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ORIGINAL

Mechanical power and mortality: analysis of a prospective cohort of ventilated patients

Poder mecánico y mortalidad: análisis de una cohorte prospectiva de pacientes ventilados

Yudiel Pérez Yero[1], Ariel Sosa Remón[2], Jhossmar Cristians Auza-Santivañez[3], Arian Jesús Cuba Naranjo[4], Dasha María García Arias[1], Ana Esperanza Jeréz Alvarez[5], Mileydys Saborit García[1], Osman Arteaga Iriarte[6], Jose Bernardo Antezana-Muñoz[7]

[1]Universidad de Ciencias Médicas de Granma. Hospital Provincial Clínico-Quirúrgico ¨Celia Sánchez Manduley¨. Cuba.
[2]Universidad de Ciencias Médicas de La Habana. Instituto de Oncología y Radiobiología. La Habana, Cuba.
[3]Ministerio de Salud y Deportes. Instituto Académico Científico Quispe-Cornejo. La Paz, Bolivia.
[4]Universidad de Ciencias Médicas de Granma. Hospital Militar ¨Carlos Arvelo¨. Unidad de Cuidados Intensivos. Venezuela.
[5]Universidad de Ciencias Médicas de La Habana. Instituto Nacional de Oncología y Radiobiología. La Habana, Cuba.
[6]Hospital Universitario Japonés. Unidad de Cuidados Intensivos. Santa Cruz, Bolivia.
[7]Hospital Elizabeth Seton. Caja Petrolera de Salud. Cochabamba, Bolivia.

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Corresponding author: Jhossmar Cristians Auza-Santivañez

ABSTRACT

Introduction: mechanical power establishes the amount of energy per unit time transferred from the ventilator to the respiratory system. Its usefulness as a predictor of death has been demonstrated in COVID-19 or acute respiratory distress syndrome. However, its prognostic value in ventilated patients without these conditions is unknown.
Objective: to determine the association of mechanical power with the incidence of mortality in patients with invasive artificial ventilation in the Intensive Care Unit.
Method: a prospective cohort study in 52 patients ventilated invasively in an Intensive Care Unit of a Cuban hospital. The final variable of interest was mortality. Sociodemographic and ventilatory variables were studied. The level of significance was found according to p value ≤ 0,05 through hypothesis testing of differences in means and proportions and the the area under the ROC curve.
Results: mortality predominated in female patients, with a mean age of 51,76 ± 21,76 years. The main causes of ventilation were respiratory. High APACHE II score, SOFA and a mean mechanical power value of 14,82 ± 1,67 J/min were associated with mortality. On analysis of the area under the ROC curve, mechanical power yielded adequate discriminative ability for mortality (AROC: 0,993; 95 % CI: 0,979 - 1; p = 0,000).
Conclusions: in this series of ventilated patients the mechanical power value proved to be a factor associated with mortality.

Keyword: Mechanical Power; Mortality; Artificial Mechanical Ventilation; APACHE II; SOFA; Driving Pressure; Pneumonia.

RESUMEN

Introducción: el poder mecánico establece la cantidad de energía por unidad de tiempo transferida desde

el ventilador al sistema respiratorio. Su utilidad como predictor de muerte ha sido demostrada en la COVID-19 o el síndrome de dificultad respiratoria aguda. Sin embargo, se desconoce su valor pronostico en ventilados sin estas condiciones.
Objetivo: determinar la asociación del poder mecánico con la incidencia de mortalidad en pacientes con ventilación mecánica artificial invasiva en la Unidad de Cuidados Intensivos.
Método: estudio prospectivo de cohorte en 52 pacientes ventilados invasivamente en Terapia Intensiva de un hospital cubano. La variable de interés final fue la mortalidad. Se estudiaron variables sociodemográficas y ventilatorias. El nivel de significación se halló según p valor ≤ 0,05 a través de las pruebas de hipótesis de diferencias de medias y proporciones y el área bajo la curva operador-receptor
Resultados: la mortalidad predominó en pacientes femeninas, la edad promedio de 51,76 ± 21,76 años. Las principales causas de ventilación fueron las respiratorias. Se asociaron a la mortalidad la puntuación elevada del APACHE II, SOFA y un valor promedio del poder mecánico en 14,82 ± 1,67 J/min. Al análisis del área bajo la curva operador-receptor, el poder mecánico arrojó adecuada capacidad discriminativa para la mortalidad (AROC: 0,993; IC 95 %: 0,979 – 1; p = 0,000).
Conclusiones: en esta serie de pacientes ventilados el valor del poder mecánico resultó ser un factor asociado a la mortalidad.

