to 1	0.46	0 to 0.95
P_{es}EIO (cmH_2O)	3.04	- 0.13 to 11.99	0.48	0 to 1	-	-
PL_{es}EIO (cmH_2O)	2.95	- 0.25 to 11.87	-	-	-	-
P_{plat} (cmH_2O)	- 2.43	- 11.34 to 0.79	-	-	0.42	0 to 0.95
DP (cmH_2O)	-	-	0.02	- 1.06 to 1.07	- 0.02	- 0.94 to 0.94
Strain-rate (L/s/cmH_2O)	- 1.49	- 1.98 to -1	-	-	-	-
V_T (ml)	0.05	0.04 to 0.06	0.05	0.04 to 0.05	0.04	0.04 to 0.05
Elastic Static Power						
RR (rpm)	0.39	0.31 to 0.48	0.6	0.47 to 0.72	0.57	0.48 to 0.67
PEEP (cmH_2O)	0.97	0.88 to 1.05	0.88	0.77 to 0.99	0.91	0.82 to 1
V_T (ml)	0.03	0.02 to 0.03	0.04	0.03 to 0.04	0.03	0.03 to 0.04

Mean, average *a posteriori*. Cred Interval, credibility interval.
RR, respiratory rate. P_{es}EIO, end-inspiratory esophageal pressure. PL_{es}EIO, end-inspiratory transpulmonary pressure. P_{peak}, peak pressure. PEEP, positive end-expiratory pressure. P_{plat}, plateau pressure. DP, driving pressure. V_T, tidal volume. Strain-rate, subrogated strain rate.
The absence of data for some variables in their time sequence means that for that particular model they did not present a relevant probability of inclusion *a posteriori*.

