





OPEN

DOI: https://doi.org/10.5554/22562087.e1037

Mechanical power measurement during mechanical ventilation of SARS-CoV-2 critically ill patients. A cohort study

Medicion del poder mecánico durante ventilacion mecanica en pacientes críticamente enfermos con SARS-CoV-2. Estudio de cohorte

Alejandro Rivera Palacios ^a, Johana Andrea España ^a, José Fernando Gómez González^{a,b}, Guillermo Salazar Gutierrez^a, Diana Ávila Reyes^{a,b}, Paula Moreno^c, Angie Vanessa Lara Martinez^d, Mateo Aguirre-Flórez^e, Adrian Giraldo-Diaconeasa^e

^aCritical Medicine and Intensive Care, Universidad Tecnológica de Pereira. Pereira, Colombia.

^bCritical Medicine and Intensive Care Research Group GIMCCI. Universidad Tecnológica de Pereira, Colombia. Pereira, Colombia.

^c Fundación Universitaria Autónoma de las Américas. Pereira, Colombia.

^d Clínica Los Rosales. Pereira, Colombia.

^e School of Health Sciences, Medicine Program, Universidad Tecnológica de Pereira. Pereira, Colombia.

Correspondence: Facultad de Ciencias de la Salud, Universidad Tecnologica de Pereira. Carrera 27 No. 10-02. Pereira, Colombia. E-mail: diana.avila@utp.edu.co

What is already known on this subject?

- VILI originates from the interchange of energy, or mechanical power between the ventilator and the lung parenchyma, among other factors.

- Mechanical power is also associated with ICU mortality, 30-day mortality, and with days free of mechanical ventilation, even with a low tidal volume; high mechanical power (MP) was also associated with in-hospital mortality.

- A mechanical power greater than 17 Jules/min results in a constantly increasing risk as reported in the literature.

What does this study contribute?

- This study evaluates the clinical outcomes related to mechanical power in patients ventilated for different causes, including patients with SARS-CoV-2 infection in the context of the pandemic.

- Notwithstanding some knowledge gaps, there is evidence that mechanical power variables should be managed with caution to provide safe mechanical ventilation and deliver less energy or mechanical power transmission to the already injured lung parenchyma during each breath, thus avoiding the exponential increase in VILI.

How to cite this article:

Rivera Palacios A, España JA, Gómez González JF, Salazar Gutierrez G, Ávila Reyes D, Moreno P, et al. Mechanical power measurement during mechanical ventilation of sars-cov-2 critically ill patients. a cohort study. Colombian Journal of Anesthesiology. 2022;50:e1037.

Abstract

Introduction: The ventilator-induced lung injury (VILI) depends on the amount of energy per minute transferred by the ventilator to the lung measured in Joules, which is called mechanical power. Mechanical power is a development variable probably associated with outcomes in ventilated patients.

Objective: To describe the value of mechanical power in patients with SARS-CoV-2 infection and ventilated for other causes and its relationship between days of mechanical ventilation, length of stay in the intensive care unit (ICU), and mortality.

Methods: A multicenter, analytical, observational cohort study was conducted in patients with SARS-CoV-2 infection who required invasive mechanical ventilation and patients ventilated for other causes for more than 24 hours.

Results: The cohort included 91 patients on mechanical ventilation in three tertiary care centers in the city of Pereira, Colombia. The average value of the mechanical power found was 22.7 ± 1 Joules/ min. In the subgroup of patients with SARS-CoV-2 infection, the value of mechanical power was higher 26.8 ± 9 than in the subgroup of patients without a diagnosis of SARS-CoV-2 infection 18.2 ± 1 (p <0.001).

Conclusions: Mechanical power is an important variable to consider during the monitoring of mechanical ventilation. This study found an average value of mechanical power of 22.7 ± 1 Joules/min, being higher in patients with SARS-CoV-2 infection related to longer days of mechanical ventilation and a longer stay in the ICU.

Keywords: Respiratory distress syndrome; Artificial respiration; SARS-CoV-2 infection; Coronavirus; Critical care; Anesthesiology.

Copyright © 2022 Sociedad Colombiana de Anestesiología y Reanimación (S.C.A.R.E.). This is an open access article under the CC BY-NC-ND license (http://creativecommons.org/licenses/by-nc-nd/4.0/).

Resumen

Introducción: La lesión pulmonar inducida por la ventilación mecánica (LPIVM) depende, entre otras variables, de la cantidad de energía -medida en Joules- por unidad de tiempo transferida desde el ventilador al paciente, también llamada poder mecánico. El poder mecánico es una variable de desarrollo, posiblemente asociada a los desenlaces en pacientes sometidos a ventilación.

Objetivo: Describir el valor del poder mecánico en pacientes con infección por SARS-CoV-2 y ventilados por otras causas y la relación entre días de ventilación mecánica, estancia en la UCI y mortalidad.

Métodos: Estudio multicéntrico, analítico y observacional de cohorte realizado en pacientes con diagnóstico de infección por SARS-CoV-2 que requirieron soporte ventilatorio mecánico invasivo y pacientes ventilados por otras causas, durante más de 24 horas.

Resultados: La cohorte incluyó 91 pacientes que recibieron ventilación mecánica en 3 centros de tercer nivel de la ciudad de Pereira, Colombia. El valor promedio del poder mecánico obtenido fue 22,7 ± 1 Joules/min. En el grupo de pacientes con infección por SARS-CoV-2 el valor obtenido fue mayor (26,8 ± 9), comparado con el grupo de pacientes sin infección por SARS-CoV-2 (18,2 ± 1) (p <0,001).