Palabras clave: Poder Mecánico; Mortalidad; Ventilación Mecánica Artificial; APACHE II; SOFA; Presión de Distensión Alveolar; Neumonía.

INTRODUCTION

Artificial mechanical ventilation (AMV) is an essential component of critical care that can also damage the lungs, an event known as ventilator-induced lung injury (VILI). Therefore, the main objective of AMV is to maintain adequate gas exchange and reduce the work of breathing while minimizing VILI. To achieve this goal, lung-protective strategies have been widely adopted, in which tidal volume (Vt) and plateau pressure (P_2) are limited. However, it has also been shown that other variables, such as respiratory rate (RR) and driving pressure (DP), are associated with the development of VILI and, thus, multiple organ failure and mortality.[1,2]

It is, therefore, practical to benefit from a variable that combines all the possible factors associated with VILI and mortality, which could be quickly evaluated at the patient's bedside. In this sense, an attractive concept is the use of mechanical power (MP) to configure an artificial ventilator, as it combines the effects mentioned above and describes the energy delivered to the respiratory system and the lung over time (amount of energy per unit of time [J/min] transferred from the ventilator to the respiratory system and lung tissue, and can be calculated as the product of VT, RR and the difference between peak pressure [P_1] and 0,5 × DP). Changing just one parameter does not always protect the lungs if it does not change the amount of energy delivered to the lung tissue.[2,3]

Both DP and MP have been evaluated as excellent predictors of VILI and mortality in different studies of patients with acute respiratory distress syndrome (ARDS) and COVID-19. However, it has been scarcely investigated in populations of ventilated patients without the conditions above, and it is not known for sure if there is a similar association. Furthermore, its validity as an outcome predictor shows inconsistencies with current evidence due to different cut-off points and factors that can modify its interpretation. So far, it is unknown whether any published meta-analyses demonstrate a cut-off point as a predictor of mortality in the different clinical scenarios where it can be used.[2,4,5,6] In Cuba, studies on the subject are scarce and show diverse results regarding the predictive capacity of MP.[7,8] Based on the above; this research aims to determine the association of MP with the incidence of mortality in patients with invasive VMA in the ICU.

METHOD

Design and population. An observational, prospective, and analytical cohort study in the Provincial Clinical Surgical Hospital "Celia Sánchez Manduley" ICU in Granma, Cuba. Universe of 52 patients admitted between January and December 2023 who required invasive MV > 24 hours and met the inclusion criteria: 1) over 18 years of age, 2) need for invasive MV for more than 48 hours, 3) diagnosis other than COVID-19 pneumonia or ARDS and 4) measurement and mathematical calculation of the variables studied was feasible. The following were excluded from the present investigation: 1) patients under 18 years of age, 2) those who received AMV for less than 48 hours, 3) pregnant patients, and 4) those who were ventilated in the first 48 hours in a modality other than volume-controlled ventilation (VCV). A total of 52 patients were recruited for the study, of whom 35 were alive and 17 deceased.

Clinical and ventilatory data. Variables used: age (years completed to date), sex (patient's gender), reason for respiratory AMV (severe pneumonia, aspiration of gastric contents, COPD-severe asthma), cardiovascular (acute myocardial infarction, acute pulmonary edema, cardiogenic shock), sepsis or septic shock, neurological (cerebrovascular accident, neuromuscular disease, severe encephalopathy, coma) and others such as pulmonary embolism, acute pancreatitis, acute intoxication. Isogravity scores[9] at the start of the AMV (APACHE II and SOFA) and ventilatory variables[10] at the beginning of the AMV, Tidal volume (Vt): Volume of the mixture of air blown into the lungs in each respiratory cycle / Peak inspiratory pressure (P_1): Maximum pressure reached in the airway during inspiration / Plateau or plateau pressure (P_2): pressure reached at the end of inspiration / Mean airway pressure (mean P): average pressure generated throughout the respiratory cycle / PEEP: Pressure reached in the airway at the end of the expiratory phase, which is preset by the operator / Driving pressure (DP): Difference between P_2 and PEEP as a surrogate variable for intra-alveolar distension / Compliance: lung distensibility in the period without gas flows and the MP.

