Mechanical power in AVM-2 versus conventional ventilation modes in various ARDS lung models. Bench study

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DOI: https://doi.org/10.53097/JMV.10056

Cite: Yeo J, Shah P, Koichi K, Franck CL, Daoud EG. Mechanical power in AVM-2 versus conventional ventilation modes in in various ARDS lung models: A bench study. J Mech Vent 2022; 3(3):110-122.

Abstract

Introduction

Mechanical power has been linked to ventilator induced lung injury and mortality in acute respiratory distress syndrome (ARDS). Adaptive Ventilator Mode-2 (AVM-2) is a closed-loop pressure-controlled mode with an optimal targeting scheme based on the inspiratory power equation that adjusts the respiratory rate and tidal volume to achieve a target minute ventilation. Conceptually, this mode should reduce the mechanical power delivered to the patients and thus reduce the incidence of ventilator induced lung injury.

Methods

A bench study using a lung simulator was conducted. We constructed three passive single compartment ARDS models (Mild, Moderate, Severe) with compliance of 40, 30, 20 ml/cmH_2O respectively, and resistance of 10 cmH_2O/L/s, with IBW 70 kg. We compared three different ventilator modes: AVM-2, Pressure Regulated Volume Control (PRVC), and Volume Controlled Ventilation (VCV) in six different scenarios: 3 levels of minute ventilation 7, 10.5, and 14 Lit/min (Experiment 1, 2, and 3 respectively), each with 3 different PEEP levels 10, 15, and 20 cmH_2O (Experiment A, B, and C respectively) termed 1A, 1B, 1C, 2A, 2B, 2C, 3A, 3B, 3C respectively for a total of 81 experiments.

The AVM-2 mode automatically selects the optimal tidal volume and respiratory rate per the dialed percent minute ventilation with an I:E ratio of 1:1. In the PRVC and VCV (constant flow) we selected target tidal volume 6ml/kg/IBW (420 ml) and respiratory rate adjusted to match the minute ventilation for the AVM-2 mode. I:E ratio was kept 1:2.

The mechanical power delivered by the ventilator for each mode was computed and compared between the three modes in each experiment. Statistical analysis was done using Kruskal-Wallis test to analyze the difference between the three modes, post HOC Tukey test was used to analyze the difference between each mode where $P < 0.05$ was considered statistically significant. The Power Compliance Index was calculated and compared in each experiment. Multiple regression analysis was performed in each mode to test the correlation of the variables of mechanical power to the total calculated power.

Results

There were statistically significant differences ($P < 0.001$) between all the three modes regarding the ventilator delivered mechanical power. AVM-2 mode delivered significantly less mechanical power than VCV which in turn was less than PRVC. The Power Compliance index was also significantly lower ($P < 0.01$) in the AVM-2 mode compared to the other conventional modes. Multiple regression analysis indicated that in AVM-2 mode, the driving pressure ($P = 0.004$), tidal volume ($P < 0.001$), respiratory rate (P 0.011) and PEEP ($P < 0.001$) were significant predictors in the model. In the VCV mode, the respiratory rate ($P < 0.001$) and PEEP ($P < 0.001$) were significant predictors, but the driving pressure was a non-significant predictor (P 0.08). In PRVC mode, the respiratory rate ($P < 0.001$), PEEP ($P < 0.001$) and driving pressure ($P < 0.001$) were significant predictors.

Conclusion

AVM-2 mode delivered less mechanical power compared to two conventional modes using low tidal volume in an ARDS lung model with different severities. This might translate to the reduction of the incidence of ventilator induced lung injury. Results need to be validated in clinical studies.