Conclusiones: El poder mecánico es una variable importante a tener en cuenta en el monitoreo de la ventilación mecánica. El presente estudio encontró un valor promedio de poder mecánico de 22,7±1 Joules/min, siendo mayor en los pacientes con infección por SARS-CoV-2 en relación con más días de ventilación mecánica y estancia en UCI más prolongada.

Palabras clave: Síndrome de dificultad respiratoria; Respiración artificial; Infección por SARS-CoV-2; Coronavirus; Cuidado crítico; Anestesiología.

INTRODUCTION

Acute respiratory failure is one of the main reasons for admission to the intensive care unit (ICU), and mechanical ventilation is the approach to maintain respiratory function and until the patient's clinical condition resolves.(1) The principles of mechanical ventilation are to improve gas exchange, decrease the patient's respiratory work, and buy time while re-establishing respiratory and systemic physiology. The decision to ventilate a patient will depend on multiple factors(1) and has precise indications. Mechanical ventilation is prescribed to achieve therapeutic goals and it requires monitoring and control to limit any potential deleterious effects, which are included in the concept of ventilatorinduced lung injury (VILI).(2,3)

In addition to the mechanism responsible for the injury, the heterogeneity of the sick lung must be considered, which determines the presence of regional variations with collapsed or occupied alveolar units and distended alveolar regions, subjecting certain pulmonary areas to greater stress and cyclical collapse.

The determinants of VILI include delivered pressures, volume, and flow,

as well as the times these variables are administered per unit of time. (4) It has been argued that VILI depends on the amount of energy per minute delivered to the lung by the ventilator measured in Joules, which is called mechanical power. (2) (5) (6) The energy is used mainly to overcome airway resistance and to expand the chest wall; such energy may also lead to cell damage. (7-9)

Our objective was to describe the value of mechanical power in patients with SARS-CoV-2 infection and ventilated for other causes and its relationship with days of mechanical ventilation, ICU length of stay and mortality, in patients receiving mechanical ventilation in a volumecontrolled mode for more than 24 hours in three ICU in the city of Pereira, between July and August 2020. As a secondary objective, the demographic, clinical and ventilatory parameters used in the study subgroups are described.

METHODS

Multicenter, analytical cohort observational study. The protocol of this study was approved by the Ethics Committee of Universidad Tecnológica de Pereira under number 04-010620 dated June 4, 2020. This study includes patients admitted to the ICU of three institutions: Hospital Universitario San Jorge, Clínica Los Rosales, and Clínica Comfamiliar in Pereira - Colombia, between July 1 and August 31, 2020; the patients required invasive ventilatory support in a volume-controlled mode for more than 24 hours. Convenience sampling was used including all hospitalized patients in the study centers that met the inclusion criteria.

We included patients older than 18 years, with mechanical ventilation in a volume-controlled mode for more than 24 hours. Patients were excluded if they had a history of exposure to mechanical ventilation in the previous 30 days, pregnant women, patients with mechanical ventilation in modes other than volume controlled, and duplicate or incomplete medical records.

The data were collected by the study authors and collaborators between July and August 2020 using a written information collection form (Complementary material 1) and obtaining data from the electronic medical record. The mechanical ventilation monitoring sheet of each institution was reviewed to obtain the ventilatory parameters. For the calculation of mechanical power, two measurements were taken to produce the data and as input for the equation. Measurements were taken at the time of intubation and at the start of mechanical ventilation in the patients; the second measurement was recorded 24 hours after the first measurement. The measurements were taken by a respiratory therapist or a physiotherapist experienced in adult respiratory critical care, in accordance with the protocol described under Complementary material 2.

The following variables were recorded: demographics (age, sex, previous diseases), needforinotropicsupportandrenaltherapy, diagnoses, vital signs, ICU severity scores (APACHE II and SOFA) measured during ICU admission. Ventilatory parameters including tidal or tidal volume (Vt), Positive end-expiratory pressure (PEEP), maximum or peak pressure (Ppeak), respiratory rate (Rr), inspiration: expiration ratio (I: E), inspiratory time (It), and during a pause at the end of inspiration, and plateau airway pressure (Pplat), were also recorded.

Secondary variables were calculated as follows:

• Compliance (C) = Vt / (Pplat - PEEP) (5), the dynamic and static Compliance measurements were taken, though the latter only if the patient was under neuromuscular relaxation for medical indication. The dynamic compliance calculation was based on a <10% asynchronous index to ensure the reliability of the measurement.(5)

 \cdot Elastance (E) = 1 / C, as the inverse of compliance.

· Airway conduction pressure (Δ Paw)

 Δ Paw: Pplat - PEEP. => Vt / C => E x Vt.(5)

For the calculation of mechanical power (MP), the simplified formula proposed by Gattinoni at al.(5) was used. Mechanical power (Joule / min) = 0.098 x (respiratory rate) x (tidal volume) x [peak pressure - ($\Delta P/2$).(5)

The primary outcomes of the study were the number of days in the ICU, and the

number of days under invasive mechanical ventilation. Patients were followed-up until death or ICU discharge. Potential selection biases were controlled with strict compliance with the inclusion and exclusion criteria; information biases were controlled with the requirement to clearly and fully complete the data collection instrument and rejecting any duplicate or incomplete records. Additionally, a subgroup analysis was conducted when the requirement for mechanical ventilatory support was due to the presence of SARS-CoV-2. Observerrelated errors were controlled based on the homogeneity of the concepts used for the inclusion, exclusion, and definition of terms by the respiratory therapists and physiotherapists.