The following equations were calculated in the first 48 hours of VMA:[4]

$$DP = \frac{P_2}{PEEP}$$

PM:

$$PDA = 0{,}098 \times (P_2 - PEEP) \times Vt \times FR$$

A simplification equivalent to Gattinoni's original equation for VCV. In which 0,098 is a constant.[4,11]

Compliance:

$$= \frac{Vt}{P_2 - PEEP}$$

All patients underwent invasive MVA in VCV under a lung-protective ventilation protocol.[10]

An instrument for recording the data. A database was created using SPSS 22.0 software.

The analysis results were consulted in different bibliographic databases such as Pubmed/Medline, Google Scholar, and Scielo to cross-check the information obtained. Summary measures of descriptive statistics were applied to characterize the study population. For qualitative variables, absolute and relative frequencies (percentages) were obtained; for quantitative variables, means and standard deviations. To establish significant statistical differences between the two subgroups, the hypothesis test of differences of proportions was used for qualitative variables and the hypothesis test of differences of means for quantitative variables, using a significance level of 0,05. A classification and regression tree (CART) was constructed based on the predictor variables with the statistical program SPSS 22.0. CART analysis is a form of binary partitioning that uses nodes, which can be divided into two branches that obtain a form of classification that is simpler to interpret; it is non-parametric, so it does not have to meet the assumptions regarding the distribution of the variables with prognostic capacity, it can handle both biased or multimodal numerical variables, as well as categorical variables, with ordinal or non-ordinal structure.[12]

The discriminatory capacity of the statistically significant variables was evaluated using the Area Under the Receiver Operating Characteristic Curve (AUC). The fixed variable was determined as intra-ICU mortality. Ethical aspects. Authorization was requested from the hospital management, the Research Ethics Committee, and the Institutional Scientific Council to carry out all the research steps. The anonymity of the patients in the study was maintained at all times, and only the authors handled the information referring to the patients. The consent of the relatives to participate in the study was obtained due to the patient's incapacity due to ventilatory compromise.

RESULTS

Table 1 shows the general characteristics of the study population. Among the deceased, the average age was 51,76 ±21,76 years, females predominated and patients ventilated for respiratory causes (35,7 %), and the Isogravity scores were higher (APACHE II: 16 ±6 points and 7 ±3 SOFA points). For the ventilation variables, there were similar values between both subgroups. At the same time, the MP value was higher in the deceased (14,82 ±1,67 J/min vs. 10,89 ±1,02 J/min). The statistical analysis established statistically significant differences between the two groups and mortality for variables such as APACHE II, SOFA, and MP ($p<0{,}05$ in all three variables [hypothesis test of differences of means]). This behavior is shown in figure 1.

The CART model shows the pattern of the variables that lead to a higher predisposition to die while using HAART. The PM value determined that scores between 12 and 13 established a mortality rate of 66,7 %, while mortality was 100 % for higher scores (p = 0,000) (figure 2).

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Table 1. General characteristics and ventilatory parameters of the study population

Variables	Variables	Alive (n=35)		Deceased (n=17)	
		M±DS	Límit	M±DS	Límit
Category		58,54±17,04	18 - 85	51,76±21,76	20 - 84
		18 (66,7 %)		9 (33,3 %)	
Age	Age	17 (68,0 %)		8 (32,0 %)	
		8 (22,8 %)		6 (35,9 %)	
Gender (*)	Gender (*)	2 (5,7 %)		1 (5,8 %)	
Male	Male	9 (25,7 %)		5 (29,4 %)	
	Neurological	10 (28,5 %)		3 (17,6 %)	
	Other	5 (14,2 %)		2 (11,7 %)	
Score by	APACHE II *	10±3	6 - 16	16±6	8 - 25
Isogravity	SOFA *	4±1	1 - 7	7±3	2 - 13
	VT	395±43	320 - 480	398±43	340 - 480
	P1	28±3	23 - 35	29±3	26 - 35
	Mean P	8±2	15 - 25	20±3	15 - 25
	PEEP	8±2	5 - 14	9±3	5 - 14
	P2	23±3	17 – 28	24±3	17 - 30
	Driving pressure	14±2	12 – 20	15±2	12 - 21
	Compliance	57±18	34 – 98	47±17	31 - 89
	Mechanical power*	10,89±1,02	10 - 13	14,82±1,67	13 - 18

M: mean. SD: standard deviation. (*) Numbers and percent (calculated based on n). *Hypothesis test of differences of means p<0,05. CVC: cardiovascular. APACHE II: acute physiology and chronic health evaluation II. SOFA: sepsis related organ failure assessment. VT: tidal volume. P_1: peak inspiratory pressure. PEEP: positive end-expiratory pressure. P_2: plateau pressure.

