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# 4DPRR- Index for predicting mortality in COVID-19 ARDS

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**Abstract**

**Background**

Mortality in ARDS was reduced significantly after the introduction of the low tidal volume ventilation strategy. It has been recently shown that lung-protective ventilation strategies should primarily target driving pressure rather than Vt and that ventilator induced lung injury is not just dependent on tidal volume but also other factors like respiratory rate and driving pressure. Ventilator induced lung injury is also thought to be dependent on the amount of energy transferred by the ventilator to the patient which in turn is dependent on tidal volume size ($V_T$), plateau pressure (Pplat), respiratory rate (RR). Mechanical power can be calculated accurately through power equations which can increase their applicability in clinical practice. One simple composite equation (driving pressure multiplied by four plus respiratory rate [4DPRR]) has been recently suggested as a simple surrogate for the power equation. This equation also doesn't include PEEP as it has been theorized that it is the only elastic dynamic component of driving energy which affects the outcome and not the elastic static component (i.e., PEEP) and the resistive power (related to flow and airway resistance).

**Objectives**

To assess the mechanical power as measured by 4DPRR in mechanically ventilated patients who have moderate to severe COVID-19 ARDS. Methods: We obtained data on ventilatory variables and mechanical power from the patients who were admitted with moderate to severe COVID ARDS in our hospital from March 2021 to June 2021.

**Results**

We included 34 patients (28% women; mean age, 57 ± 17 yrs.). The average ΔP was 21.44 ± 3.98 $cmH_2O$, the RR was 23.8 ± 3.84 breaths/min, and the mean driving pressure was 21.4 $cmH_2O$. 28% (n = 10) of patients expired. There was no significant association of 4DPRR (P 0.72), Pplat (P 0.79).and RR (P 0.21) with mortality as predicted by area under ROC curves.

**Conclusions**

Driving power and plateau pressure were associated with mortality during controlled mechanical ventilation in COVID ARDS, but a simpler model of mechanical power using only the driving pressure and respiratory rate was found to be a poor predictor of mortality.

**Keywords:** COVID-19, ARDS, Mechanical power, Driving pressure, Plateau pressure

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## Introduction

Ventilation in ARDS is a double-edged sword. Although the low tidal volume lung protective ventilation strategy has significantly reduced mortality in ARDS patients, mechanical ventilation (MV) itself has been recognized as a cause of pulmonary parenchymal injury and it was only in 1993 that the term ventilator-induced lung injury (VILI) was coined. [1]

The understanding of mechanisms for VILI has evolved from the initial pressure mediated injury (barotrauma) to volutrauma, atelectotrauma to biotrauma and ergotrauma. The effects range from micro-fractures to alveolar ruptures, from cytokine production to intra-alveolar haemorrhage.

It has been recently shown that the mortality benefit of ventilation with lower tidal volume (Vt) in ARDS varies according to elastance, suggesting that lung-protective ventilation strategies should primarily target driving pressure rather than $V_t$. [2]Previous studies have also shown that driving pressure correlates with mortality, however this observed association does not necessarily mean that driving pressure is the causal determinant of benefit from lower tidal volume ventilation.[3,4] This is particularly because there are potential residual confounding effects and mathematical coupling of various factors like elastance, tidal volume and energy dissipation by the mechanical ventilator. Hence, it has also been recently postulated that ventilator-induced lung injury is not just dependent on tidal volume but other factors like respiratory rate (RR), driving pressure (DP) and inspiratory flow also plays a significant role.

Moreover, ventilator-induced lung injury is thought to be dependent on the amount of energy transferred by the ventilator to the patient. The energy transferred to the lungs from the ventilator can be either stored in the form of elastic energy or is dissipated to overcome the friction of air during airflow through the endotracheal tube and airways. This energy in turn is dependent on tidal volume, plateau pressure (Pplat), and respiratory rate (RR) and is also associated with increased mortality.[5,6]

Mechanical power has been recently proposed as a unifying metric for estimating the risk of VILI. It can be calculated accurately through power equations (Table 1), which can increase its applicability in clinical practice. [7,8] This study aimed to calculate mechanical power using a simplified equation and find its association with mortality in COVID -19ARDS patients.