Statistical analysis

The data were analyzed using the R studio 1.2.5 software for Windows. Descriptive statistics were used to summarize the clinical characteristics of the study population according to the type of variable, for nominal variables, tables of frequency distribution, percentages, and ratios. For quantitative variables, in addition to the above, measures of central tendency (mean, median) and dispersion (variance, standard deviation, interquartile range) were used. The patients' characteristics with and without SARS-CoV-2 infection were compared using the Student's t-test for numerical variables and Pearson's chi-square for categorical variables at baseline. The correlation between ventilatory parameters and clinical outcomes (days of ICU stay and days of invasive mechanical ventilation) was reported using Spearman's Rho.

For primary outcomes, dependency relationships were established through the chi-square test to compare nominal or ordinal variables. The type of distribution was established to compare the quantitative variables; when the normal distribution assumptions were met, parametric tests were used (Student's t, anova); if these assumptions were not met, non-parametric tests were used (Mann-Whitney U, Kruskal Wallis). The number of days on mechanical ventilation were compared between the subgroups according to the value of the mechanical power discriminated in terciles, and survival analysis was performed using Cox regression. Death was considered the final outcome. Adjusted analyzes were controlled for sex, age, renal replacement therapy, inotropic support, neuromuscular relaxation, SARS-CoV-2 infection, and ventilatory parameters. Multivariate model 1 was adjusted for respiratory rate, tidal volume, and conduction pressure, while model 2 was adjusted for mechanical power. Hazard ratios were obtained and reported, and significance was determined based on a 95% confidence interval (95% CI).

RESULTS

The cohort included a total of 91 patients, who were admitted to 3 ICUs in the city of Pereira between June and October 2020. 72.5% (n = 66) of the patients were males and the average age was 59.6 \pm 14.9 years. The average APACHE II score was 14.5 \pm 7.9 and SOFA 8.6 \pm 3.4. SARS-CoV-2 infection was diagnosed in 51.6% (n = 47) patients and 62.6% (n = 57) died. Twelve percent (n = 11) of the patients required renal replacement therapy, 41.8% (n = 38) received inotropic and / or vasopressor support and 64.8% (n = 59) were under neuromuscular relaxation.

Table 1 shows the characteristics of the patients included, as well as the comparison between patients with SARS-CoV-2 infection and patients without the infection. Regarding the clinical outcomes, no differences were found between the groups of patients.

Ventilatory parameters

Table 2 shows the ventilatory parameters at the beginning and 24 hours after the initiation of invasive mechanical ventilation. There was a reduction in FiO2 between the first and second measurement (from 56 \pm 21 to 41 \pm 15, p <0.001) and in the I:E ratio (from 2.7 \pm 0.8 to 2.4 \pm 0.7, p = 0.016, which was similar according to the SARS-CoV-2 infection status. Respiratory rate (p <0.001), I: E ratio (p = 0.025), FiO2 (p = 0.003), PEEP (p <0.001), peak pressure (p = 0.001), plateau pressure (p <0.001), pressure conduction and mechanical power (p <0.001) were higher in patients with SARS-CoV-2 infection, while dynamic compliance (p = 0.003) and static compliance (p = 0.001) were higher in patients without SARS-CoV-2 infection.

Mechanical power

The average mechanical power value was 22.7 \pm 1 Joules/min. In the subgroup of patients with SARS-CoV-2 infection, the mechanical power was higher (26.8 \pm 9 Joules/min) than in the subgroup of patients without a diagnosis of SARS-CoV-2 infection (18.2 \pm 1 Joules/min) (p <0.001).

Table 1. Characteristics of patients with mechanical ventilation.

Iotal (n=91) $Iotal (n=91)$ $Iotal$						
Female 25 (27.5) 14 (31.8) 11 (23.4) Male 66 (72.5) 30 (68.2) 36 (76.6) Age 59.6±14.9 61.3±17.0 58.1±12.5 <45 years 15 (16.5) 9 (20.5) 6 (12.8) 45-64 38 (41.8) 24 (54.5) 14 (29.8) >65 years 38 (41.8) 11 (25) 27 (57.4) Previous respiratory disease 21 (23.1) 12 (27.3) 9 (19.1) Severe ARDS 34 (37.4) 13 (29.5) 21 (44.7)						
Male 66 (72.5) 30 (68.2) 36 (76.6) Age 59.6±14.9 61.3±17.0 58.1±12.5 <45 years						
Age 59.6±14.9 61.3±17.0 58.1±12.5 <45 years 15 (16.5) 9 (20.5) 6 (12.8) 45-64 38 (41.8) 24 (54.5) 14 (29.8) >65 years 38 (41.8) 11 (25) 27 (57.4) Previous respiratory disease 21 (23.1) 12 (27.3) 9 (19.1) Severe ARDS 34 (37.4) 13 (29.5) 21 (44.7)						
<45 years						
45-64 38 (41.8) 24 (54.5) 14 (29.8) >65 years 38 (41.8) 11 (25) 27 (57.4) Previous respiratory disease 21 (23.1) 12 (27.3) 9 (19.1) Severe ARDS 34 (37.4) 13 (29.5) 21 (44.7)						
>65 years 38 (41.8) 11 (25) 27 (57.4) Previous respiratory disease 21 (23.1) 12 (27.3) 9 (19.1) Severe ARDS 34 (37.4) 13 (29.5) 21 (44.7)						
Previous respiratory disease 21 (23.1) 12 (27.3) 9 (19.1) Severe ARDS 34 (37.4) 13 (29.5) 21 (44.7)						
Severe ARDS 34 (37.4) 13 (29.5) 21 (44.7)						
APACHE II 14.5±7.9 15.6±4.7 13.9±9.5						
SOFA 8.6±3.4 9.0±4.0 8.2±2.7						
Renal replacement therapy 11 (12.1) 6 (13.6) 5 (10.6)						
Inotropic / vasopressor support 38 (41.8) 23 (52.3) 15 (31.9)						
Neuromuscular relaxation 59 (64.8) 13 (29.5) 46 (97.9)						
Outcomes						
ICU days 12.3±6.2 11.5±7.1 13.2±5.1						
IMV support days 9.2±5.6 9.1±5.1 11.1±4.7						
Ventilation-free days 2.3±3.1 2.2±3.5 2.0±2.7						
Death 57 (62.6) 26 (59.1) 31 (66)						

Source: Authors.