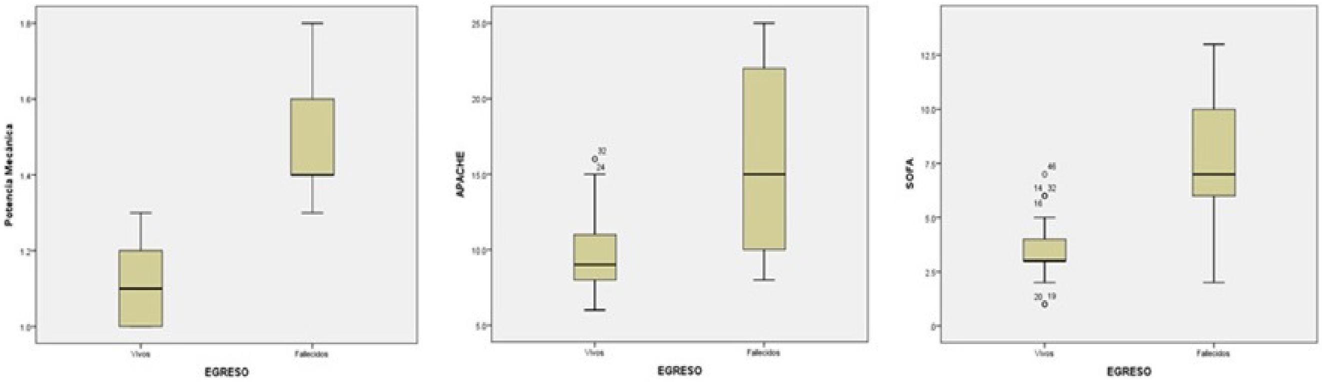

Figure 1. Quantitative variables with statistically significant differences. Hypothesis test of means

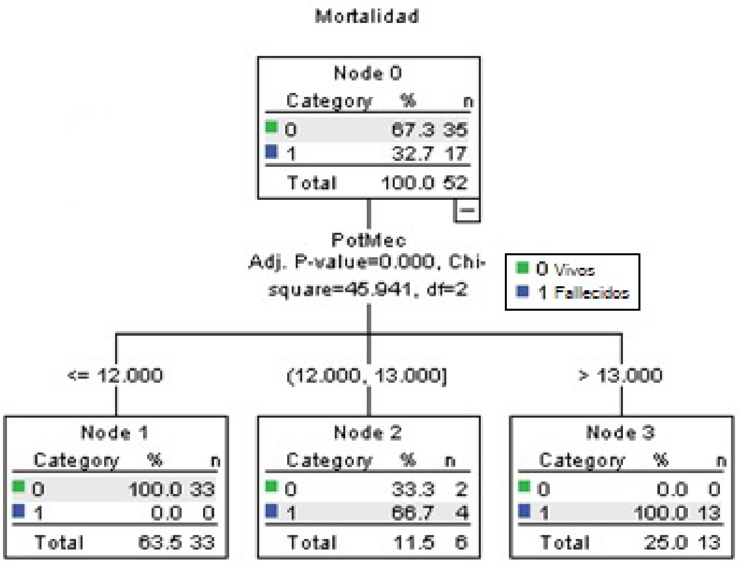

Figure 2. Quantitative variables with statistically significant differences. Hypothesis test of means