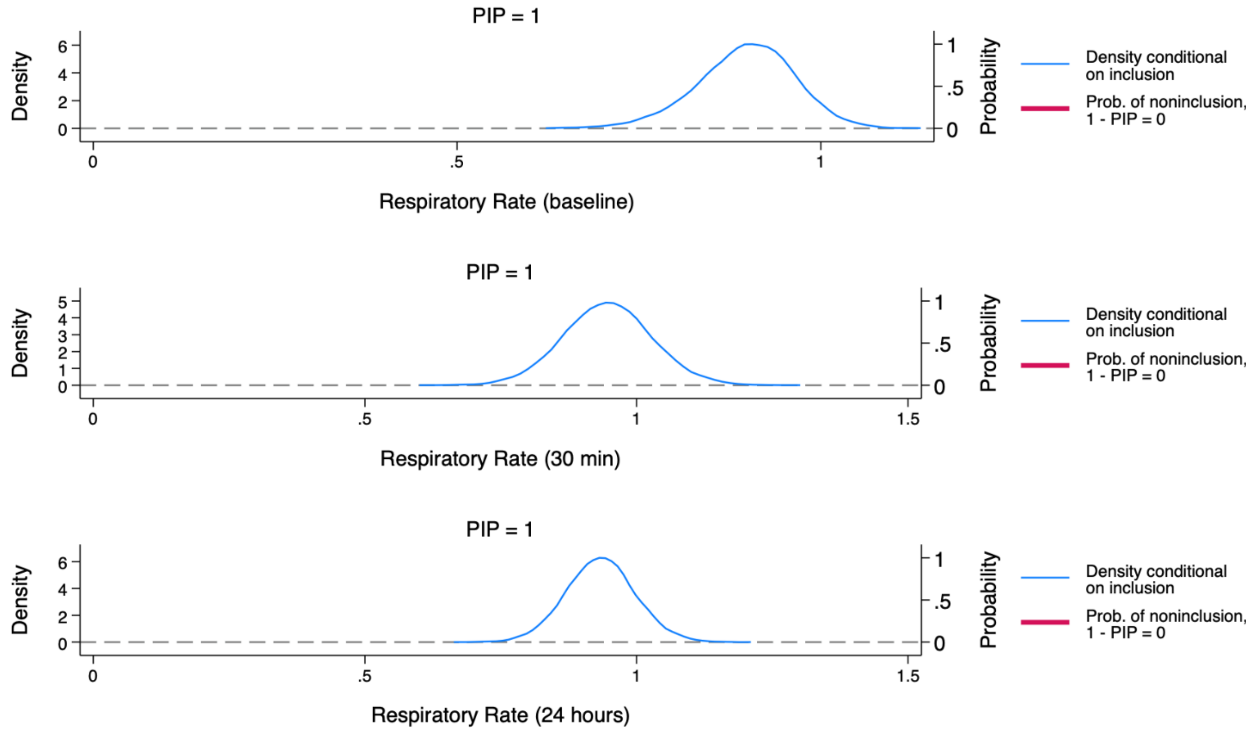

Figure 1: *A posteriori* inclusion probability (PIP) for respiratory rate, in the three chronological measurements, of the multivariate models for the MPGattinoni analysis. On the abscissa (X) axis are represented the *posterior* means. On the ordinate (Y) axis, on the left is represented the density, and on the right the *a posteriori* inclusion probability.

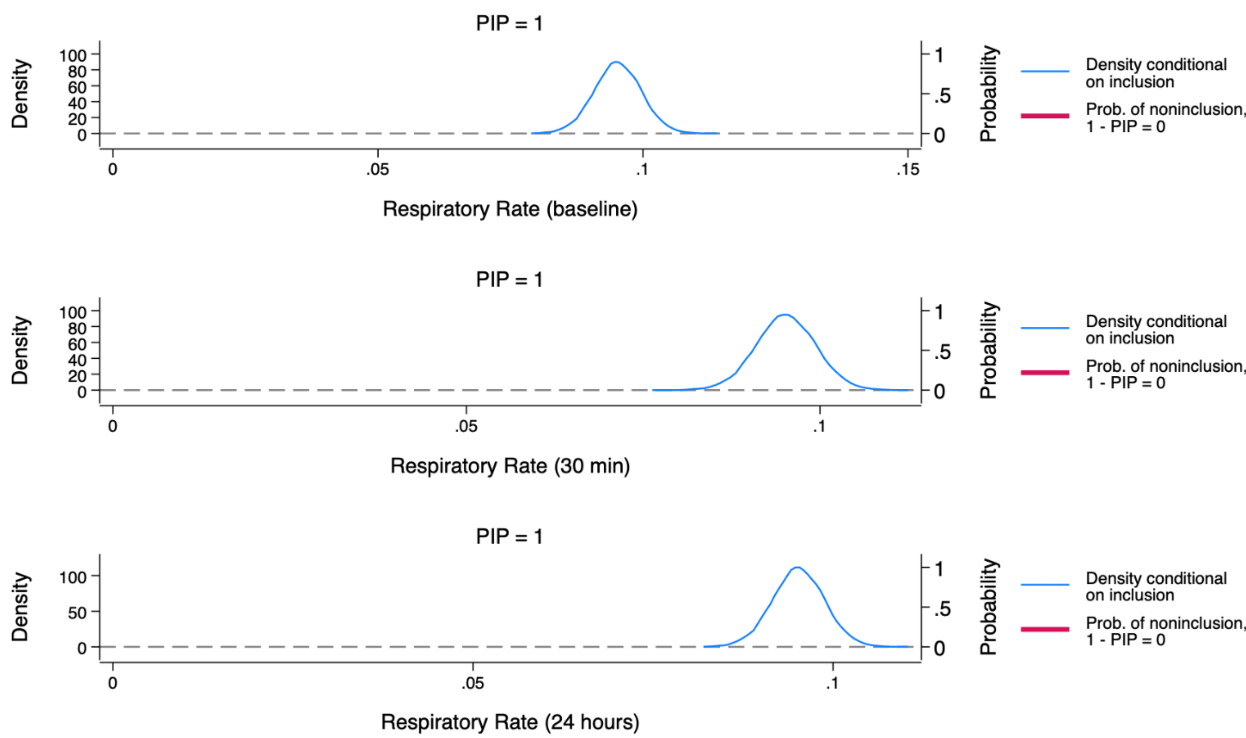

Figure 2: A posteriori inclusion probability (PIP) for respiratory rate, in the three chronological measurements of the multivariate models for the MPModesto analysis. On the abscissa (X) axis are represented the *a posteriori* means. On the ordinate (Y) axis, on the left is represented the density, and on the right the a posteriori inclusion probability