Keywords: Mechanical power, Power Compliance Index, AVM-2

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Conflict of interest/Disclosures: Bellavista ventilator donated by Vyaire. Data collection, analysis, manuscript preparation done independently by the authors. Lung simulator donated by Michigan Instruments
Funding: None

Introduction

Acute respiratory distress syndrome (ARDS) is defined according to the "Berlin Definition of ARDS" as the acute onset of hypoxia and bilateral pulmonary opacities not fully explained by a cardiac cause. [1] It occurs when a variety of etiologies trigger acute bilateral pulmonary inflammation and increased pulmonary capillary permeability leading to acute hypoxic respiratory failure. Although ARDS is common with significant morbidity and mortality, there are limited therapeutic options and supportive care with mechanical ventilation remains the key to patient management. [2,3] However, mechanical ventilation itself can cause ventilator-induced lung injury (VILI). [4,5]

Volutrauma and barotrauma are well known principal mechanisms of VILI. The landmark ARDS Network trial demonstrated that limiting tidal volume (6 vs.12 mL/kg predicted body weight) and plateau airway pressure (≤ 30 vs. ≤ 50 cmH_2O) improved survival in patients with ARDS. [6] Other trials also support lung protective effects of lowering the tidal volume (V_T) in patients with ARDS. [7] In addition, it is hypothesized that the driving pressures (DP) may play an important role in the development of VILI and is correlated to mortality. [8] The DP is considered to express the lung stress (transpulmonary pressure) while the V_T expresses the lung strain (inflated volume to functional residual capacity ratio).

Atelectrauma is another important form of VILI and describes the repeated opening and closure of alveoli during the respiratory cycle. [9] The term ergotrauma has been coined to describe the energy and power applied to the lung and to their potential contribution to VILI. [10,11]

Mechanical power (J/min) is the product of the work applied to the respiratory system as a result of the interaction of the patient work if present, along the various ventilator parameters (V_T, DP, inspiratory flow, and positive end-expiratory pressure [PEEP]) multiplied by the respiratory frequency per min. [12] Conceptually, this can be thought of as the energy or work transferred to the lungs and the number of times that work is applied per minute.

In clinical practice, much emphasis has been placed on reducing the V_T and DP, and often the respiratory rate has to be increased to compensate for the lower minute ventilation but this may lead to lung injury when the total mechanical power delivered to the lung exceeds some threshold. [13] Several studies have shown an association between the mechanical power to VILI and mortality, [14,15] while others failed to show such association. [16]

The mechanical energy and power supplied by the ventilator can be calculated through different means including the analysis of the pressure-volume curve (the integral of the volume X pressure) and through different complex and simplified equations derived from the equation of motion. [12, 17]

The area of pressure-volume curve and the mechanical power can be subdivided into: Elastic, Resistive and Kinetic (PEEP is static elastic) energy components. [17, 18] The product of the tidal volume per plateau pressure defines the total elastic power, [18] which is subdivided into dynamic and static elastic powers. The dynamic one is equal to the energy necessary to inflate the lungs, whereas the static one is the energy required to balance out the potential energy stored in the respiratory system by the PEEP. [19] The total inflation energy, that is, the mechanical power is equal to the total elastic power plus the total kinetic power, which is the energy spent on overcoming the airway and tissue resistance to the flow. [18,19] The product of these equations by the respiratory rate and by the conversion constant 0.098 results in Joules per minute.

However, it is still unclear which of those components either alone or in combination can cause the highest risk. There are no clinical studies that have evaluated the effects of those components in clinical practice.
Given the association between mechanical power and mortality, adaptive ventilation modes were designed to ensure optimization of the patient's work of breathing while providing protective lung ventilation strategies. Adaptive ventilation modes like Adaptive Support Ventilation (ASV) and Adaptive Ventilation Mode-2 (AVM-2) are closed loop ventilator modes that automatically adjust based on an optimum

targeting scheme which targets the lowest "cost" to the patient according to different algorithms. [20]

AVM-2 is a pressure-controlled ventilator mode developed in 2017 that uses the mean inspiratory power delivered by the ventilator as the basis for its optimum targeting scheme to reduce mechanical power. The algorithm adjusts the tidal volume, respiratory rate and I:E ratio according to the actual dead space (if measured) or expected (2.2 ml/kg) according to the desired minute ventilation set by the clinician to minimize the tidal volume and driving pressure while avoiding auto-PEEP. [20]

In a previous study, our group demonstrated that AVM-2 mode provided less mechanical power compared with conventional ventilation modes in a normal lung model using a lung simulator. [21] Another study compared AVM-2 to AVM (the older version of the mode that adjusts its output according to the Otis equation) in ARDS patients. [22] However, so far, there is no bench or clinical studies comparing AVM-2 to other conventional ventilation modes in the diseased lung.