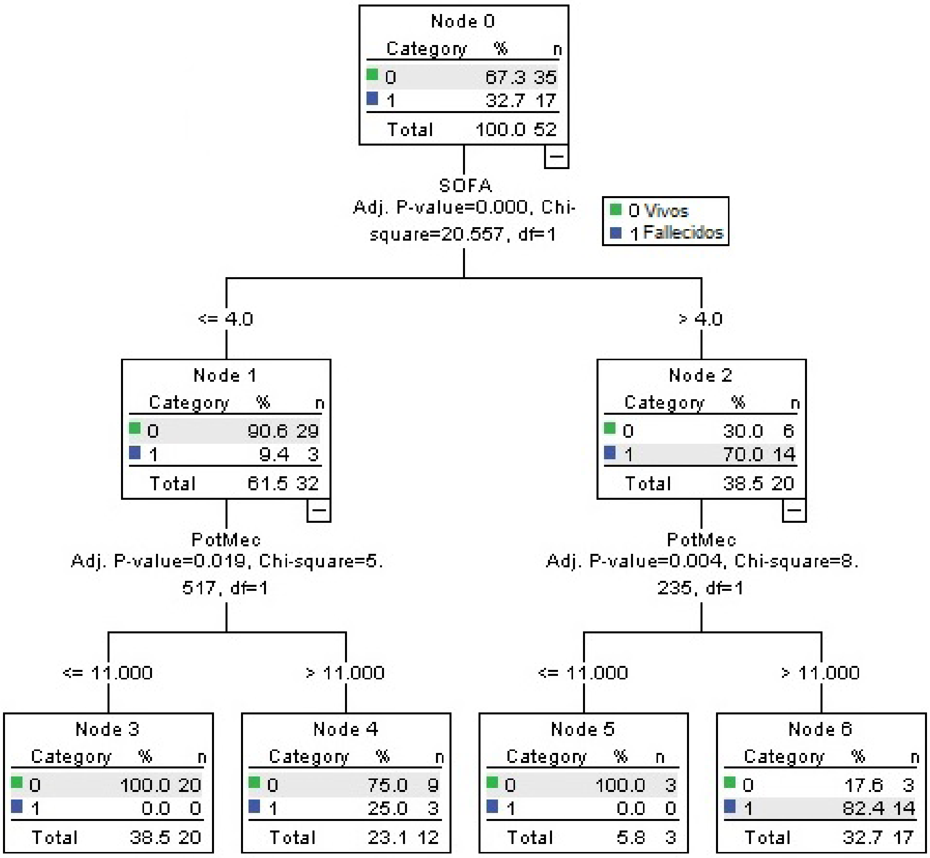

Figure 3. Regression tree and classification of SOFA, Mechanical Power and mortality

On analyzing the area under the ROC curve (figure 4), the MP (ROC: 0,993; 95 % CI: 0,979-1; p = 0,000) showed an adequate discriminatory capacity superior to the APACHE II (ROC: 0,806; 95 % CI: 0,666-0,937; p = 0,000) and SOFA respectively (ROC: 0,878; 95 % CI: 0,764 - 0,993; p = 0,000).

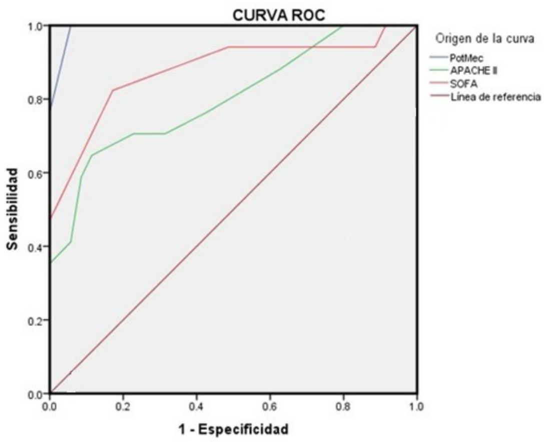

Figure 4. ROC curve of the variables associated with mortality

DISCUSSION

A safe MP threshold for critically ill patients with or without ARDS has yet to be defined. However, the available evidence points to a cut-off point ≥ 12 J/min as an excellent discriminator for the onset of VILI or mortality.[2] However, the only meta-analysis published and referenced by the authors of this research is that carried out by Huerta et al.[5] which included six cohort studies and a secondary analysis of randomized controlled trials (n = 3775), a low MP value (mean of 17 J/min) was associated with increased survival (OR: 0,45; 95 % CI: 0,34-0,59; I2: 56 %). All the research reviewed and included in the meta-analysis was in patients with ARDS, so the results differed from those reported in the present research, among other variables, and may be related to the type of patient invasively ventilated. About the general characteristics of the study population, age, and sex were similar to those presented by Rodríguez-de-Molina et al.[13] who studied a population of ventilated patients for multiple causes, and the average age was 55 ±17,4 (p < 0,0001). In a Cuban cohort of patients ventilated for various reasons, Hernández-Jiménez et al.[14] the subgroup of deceased patients was older (62,9 ±17,1 years).