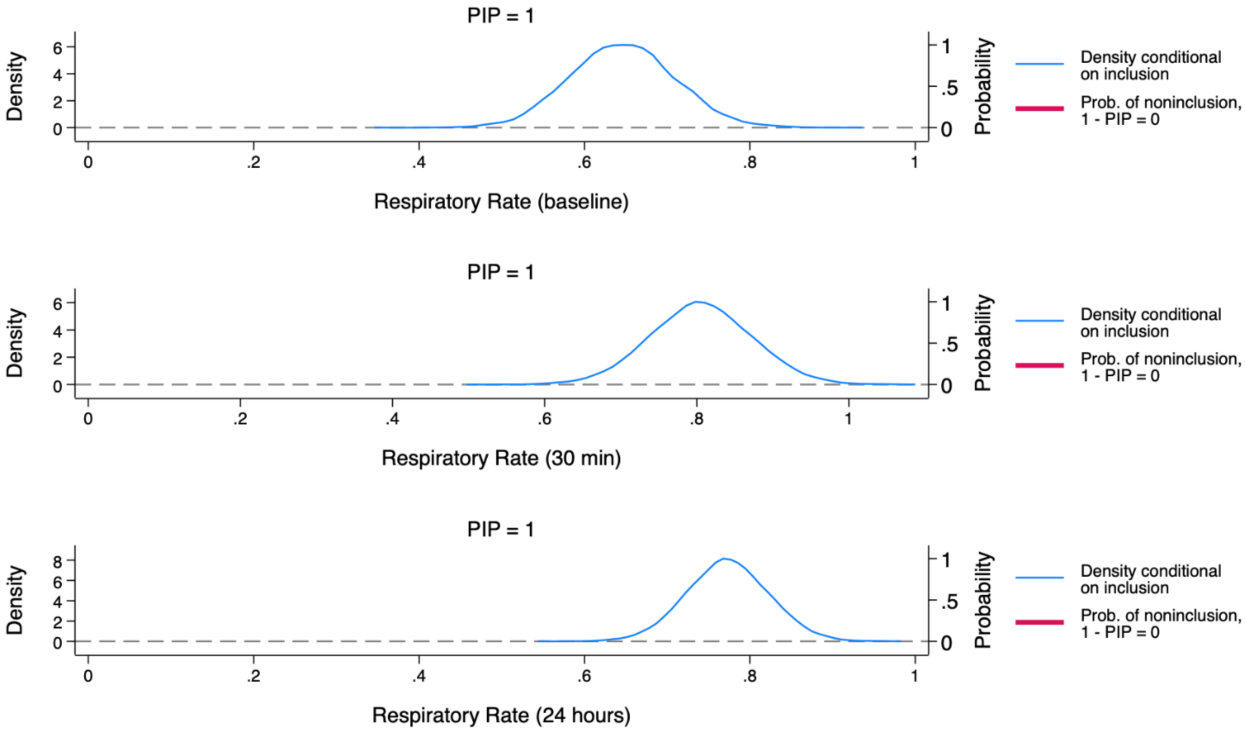

Figure 3 A *posteriori* inclusion probability (PIP) for respiratory rate, in the three chronological measurements of the multivariate models for the Total Elastic Power analysis. On the abscissa (X) axis are represented the *a posteriori* means. On the ordinate (Y) axis, on the left is represented the density, and on the right the *a posteriori* inclusion probability.