**Highlights**

A simple model for calculation of mechanical power, using only Driving pressure and respiratory rate, was not found shown to be useful in predicting mortality in COVID-19 ARDS patients. This is one of the first study from an Asian country to study the association of mechanical power calculated using 4DPRR with mortality

## Objectives

To evaluate the association of 60-day mortality with total mechanical power using the empirical formula →4DPRR

## Methods

This was a single center, retrospective, observational study conducted in a tertiary care teaching institute, after approval of the institutional ethical committee for a period of 3 months from March 2021 to June 2021. Consent was waived off being retrospective and observational study.

Data was collected from records of adult patients admitted to COVID intensive care unit, over a period of three months. ARDS was defined according to the Berlin criteria for ARDS. All adult patients with moderate-to-severe ARDS with a duration of 36 hours or less from meeting the Berlin criterion[9] were included in the study.

The patients on mechanical ventilation (MV) for more than 96 h or less than 24 hours, history of lung or liver transplantation, evidence of active air leak from the lung (including bronchopleural fistula, pneumothorax, pneumo-mediastinum or air leak from existing chest tube), on rescue therapies for COVID-19 before enrolment (ECMO, prone positioning) were excluded from the study.

Ventilatory variables extracted from records included plateau pressure (Pplat), driving pressure above PEEP (DP), respiratory rate (RR) and outcome mortality at hospital discharge. All the patients were ventilated as per Surviving Sepsis Campaign Covid 19 guidelines.[10]

**4DPRR = 4 X Driving pressure + Respiratory Rate**

Mechanical power was calculated using the 4DPRR formula. Values of variables at admission & 24 hours after initiating MV were used for calculation. Data were described in terms of range; mean ± standard deviation (± SD), frequencies (number of cases) and relative frequencies (percentages) as appropriate. Receiver operator characteristics (ROC) curve was done, and the criterion value was estimated depending on the specificity and sensitivity.

The area under curve (AUC) was measured. A probability value (P value) less than 0.05 was considered statistically significant. All statistical calculations were done using (Statistical Package for the Social Science) SPSS 21version (SPSS Inc., Chicago, IL, USA) statistical program for Microsoft Windows.

| | | | **MECHANICAL POWER (J/MIN)** | | | | | |
|---|---|---|---|---|---|---|---|---|
| | | | **POWER OF INSPIRATION (cmH$_2$0.L/min)** | | | | | **Conversion factor** |
| | | | **WORK OF INSPIRATION (cmH$_2$0.L)** | | | | **RR (BPM)** | |
| | | | **VOLUME X** | **PRESSURE (cm H$_2$0)** | | | | |
| | | | | **Elastic + static component** | **Elastic + dynamic component** | **Resistive component** | | |
| **VCV** | Simplified equation | Gattinoni et al | ΔV | Peak pressure- (plateau pressure- PEEP) / 20 | | | RR | 0.098 |
| | Surrogate | Giosa et al | ΔV | (Peak pressure + PEEP+F/6) /20 | | | RR | 0.1 |
| **PCV** | Surrogate | Becher et al | ΔV | PEEP | Pinsp. $(1 - e^{-Tinsp/T})$ | | RR | 0.098 |
| | Simplified equation | Becher et al | ΔV | PEEP | Pinsp | | RR | 0.098 |

Table 1: Formulae for calculation of Mechanical Power

## Results

We had a total of 50 ventilated patients with ARDS in COVID unit during the study period. Among them, 34 patients satisfied the inclusion criteria. The mean age of patients in our cohort was 57 ± 17 years and there were 28% females (n=10). The Mean Pplat was 21.44 ± 3.98 cmH$_2$O, the mean RR was 23.8 ± 3.84 breaths/min and the mean driving pressure was 21.4 cmH$_2$O. In our study 10 patients expired, accounting for a mortality rate of 28%.