Clinical outcomes

The clinical outcomes of the patients is shown in Table 1. On average, the patients spent 12.3 \pm 6.2 days in the ICU and 9.2 \pm 5.6 days with invasive mechanical ventilatory support. ICU mortality was 62.6% (n = 57 patients). The occurrence of outcomes was similar between the groups with and without SARS-CoV-2 infection.

Table 3 shows the survival analysis using Cox regression for the risk of death, controlled by sex, age, static compliance, renal replacement therapy, inotropic support, neuromuscular relaxation, SARS-CoV-2 infection, and ventilatory parameters. A protective association was found between neuromuscular relaxation and time to death in model 1 (HR = 0.175, 95%CI 0.043-0.712) but not in model 2.

Figure 1 shows the average days in an ICU and days of invasive mechanical ventilation (IMV) according to the terciles of ventilatory parameters. Figure 2 shows the survival of patients with invasive mechanical ventilation. Panel A shows survival according to the terciles of mechanical power with no group differences identified. Panel B shows survival according to the use of neuromuscular relaxation, observing a higher percentage of survival and fewer days of ICU stay in the group of patients with neuromuscular relaxation.

DISCUSSION

VILI is the result of the relationship between the energy delivered by the ventilator to the lung parenchyma and how the lung responds. On one hand, there are the causes of ventilator generated VILI, including pressures, volume, flow, and respiratory rate. On the other hand, there are the conditions favoring lung injury; i.e. the amount of pulmonary edema, lung volume reduction, lung heterogeneity, cyclical collapse and loss of compliance, in addition to extrapulmonary factors such as perfusion, pH, and temperature during mechanical ventilatory support. All of these factors interact.(10-11)

Ventilatory parameters	Total (n=91)			SARS-CoV-2 infection Negative (n=44)			SARS-CoV-2 infection Positive (n=47)			Valor p*
	То	T24	p value	То	T24	p value	То	T24	p value	
Breathing frequency	21 <u>+</u> 5	20 <u>+</u> 6	0.100	18 <u>+</u> 4	17 <u>+</u> 6	0.811	23±5	24 <u>+</u> 4	0.049	<0.001
I:E ratio	2.7 <u>+</u> 0.8	2.4 <u>+</u> 0.7	0.016	2.8 <u>+</u> 0.9	2.6 <u>+</u> 0.8	0.050	2.5 <u>+</u> 0.6	2.3 <u>+</u> 0.4	0.066	0.025
Tidal volume	434±50	431 <u>+</u> 50	0.857	433±54	427±54	0.312	435±46	435±45	0.299	0.82
Volume (mL/Kg)	6.95 <u>+</u> 0.84	6.91 <u>+</u> 0.87	0.954	7.04±0.97	6.95 <u>+</u> 1.01	0.362	6.87 <u>+</u> 0.68	6.87 <u>+</u> 0.73	0.329	0.328
FiO2	56 <u>+</u> 21	41±15	<0.001	50±19	38 <u>+</u> 13	<0.001	63 <u>+</u> 22	43±17	<0.001	0.003
PaFi	135 <u>+</u> 65			164±74			107 <u>+</u> 39			<0.001
PEEP (cm H2O)	9±2	9±2	0.146	8 <u>+</u> 2	9±3	0.845	10 <u>+</u> 2	10 <u>+</u> 1	0.225	<0.001
Peak pressure	31 <u>+</u> 8.7	30 <u>+</u> 8	0.091	27.8 <u>+</u> 9.6	28 <u>+</u> 10	0.282	34 <u>+</u> 6.6	32 <u>+</u> 6	0.900	0.001
Plateau pressure	21 <u>+</u> 6	20 <u>+</u> 4	0.034	18 <u>+</u> 5	19±4	0.226	23±5	22 <u>+</u> 4	0.510	<0.001
Driving pressure	11 <u>+</u> 5	11 <u>+</u> 3	0.075	10 <u>+</u> 4	10 <u>+</u> 3	0.221	13 <u>+</u> 5	12 <u>+</u> 3	0.849	0.002
Dynamic compliance	23.7 <u>+</u> 11.1	23.34 <u>+</u> 9.21	0.479	27.3 <u>+</u> 13.1	25.9 <u>+</u> 10.8	0.732	20.2 <u>+</u> 7.4	20.9 <u>+</u> 6.7	0.381	0.003
Static compliance	44.6 <u>+</u> 20.0	43.8 <u>+</u> 15.8	0.157	52.1 <u>+</u> 24.5	48.4 <u>+</u> 19.0	0.684	37.6 <u>+</u> 10.9	39.6 <u>+</u> 10.5	0.273	0.001
Power or mechanical power	22.7 <u>+</u> 11.0	22.4 <u>+</u> 11.3	0.767	18.2 <u>+</u> 11.2	17.2 <u>+</u> 11.0	0.741	26.8 <u>+</u> 9.2	27.2 <u>+</u> 9.4	0.351	<0.001

Table 2. Initial ventilatory parameters and 24 hours after IMV support in three hospitals in Pereira, Colombia.