Regarding the reason for ventilation, Rodríguez-de-Molina et al.[13] found that it was mainly performed on patients with sepsis, associating it with death (p<0,001), as did Sim et al.[1] These data are consistent with the results of the present study.

The authors consider it relevant to highlight the effect of PE when studying different ventilatory variables. It has been proposed that in patients without ARDS, PE represents a risk factor for mortality and ARDS. Wu et al.[15] in 207 patients with severe pneumonia without ARDS, correlated PE > 19 cmH_2O with mortality at day 28 (p = 0,002; sensitivity: 62,5 %, specificity: 60,9 %; OR: 1,110; 95 % CI: 1,013–1,217; p = 0,026). Van-Meenen et al.[3] obtained similar results in 839 ventilated patients with multiple causes (616 without ARDS). A cut-off for PD > 19 cmH2O resulted in a 90-day mortality prognosis (OR: 1,05 95 % CI: 1,03–1,08; P < 0,001). However, Schmidt et al.[16] found no statistical association with mortality in a multicenter retrospective analysis of 622 ventilated adults without ARDS. These results suggest the need for further research in this clinical context. A higher risk of death is indicated with a PD > 14 cmH_2O, although a well-tolerated threshold has not yet been identified. The prone position and simple ventilatory adjustments to facilitate CO_2 elimination can help reduce PE.[4] Different authors have studied the other ventilatory variables presented in this research; the results are diverse, and it has not been possible to establish each of them separately as a predictor of fatal outcomes in a reliable way.[1,13,17,18]

The need to evaluate medical care in seriously ill patients and predict their evolution led to the emergence of prognostic evolution models. APACHE II and SOFA have been the most universally used in this context.[9] Wu et al.[19] found APACHE II scores higher than those of this study in patients ventilated for pneumonia (mean: 25,3 ±6,8) although lower than those with ARDS (27,6 ±8,7; p<0,05). As did Sahitya et al.[20] in a ventilated group without ARDS (APACHE II average: 20,2 points; OR: 1,08; 95 % CI: 1,04–1,11; p<0,001). On the other hand, Hernández-Jiménez et al.[14] showed APACHE II values similar to the present investigation (16.6±4.5), with statistical correlation to mortality. 33,6 % of the patients presented an APACHE II between 15-19 points 24 hours after admission, of whom 75 % died. In addition, it was observed that the ratio of survivors to deceased decreased as the score on the scale increased (p<0,01).

A similar situation was shown with the SOFA score; rodríguez-de-Molina et al.[14] described a mean of 9,1 ±4,5 points correlated with mortality (p<0,001). The APACHE II and SOFA scores have shown their predictive utility in the outcome of ventilated patients in different clinical scenarios, although with different cut-off points. The main strength of these scores' usefulness (including others developed from them, such as APACHE III and IV or SAPS) lies in the positive correlation with mortality as the scores increase.[1,7,19,20,21] The CART analysis in the present study showed a more significant association with mortality of the MP when combined with a SOFA score greater than 4 points. This allowed the influence of these factors on mortality to be modeled, correctly classifying it in 82,4 % of cases.

The concept of MP aimed to quantify the contribution of RF and PEEP to the total power supplied by the ventilator. These variables are aggregated into a single physical measure, the value of which could be related to the risk of VAP. However, due to the complexity of the calculation and specific limitations in the equations estimated for the modes of AMV, the calculation is currently rarely provided directly by the ventilators, and the estimation at the bedside must be done manually based on the values provided by the ventilator, supported by precisely measured parameters. The complexity of lung disease and ventilator settings do not allow PM to be used as the sole parameter. The best approach lies in individualizing AMV, considering PM as a summary parameter.[22,23] The definition of appropriate upper and lower safety thresholds is debated. A "normal" PM provides acceptable PO_2 and PCO_2. Experimentally, an upper threshold of 12 J/min and a lower threshold of 4-7 J/min are estimated. However, these are only average values, and, in theory, the distribution of MP within the respiratory cycle can play an equally important role. MP is concentrated at the beginning of inspiration during pressure support ventilation, while in VCV, the distribution of MP is more evenly distributed throughout the inspiratory time. In addition, the dissipation of MP during expiration can be more uniform if the expiratory flow is constant.[2,22]