All patients had driving pressure greater than 15 and the distribution of patients according to DP is shown in Figure 1a.11 patients had driving pressure in the range of 16-19 and 20 -23 cmH$_2$O, respectively whereas 10 and 2 patients had driving pressure in the range of 24 to27 and 28 to 31 cmH$_2$O, respectively.

The distribution of patients according to plateau pressure (Pplat) is shown in Figure 1b.2 patients had Pplat in the range of 22-26 cmH$_2$O, 14 patients in the range of 26-30 cmH$_2$O, 3 patients in the range of 30-34cmH$_2$O and

12 in the range of 34-38 cmH$_2$O and 3 had had plateau pressure in the range of 38-42 cmH$_2$O.

4DPRR was calculated using the above equation and ranged between 80 and 150. The distribution of patients according to mechanical power is shown in Figure 1c. 3 patients each had a 4DPRR score of 80 - 90 and 90-100. 12 patients had a score of 100-110, and 6 patients had a score of 110-120. 7 patients had a score of 120-130, and 1 patient had a score of 130 to 140. and 2 patients had a score of 140-150 each.

There was no significant association of 4DPRR (P 0.72), Pplat (P 0.79), and RR (P 0.212)with mortality as predicted by area under ROC curves.(Figure 2)

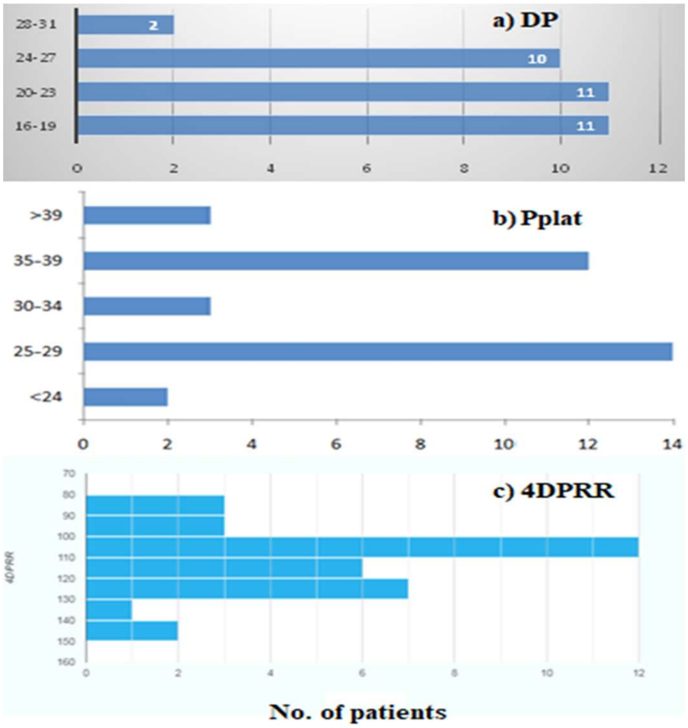


Figure 1: showing distribution of patients of COVID-19 ARDS according to a) driving pressure; b) Plateau pressure (Pplat); c) Mechanical power calculated by 4DPRR