* p-value for the difference between patients with and without SARS-CoV-2 infection. **Source:** Authors.

Figure 1. Average days in an ICU and days of IMV according to the terciles of ventilatory parameters in patients with invasive mechanical ventilation in 3 ICUs in Pereira, Colombia.

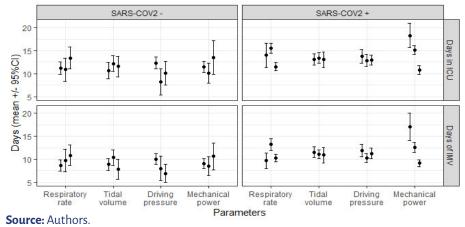
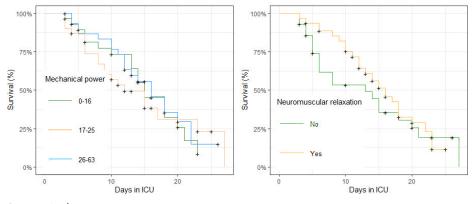


Figure 2. Survival of patients with invasive mechanical ventilation in 3 ICUs in Pereira, Colombia. Graph A shows survival according to the mechanical power terciles and B according to the use of neuromuscular relaxation at the time of intubation.



Most studies on VILI focus on the static components of ventilation. However, another important factor is the respiratory rate which determines the number of times potential barotrauma or volutrauma is induced per minute.(12, 13) The inspiratory flow is another variable related to the development of VILI and the assumption could be made that the flow velocity plays a more significant role in a mechanically heterogeneous lung.(14) The dynamic and static predictors are available, but traditionally lung-protective ventilation strategies have focused on measures and static characteristics of the tidal cycle such as tidal volume (Tv), plateau pressure (Pplat), PEEP, and recently driving pressure (ΔP) ; the importance of these measures is based on animal experiments and clinical data supporting their relevance.(14-25)

Gattinoni's group states that all the mechanical factors involved in ventilation, i.e. tidal volume, conduction pressure, flow, resistance, respiratory rate, and PEEP, are but different components of one single physical variable, which is the energy supply over time, that is, mechanical power.(5) The mechanical power equation is derived from the equation of respiratory movement in which the pressure in the respiratory



Table 3. Analysis using Cox regression for the risk of death in patients with ventilatory support with and without SARS-CoV-2 infection in three hospitals in Pereira, Colombia.

Markeller -	Raw model		Adju	sted Mo	del 1*	Adjusted Model 2*			
Variables	HR	(Cl95%	HR		Cl95%	HR		Cl95%
Renal replacement therapy	1.456	0.65	3.24	1.369	0.525	3.571	1.423	0.56	3.615
Inotropic/ vasopressor support	0.88	0.51	1.51	0.556	0.243	1.271	0.764	0.398	1.468
Neuromuscular relaxation	0.77	0.44	1.34	0.175	0.043	0.712	0.358	0.121	1.057
SARS-CoV-2 infection	1.03	0.6	1.75	1.116	0.418	2.976	1.496	0.613	3.651
Ventilatory parameters									
Breathing Frequency									
12 to 17	1			1					
18 to 21	0.906	0.462	1.775	3.033	0.791	11.629			
26 to 35	1.306	0.697	2.445	4.178	0.983	17.761			
Tidal volume									
330 to 399	1			1					
400 to 459	0.94	0.52	1.7	1.015	0.501	2.058			
460 to 562	0.603	0.28	1.301	0.381	0.132	1.100			
Driving pressure									
3 to 9	1			1					
10 to 11	1.453	0.742	2.845	2.219	0.782	6.301			
12 to 26	1.39	0.753	2.566	3.119	0.737	13.200			
Mechanical power									
4 to 16	1								
17 to 25	0.89	0.466	1.698				1.141	0.503	2.589
26 to 63	1.095	0.572	2.096				1.52	0.664	3.479

*Adjusted by sex, age, and static compliance. **Source:** Authors.

system has an elastic component necessary to distend the lung parenchyma, a resistive component necessary to advance the flow of air against the resistance of the airway and an inertial component due to changes in the lung parenchyma caused by volume acceleration.(3,4) With the addition of PEEP at any given time, the pressure in the entire respiratory system equals:

 $P = ELrs \cdot \Delta V + Raw \cdot F + PEEP$

(P: pressure in the respiratory system at any given time. ELrs: total elastance of

the respiratory system. ΔV : tidal volume. Raw: resistance of the respiratory tract. F: flow. PEEP: positive pressure at the end of expiration.)

Therefore, VILI is the result of energy interchange, or mechanical power between the ventilator and the lung parenchyma, among other factors. In our study, the main reason for using mechanical ventilation in patients without a diagnosis of SARS-CoV-2 infection was hypoxemic respiratory failure secondary to acute respiratory tract infection; pressure conduction and mechanical power were higher in patients with SARS-CoV-2 infection, while both dynamic and static compliance were higher in patients without SARS-CoV-2 infection.

The mechanical power values found are consistent with those reported by cohort studies in international databases; a higher mechanical power value was documented in patients with SARS-CoV-2 infection and in the tercile analysis no significant differences were observed between groups, and no significant differences were found in the survival analysis using Cox regression for the risk of death. However, there is no conclusive scientific evidence to date that indicates which is the limit value of mechanical power in the population with SARS-CoV-2 infection under invasive mechanical ventilation, and even in the population with ARDS due to other causes; the mechanical power values have been heterogeneous in the different studies published so far.