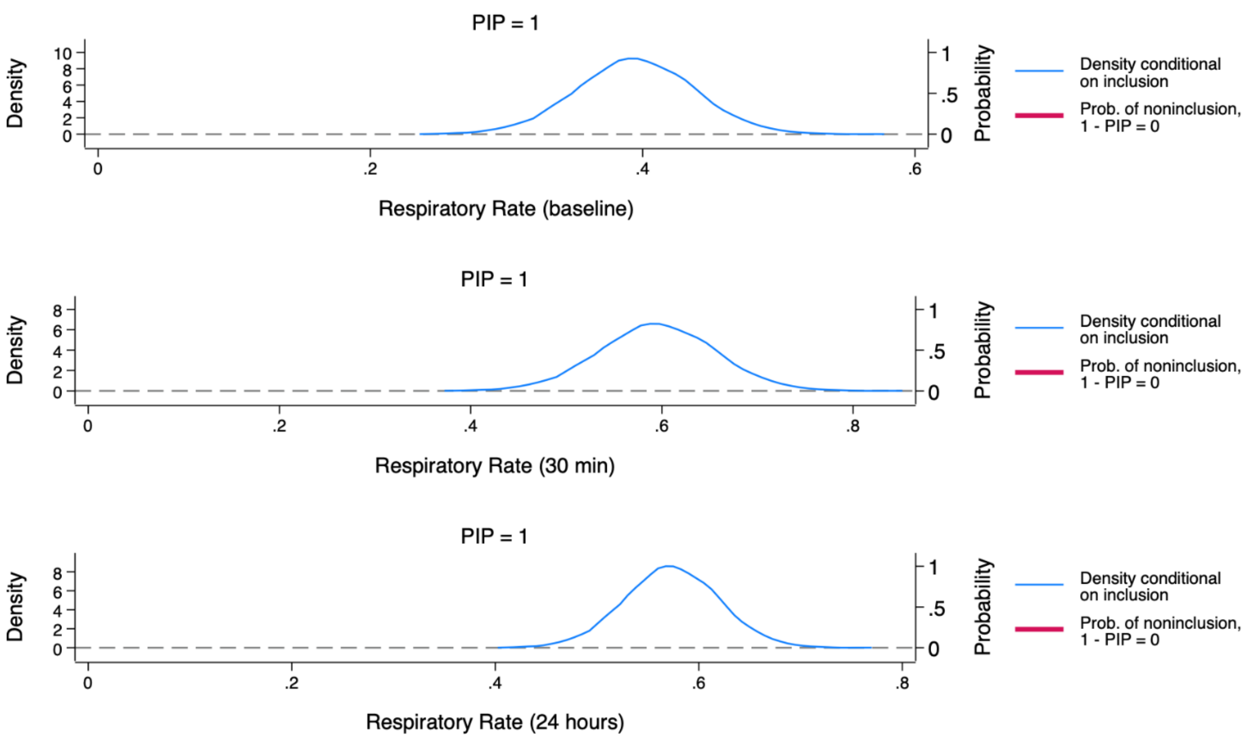

Figure 4 A posteriori inclusion probability (PIP) for respiratory rate, in the three chronological measurements of the multivariate models for the Elastic Static Power analysis. On the abscissa (X) axis are represented the *a posteriori* means. On the ordinate (Y) axis, on the left is represented the density, and on the right the *a posterior* inclusion probability.

Discussion

In this study we tried to find which of all the variables that make up the mechanical power formula, regardless of the design of its calculation, is associated with the greatest relevance with respect to cyclic power transmission. We observed that both the baseline measurement of the variables, prior to the installation of the esophageal catheter, and those obtained 30 minutes and 24 hours after its installation, the energy transfer measurement variables always showed levels higher than those universally accepted as safe. The $MP_{Gattinoni}$, in the baseline measurement, was 21.4 J/min, while its maximum accepted value is 17 J/min. Likewise, we found a basal total elastic power of 16.6 J/min, while its maximum accepted value is 3.3 J/min in experimental models.

Our multivariate Bayesian models showed that respiratory rate was the only variable of relevance that was present both in the three chronological sequential times and in the different analyses of the energy transfer measurement equations (*a posteriori* inclusion probability (PIP)=1) (Figures 1 to 3). This confirms that respiratory rate, in the models described, is the variable that best fits the data according to the estimated maximum likelihood, for patients with severe ARDS. That is, for this cohort, a programmed respiratory frequency ≥ 25 per minute, is transversely present in all power transmission measurements, when patients with severe ARDS were analyzed.