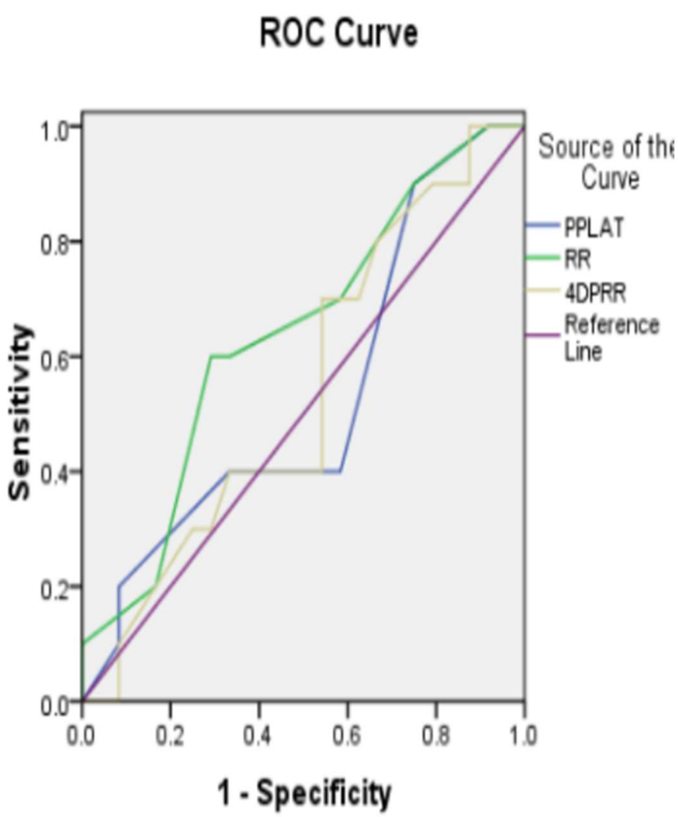


Figure 2: ROC curves

## Discussion

This observational trial was conducted to study the relation of mechanical power as predicted by a simple formula 4DPRR with mortality in COVID associated ARDS patients. Mechanical power is a more physiological way to summarize the physical contributions of the ventilator settings expressed in meaningful and understandable physical units (J/min). However, minimizing mechanical power at the bedside is challenging because the components of mechanical power move in the opposite direction i.e. lowering of power by reducing VT and Pplat may be accompanied by compensatory increases in RR, nullifying its effect.

Many proposals have been made to simplify its computation so that it is possible to estimate the mechanical power by just looking at the ventilator settings, without any intervention so that it can be of clinically relevant utility.[7,8]One simple composite equation (product of driving pressure by four-plus respiratory rate [4DPRR] has been recently suggested as a simple surrogate for the power equation (Figure1).[11] It is interesting to note that this equation does not include PEEP, as it has been theorized that only an elastic dynamic component of driving energy affects the outcome and not the elastic static component (i.e. PEEP) and the resistive power (related to flow and airway resistance). PEEP expands the lungs once and this expansion is sustained throughout the ventilatory support unless PEEP has been changed.

Costa et al assessed the impact of mechanical power on mortality in 4,549 patients with ARDS as compared to standard respiratory variables (ΔP, VT, and RR). They concluded that significant predictors of mortality in adjusted analyses were driving pressure, RR, and mechanical power and the impact of DP on mortality was four times as large as that of the RR. Hence, computing the bedside formula for mechanical power calculation as 4DPRR.

Although, mechanical power was associated with mortality during controlled mechanical ventilation in COVID ARDS, but our results show that this simpler model using the ΔP and RR was not associated with mortality. The reason may be related to different phenotypes of COVID ARDS which have varying degrees of pulmonary microvascular and macrovascular involvement, and all may not have benefited from the conventional ventilation strategies adopted for ARDS.[12] Also, only moderate to severe ARDS patients who were passively ventilated were selected for this study and PEEP may have played an important role in COVID ARDS in High elastance phenotype (H type) although changes in PEEP did not affect the mechanical power when using the 4DPRR equation. No equation or algorithm can hence supplant the role of an informed clinical judgment guiding bedside mechanical ventilation titration.

Pplat also showed poor association with mortality in our study. Though 4DPRR has been used for estimating the risk of VILI and mortality in ARDS patients, our results suggest that the same may not be true for COVID-ARDS.

Our study has some limitations. The mechanical power could not be compared with the conventional formulas as the patients were predominantly on PC-CMV with adaptive targeting (PC-CMVa). As a result, elastic-static power related to PEEP (J/min), elastic dynamic power related to $\Delta P$ (J/min) and resistive power related to resistance in the ventilator circuit, endotracheal tube and airways could not be computed. Costa and colleagues in their study[11] found that elastic dynamic power showed a significant association with mortality.Secondly, we included a small number of patients and had retrospective data collection.

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