The results of this study should be interpreted in the light of some potential limitations: population differences in terms of the reasons for administering mechanical ventilation; and, in the context of the COVID-19 pandemic, heterogeneity of the pulmonary and ventilatory characteristics of the patients. Therefore, we conducted some subgroup analyses as described. One of the limitations of the study are the differences in recording the ventilatory mechanics by different personnel in a multicenter study, although the respiratory therapist was monitored for the correct implementation of the protocol. Concerning the position of the patients, the prone ventilation variable was not considered in the initial design, and due to physiological factors inherent to the position, these factors may alter the results of ventilatory mechanics.

In our study, both an improved survival rate and shorter ICU stay were observed in the group of patients in which neuromuscular relaxants were used; however, a specifically designed study would be required to verify this association. Further prospective studies should be conducted to assess the value of mechanical power both at admission and over a 24 to 48 hour follow-up, in addition to an assessment after 8 days of pursuing a mechanical ventilation strategy.

This study paves the way to future research in the field of mechanical power in patients with ARDS due to SARS-CoV-2 infection and raises the need for permanent monitoring of this group of patients undergoing mechanical ventilation.

In conclusion, continuous monitoring of mechanical ventilation favors a safe therapeutic approach. 26 High mechanical power is a variable that has been described as a predictor of unfavorable outcomes patients undergoing mechanical in ventilation, considering the physiological substrate of the equation of motion. However, the specific value of mechanical limit power to ensure protective ventilation in all groups of patients managed with mechanical ventilation is not yet clear. Our results open the door to future research in the field of mechanical power as a variable to be evaluated in routine monitoring of mechanical ventilation.

ETHICAL DISCLOSURES

Ethical approval

The protocol of this study was approved by the Ethics Committee of Universidad Tecnológica de Pereira under number 04-010620 dated June 4, 2020.

Protection of human and animal subjects

The authors declare that no experiments were performed on humans or animals for this study. The authors declare that the procedures followed were in accordance with the regulations of the relevant clinical research ethics commit-tee and with those of the Code of Ethics of the World Medical Association (Declaration of Helsinki).

Confidentiality of data

The authors declare that they have followed the protocols of their work center on the publication of patient data.

Right to privacy and informed consent

The authors declare that no patient data appear in this article. The authors have obtained the written informed consent of the patients or subjects mentioned in the article. The corresponding author is in possession of this document.

ACKNOWLEDGMENTS

Author Contributions

• **ARP and JAE:** Study concept and design, acquisition, analysis, and interpretation of data, drafting of the manuscript; critical revision of the manuscript for important intellectual content, original material and construction of images and tables. Administrative, technical, and material support; study supervision

• **GS**: Study concept and design; drafting of the manuscript, critical revision of the manuscript for important intellectual content, original material and construction of images and tables; study supervision.

• JFGC: Study concept and design, drafting of the manuscript, critical revision of the manuscript for important intellectual content, original material and construction of images and tables. Administrative, technical, and material study supervision.

• **DAR:** Critical revision of the manuscript for important intellectual content, study supervision. Interpretation of data, drafting of the manuscript. Administrative, technical, and material support.

• **PM:** Study concept and design, analysis, and interpretation of data, drafting of the manuscript, original material and construction of images and tables. Administrative, technical, and material support. Statistical analysis.

• **AVL:** Acquisition, analysis, and interpretation of data, construction of tables, administrative, technical, and material support. Drafting of the manuscript.

• **MAF and AGD:** Revision of the manuscript. English translation. Administrative, technical, and material support.

All authors approved the final manuscript as submitted and agree to be accountable for all aspects of the work.

Study assistance.

Respiratory therapy group of Clínica Los Rosales: Angie Vanessa Lara Martínez. Physiotherapist specialized in adult critical care.

Respiratory therapy group of Hospital Universitario San Jorge: Oscar Edwin Moncayo Arboleda. Respiratory therapist. Francia Milena Vásquez González. Respiratory therapist.

Respiratory therapy group of Clínica Comfamiliar: Ángela María Martínez Ávila. Respiratory therapist. Specialist in Critical Care Respiratory Therapy. Luz Angélica Osorio Gallo. Respiratory therapist.

Financing

Authors did not receive any financing.

Conflicts of interest

The authors have no conflicts of interest to disclose.

Appreciation

Dr. Carlos Alberto Marulanda, ICU Director at Hospital Universitario San Jorge; Dr. Carlos Mario Sánchez, ICU Director at Clínica Los Rosales; Dr. Juan Carlos Cobo, ICU Director at Clínica Comfamiliar Risaralda.