In this context and relation to the results found in the present study, the MP value was effectively correlated with mortality (AUC: 0,993; 95 % CI: 0,979–1; p = 0,000) for a cut-off point >12 J/min. Furthermore, using CART, mortality increased to 100% when the value exceeded 13 J/min and was also correlated with a SOFA score > 4 and an MP >11 J/min (p = 0,004; X2: 8,235). These data, in ventilated populations without ARDS, are similar to other research. Jiang et al.[24] in a sample of 529 ventilated neurocritical patients, of which 326 were not diagnosed with ARDS (253 patients alive and 73 deceased; p=0,045). The average cut-off point for estimating mortality was 13,4 J/min (95 % CI: 10,1–17,6; p<0,001), with adequate discrimination in the AROC (0,678; 95 % CI: 0,637–0,718). When the MP value was associated with the Glasgow coma scale score, the AROC discrimination was better (0,687; 95 % CI: 0,646–0,726). These results are particularly encouraging for the care of neurocritical patients because of the controversy surrounding establishing an adequate ventilatory strategy.

This is because VMA can induce harmful neurological effects due to the complex physiological interactions between the intrathoracic and intracranial venous compartments.[25]

The analysis by Van-Meenen et al.[6] of three multicenter randomized trials involving 1 962 ventilated patients without ARDS concluded that MP showed an independent association with mortality in ICU patients at 28 and 90 days, respectively. This finding suggests that MP has an additional predictive value over its components, which makes it an attractive measurement to monitor and use as a target in these patients. In Latin America, Rodríguez-de-Molina et al.[13] studied 63 ventilated patients, mainly for sepsis, neurocritical illness, and pneumonia. An MP value > 13 J/min was associated with an adequate discriminatory capacity for mortality according to the AROC (0,41; 95 % CI: 0,25-0,57).

Finally, Wu et al.[15] in a population of 235 ventilated patients with pneumonia without ARDS, found values much higher than in this study (25,8 ±12,2 J/min; p < 0,05; AROC: 0,735; 95 % CI; 0,655-0,814; p < 0,001). In the future, when using MP in clinical practice, one must be aware of the limitations of the particular equation used and consider its implications for treatment. MP could be used to evaluate the overall effect of AMV and help establish ventilator parameters to reduce the risk of VILI.[23]

Strengths and Limitations. The authors of this communication believe that the main strength of the above study is the weighting of the value of PM in a group of patients without ARDS not previously published in the country.

It is also considered that, as the study was carried out in a single center, the control of the clinical-ventilatory variables was strict, contributing to the reduction of biases in the study. However, the authors consider that the small study population and single-center design limit the results as they cannot be generalized.

CONCLUSIONS

In this series of invasively ventilated patients, an MP value > 12 J/min was found to be a factor associated with mortality during the stay in the ICU. These results coincide with several published studies. The predictive capacity increased when the MP was associated with the SOFA score. The area under the ROC curve showed an adequate discriminatory capacity for mortality. Finally, further research should be carried out to optimize the results found.

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CONTRIBUTION OF AUTHORSHIP
Conceptualization: Yudiel Pérez Yero.
Formal analysis: Arian Jesús Cuba Naranjo, Ariel Sosa Remón.
Research: Jhossmar Cristians Auza-Santivañez.
Methodology: Yudiel Pérez Yero, Ariel Sosa Remón, Jhossmar Cristians Auza-Santivañez.
Project administration: Yudiel Pérez Yero, Ariel Sosa Remón.
Supervision: Ana Esperanza Jeréz Alvarez.
Visualization: Dasha María García Arias.
Writing – original draft: Yudiel Pérez Yero, Ariel Sosa Remón, Jhossmar Cristians Auza-Santivañez, Arian Jesús Cuba Naranjo, Dasha María García Arias, Ana Esperanza Jeréz Alvarez, Mileydys Saborit García, Osman Arteaga Iriarte, Jose Bernardo Antezana-Muñoz.
Writing - review and editing: Yudiel Pérez Yero, Ariel Sosa Remón, Jhossmar Cristians Auza-Santivañez, Arian Jesús Cuba Naranjo, Dasha María García Arias, Ana Esperanza Jeréz Alvarez, Mileydys Saborit García, Osman Arteaga Iriarte, Jose Bernardo Antezana-Muñoz.