In addition, static measurements from the use of the esophageal catheter (esophageal pressure, transpulmonary pressure) did not show important changes for the programming of the mechanical ventilator, nor did they represent changes for the decrease in energy transfer, at 30 minutes or 24 hours after its installation.

Our study presents some strengths. First, the significant number and precision of ventilatory variables collected for each patient and at each chronological sequential time, all guided by measurements of esophageal catheter-derived variables, make this study robust in its results. Second, the complex statistical analyses confer greater certainty to the results presented, due to the high likelihood obtained through Bayesian inference. Our data coincide with the results obtained by Straub(15), who reported a higher mortality associated with respiratory rates above 27-33 per minute (OR 1.70, 95% CI: 1.69 - 1.76; P <0.05), compared with patients in whom lower respiratory rates were used.

From the pathophysiological point of view, high respiratory rates not only produce direct injury through their absolute value, but also through chemical effects on the mechanoreceptor reflex feedback system. [16] The respiratory center is especially sensitive to changes in pH, PaO_2 and $PaCO_2$. Studies suggest that hypocapnia and respiratory alkalosis resulting from the programming of high respiratory rates induce injury per se, both at the pulmonary level and in other noble organs, which is related to increased morbidity and mortality. [17]

The second law of thermodynamics states that, in any cyclic process, entropy will either increase or remain the same. Strictly speaking, entropy is a state (material) variable, and the change is defined by the reversibility of a process (T) when the heat absorbed (Q) is measured. Thus, entropy (ΔS) = Q/T. Therefore, after applying an energy input to an isolated system, the natural course of events would lead the receiving system to a state of increased disorder. There is practically no viscoelastic structure capable of absorbing the total energy input and, in turn, transforming it into an equivalent amount of work (Kelvin-Planck). [18]

In the study by Tonna et al, [19] 2452 patients with ARDS were categorized into high and low respiratory rate groups, with a cut-off point of 26 breaths per minute. What is interesting in this study is that, in the low respiratory rate group, only $MP_{Gattinoni}$ was associated with higher mortality (power [HR 1.82; 95% CI: 1.41 - 2.35, P <0.01].

Gattinoni et al, [7] in the geometrical conception of their mechanical power equation, assure that the respiratory frequency would play a secondary role in the energy transfer equation, due to a linear, but not exponential increase of the same. However, applying the science of materials engineering, the fatigue of any material is absolutely time dependent. [6] This statement has already been corroborated at experimental level, where low respiratory frequencies were associated with lower VALI [20,21] due to a shorter exposure time to stress. [22]

On the other hand, elastic power has been consolidated as an accurate variable to quantify the amount of energy delivered by the mechanical ventilator. Syed et al [9] found a high correlation between dynamic power (elastic power) and an increased risk of VALI in patients with severe ARDS. The authors conclude that there are two transcendental elements in this context: excessive *strain* per cycle and cyclic frequency.

From a clinical point of view, respiratory frequency is becoming more and more relevant, [23] and beyond the invaluable and correct recommendation of programming low V_T, low P_{plat} and DP levels, dynamic variables are beginning to consolidate as mandatory safety parameters to minimize VALI.

Limitations
Our study has severe limitations inherent mainly to its observational design; the fact that it was conceived in a single center, and the small number of patients for analysis. It is necessary to generate studies with more robust and larger designs to confirm our hypothesis.

Conclusions

The programming of invasive mechanical ventilation in patients with severe acute respiratory distress syndrome should be governed by safe limits of static variables, but also of dynamic variables. The calculation of the amount of energy transferred and assimilated, by means of equations based on the exact sciences, allows optimization and individualization of mechanical ventilation, minimizing the associated injury. In materials engineering, fatigue is the fundamental time-dependent factor that explains the potentially irreversible damage. Our results suggest that respiratory rate is probably the most relevant dynamic variable in the genesis of VALI.

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