REFERENCES

- 1. Chiappero GR, & Villarejo, F. Ventilación mecánica: libro del Comité de Neumonología Crítica de la SATI2010. ISBN 9500609010
- 2. Vasques F, Duscio E, Cipulli F, et al. Determinants and Prevention of Ventilator-Induced Lung Injury. Crit Care Clin. 2018;34(3):343-56. doi: https://doi.org/10.1016/j.ccc.2018.03.004.
- 3. Marini JJ, Jaber S. Dynamic predictors of VILI risk: beyond the driving pressure. Intensive Care Med. 2016;42(10):1597-600. doi: <u>https://</u> doi.org/10.1007/s00134-016-4534-x.
- Gattinoni L, Marini JJ, Collino F, et al. The future of mechanical ventilation: lessons from the present and the past. Crit Care. 2017;21(1):183. https://doi.org/10.1186/s13054-017-1750-x
- 5. Gattinoni L, Tonetti T, Cressoni M, et al. Ventilator-related causes of lung injury: the mechanical power. Intensive Care Med. 2016;42(10):1567-75. doi: <u>https://doi.</u> org/10.1007/s00134-016-4505-2.
- 6. Katira BH. Ventilator-Induced Lung Injury: Classic and Novel Concepts. Respir Care. 2019;64(6):629-37. doi: <u>https://doi.</u> <u>org/10.4187/respcare.07055</u>.
- Cressoni M, Gotti M, Chiurazzi C, et al. Mechanical Power and Development of Ventilator-induced Lung Injury. Anesthesiology. 2016;124(5):1100-8. doi: <u>https://doi. org/10.1097/ALN.000000000001056</u>.
- Serpa Neto A DR, Johnson AE, Bos LD. Mechanical power of ventilation is associated with mortality in critically ill patients: an analysis of patients in two observational cohorts. Intensive Care Med. 2018;44(11):1914-22. doi: https://doi.org/10.1007/s00134-018-5375-6.
- Rosas Sánchez K, Gutiérrez Zárate, D, Cerón Díaz UW. Asociación y valor predictivo del poder mecánico con los días libres de ventilación mecánica. Medicina Crítica. 2017;31(6):320-5.

- Parrillo JE. General Principles of Mechanical Ventilation. 2019. In: Critical Care Medicine: Principles of Diagnosis and Management in the Adult. 129-43. ISBN: 9780323611602
- 11. Aoyama H, Yamada Y, Fan E. The future of driving pressure: a primary goal for mechanical ventilation? J Intensive Care. 2018;6:64. doi: https://doi.org/10.1186/s40560-018-0334-4
- Beitler JR, Malhotra A, Thompson BT. Ventilator-induced Lung Injury. Clin Chest Med. 2016;37(4):633-46. doi: <u>https://doi.org/10.1016/j.ccm.2016.07.004</u>.
- 13.Silva PL, Rocco PRM. The basics of respiratory mechanics: ventilator-derived parameters. Ann Transl Med. 2018;6(19):376. doi: <u>https://</u> doi.org/10.21037/atm.2018.06.06.
- 14. Garcia-Prieto E, Amado-Rodriguez L, Albaiceta GM, et al. Monitorization of respiratory mechanics in the ventilated patient. Med Intensiva. 2014;38(1):49-55. doi: <u>https://doi.or-</u> g/10.1016/j.medin.2013.09.003.
- Brower RG, Lanken PN, MacIntyre N, et al. Higher versus lower positive end-expiratory pressures in patients with the acute respiratory distress syndrome. N Engl J Med. 2004;351(4):327-36. doi: <u>https://doi.</u> org/10.1056/NEJM0a032193.
- 16. Ferrer L. Ortiz G, Celis E. Tratado de ventilación mecánica. Un enfoque interdisciplinario.
 In: Distribuna, editor. Distribuna. ed. 2017.
 ISBN 9789588813585
- Brower RG MM, Morris A, Schoenfeld D, et al. Ventilation with lower tidal volumes as compared with traditional tidal volumes for acute lung injury and the acute respiratory distress syndrome. N Engl J Med. 2000;342(18):1301-8. doi: <u>https://doi.</u> org/10.1056/NEJM200005043421801.
- Amato MB, Meade MO, Slutsky AS, et al. Driving pressure and survival in the acute respiratory distress syndrome. N Engl J

Med. 2015;372(8):747-55. doi: <u>https://doi.</u> org/10.1056/NEJMsa1410639.

- 19. Chiumello D, Carlesso E, Brioni M, et al. Airway driving pressure and lung stress in ARDS patients. Crit Care. 2016;20:276. doi: https://doi.org/10.1186/s13054-016-1446-7.
- 20. Laffey JG, Bellani G, Pham T, et al. Potentially modifiable factors contributing to outcome from acute respiratory distress syndrome: the LUNG SAFE study. Intensive Care Med. 2016;42(12):1865-76. doi: <u>https://doi.</u> org/10.1007/s00134-016-4571-5.
- Slutsky AS, Ranieri VM. Ventilator-induced lung injury. N Engl J Med. 2013;369(22):2126-36. doi: https://doi.org/10.1056/NEJMra1208707
- 22. Yoshida T UA, Matsuura N, Mashimo T, et al. Spontaneous breathing during lung-protective ventilation in an experimental acute lung injury model: high transpulmonary pressure associated with strong spontaneous breathing effort may worsen lung injury. Crit Care Med. 2012;40(5):1578-85. doi: <u>https://doi. org/10.1097/CCM.obo13e3182451c40</u>.
- 23. Gattinoni LA, Carlesso E, Caironi P. Stress and strain within the lung. Current Opinion in Critical Care 2012;18(1):42-7. doi: <u>https://doi.</u> org/10.1097/MCC.ob013e32834f17d9.
- Rahaman U. Mathematics of Ventilator-induced Lung Injury. Indian J Crit Care Med. 2017;21(8):521-4. doi: <u>https://doi.org/10.4103/</u> ijccm.IJCCM_411_16.
- Chiumello D, Carlesso E, Cadringher P, et al. Lung stress and strain during mechanical ventilation for acute respiratory distress syndrome. Am J Respir Crit Care Med. 2008;178(4):346-55. doi: <u>https://doi.</u> org/10.1164/rccm.200710-1589OC.
- 26. Avila D, García B, Salazar G, et al. Mechanical ventilation in SARS-CoV-2 patients: state of art. narrative review. Colombian Journal of Anesthesiology. 2021. doi: <u>https://doi.</u> <u>org/10.5554/22562087.e971</u>

COMPLEMENTARY MATERIAL

Complementary material 1. Information collection instrument.

Universidad Tecnológica de Pereira

Correlation between mechanical power and days free of mechanical ventilation in three intensive care units in the city of pereira between july and august 2020

SOCIODEMOGRAPHIC DATA							
Date (D-M-Y)							
ID patient	Sex	M F					
Age (years)	Weight (kg)	Height (cm)					
HOSPITALIZATION DATA							
Hospitalization date (D-M-Y)							
Date of ICU admission (D-M-Y)							
Diagnosis for ICU admission							
CLINICAL VARIABLES	SOFA score	APACHEII					
Tidal volume	Respiratory Rate	рН					
PaCO2 mm Hg	pO2 mm Hg	PEEP					
PaFi: PaO2/ FiO2	Plateau pressure (cm H2O)						
Dilation pressure cmH20	Mechanical power J/min						
Mark	Yes	No					
Renal replacement therapy							
Vasopressor support							
Inotropic support							
Severe ARDS							
Septic shock							
OUTCOMES							
Days free from mechanical ve	ICU length of stay						
Diagnosis of pulmonary pathology Yes No							
Diagnosis of ARDS during hospitalization in ICU Yes No							
Type of acute respiratory failure I II III IV							
Respiratory failure severity classification by PaO2 / FiO2							
Mild Moderate Severe							

Complementary material 2. Ventilatory mechanics protocol.

Procedure for calculating mechanical power.

• The simplified formula suggested by Dr. Gattinoni's group will be used for the calculation of mechanical power: mechanical power (J / min) = 0.098 x(Pplateau-PEEP) x Vc x PEEP.

• The variables used to calculate the mechanical power are obtained from the mechanical ventilation monitoring sheet and the set mechanical ventilator parameters.

Ventilatory mechanics

A routine procedure in patients undergoing invasive mechanical ventilation, ideally under neuromuscular relaxation, to obtain data on the status of the respiratory system, to assist in providing safe management through the parameters programmed in the ventilator. The data obtained through monitoring of this procedure are inspiratory pressure, plateau pressure, mean pressure, dynamic compliance (expired volume divided over inspiratory pressure minus positive pressure at the end of expiration), static (expired volume divided plateau pressure minus positive pressure at the end of expiration), conduction pressure (plateau pressure minus positive pressure at the end of expiration), airway resistance (difference between peak pressure minus positive pressure at the end of expiration divided by the flow in one second).

Procedure: In patients undergoing invasive mechanical ventilation under sedation and - according to the criteria of the treating physician - with neuromuscular relaxation, respiratory mechanics will be performed, according to the above-described procedure, 24 hours after the start of ventilatory support; a second measurement shall be taken 24 hours of the first measurement. These measurements will be taken in ventilatory volume control mode; respiratory rates are programmed, tidal volume is adjusted to the ideal weight of the patient (height in cm minus 152.9, multiplied by 0.91, +45 for women and +50 for men), inspired fraction of oxygen, inspiratory time for an inspiration-expiration ratio 1: 2.0 and positive pressure at the end of expiration, which are programmed by the intensivist in charge of the patient according to the individual patient. In order to proceed with the procedure, the autoflow mode must be disabled, since it regulates the airway pressures, giving different results to the actual patient conditions. Immediately after, starting with a positive pressure at the end of expiration of 20 cmH2O for 10 respiratory cycles, an inspiratory pause of 0.3 seconds will be made observing the pressure-time graph at zero flow, monitoring the aforementioned data. Then the positive pressure at the end of expiration is decreased, reducing 2 cmH2O which is maintained for 10 breaths and followed by the next inspiratory pause; again the aforementioned data are recorded, and the cycle is successively repeated until reaching 7 cmH2O of positive pressure at the end of expiration, and then continues to increase until the optimal PEEP is reached including all PEEP values. The objective of this maneuver is to identify the positive pressure at the end of expiration value, where the best compliance is found, the lowest airway pressures that include the conduction pressure and the plateau pressure, generating the least hemodynamic compromise and decreasing the risk of loss of recruitment. These data allow us to identify the components involved in the mechanical power formula, to meet the objective of this study. It should be noted that in the case of sedation without neuromuscular relaxation, the asynchronous index (number of asynchronous events, over total respiratory rate, multiplied by 100) shall be calculated and it must be less than 10%, to ensure adequate interpretation of the data. The respective measurements shall be recorded by a respiratory therapist; the data required to calculate the formula are available through the ventilatory mechanics performed on patients in each unit and the ventilatory parameters are configured.

The records of the following variables were obtained: tidal volume (Tv), PEEP level, peak pressure (Ppeak), respiratory rate (Rr), inspiration: expiration ratio (I: E), inspiratory time (It), and during an Inspiratory pause, airway plateau pressure (Pplat) will be recorded.

The following secondary variables are calculated in the following way:

· Distensibility (C) = Tv / (Pplat-PEEP),

dynamic and static Compliance measurement will be performed, the latter will only be performed if the patient is under neuromuscular relaxation pursuant to medical indication. If the dynamic compliance calculation made, the asynchronous index should be <10% to ensure the reliability of the measurements.

 \cdot Elastance (E) = 1 / C

· Airway conduction pressure (Δ Paw) = Pplat-PEEP = Tv / C = E Tv

The mechanical power (MP) shall be calculated based on the simplified formula by Gattinoni at al.(5):

Mechanical power (Joule / min) = 0.098 x (respiratory rate) x (tidal volume) x peak pressure - ($\Delta P / 2$).