We hypothesized that when compared to other commonly used conventional mechanical ventilation modes like the volume-controlled and pressure-controlled modes (pressure-controlled ventilation or pressure regulated volume control modes), ventilator settings selected by AVM-2 would be more lung-protective in terms of mechanical power delivered by the ventilator in a diseased lung.

Methods

A bench study using a lung simulator (TTL, Michigan Instruments, Michigan, USA) was conducted. We constructed three passive single compartment ARDS models (Mild, Moderate, Severe) according to the set compliance of: 40, 30, 20 ml/cmH_2O respectively, and resistance of 10 cmH_2O/L/s, with IBW 70 kg. We compared three different ventilator modes: AVM-2, Volume Controlled Ventilation (VCV), and Pressure Regulated Volume Control (PRVC), in six different scenarios: 3 levels of minute ventilation: 7, 10.5, and 14 L/min corresponding to 100%, 150%, 200% minute ventilation percent settings in AVM-2 (Experiment 1, 2, and 3 respectively), each with 3 different PEEP levels 10, 15, and 20 cmH_2O (Experiment A, B, and C respectively) termed Experiments 1A, 1B, 1C, 2A, 2B, 2C, 3A, 3B, 3C respectively total of 81 experiments.

The AVM-2 mode automatically selects the optimal tidal volume and respiratory rate per the dialed percent minute ventilation with an I:E ratio of 1:1. In PRVC and VCV we selected a target tidal volume [6ml/kg/IBW (420 ml)] and respiratory rate adjusted to match the minute ventilation for the AVM-2 mode. I:E ratio was kept 1:2 to avoid intrinsic PEEP. The study was conducted using a Bellavista™ 1000 e Ventilator (Vyaire Medical, Illinois, USA).

The mechanical power delivered by the ventilator for each mode was computed from software on the ventilator that calculates the mechanical power on breath-to-breath intervals and compared between the three modes in each experiment. Fifty breaths over five minutes were randomly selected for analysis in each experiment.

Statistical analysis was done using Kruskal-Wallis test to analyze the difference between the three modes, post HOC Tukey test was used to analyze the difference between each mode with the confidence intervals, $P < 0.05$ was considered statistically significant. The Power Compliance Index (Mechanical power divided by the Compliance) was calculated and compared in each experiment. Multiple regression analysis was performed in each mode to test the correlation of the variables of mechanical power to the total calculated power. Correlation between variables was done using the Pearson correlation coefficient R^2

Results

The results of the study are summarized in Tables 1-4 and Figures 1 and 2. Data are presented as mean values ± SD.

The mechanical power and "Power Compliance Index "(PCI) were significantly different ($P < 0.001$) between the three modes in all of the experiments with AVM-2 being the lowest and PRVC being the highest.
Additionally, we tested the correlation between the mechanical power and the compliance (PCI) in all the experiments and there was an excellent negative correlation between the mechanical power and the compliance in all the modes in all experiments (R^2: -0.98 in AVM-2, -0.96 in VCV, - 0.96 in PRVC).

The DP was significantly less with AVM-2 followed by VCV then PRVC in the lower minute ventilation (7 L/min) but was less in the VCV followed by

AVM-2 which in turn was less than PRVC in the 10.5 and 14 L/min experiments ($P < 0.001$) (Table 2).

The VT/IBW in AVM-2 were significantly reduced in each of the set minute ventilation (ME)as the compliance was reduced. The VT/IBW was significantly correlated with the respective compliance. R^2 0.97 in the 100% ME (7 L/min), R^2 0.96 in the 150% MV (10.5 L/min), and R^2 0.98 in the 200% MV (14 L/min). (Table 3 and figure 3)

Multiple linear regression of the variables for each mode were computed, the data in each model were normally distributed per the Shapiro Wilk test, and that the variance is homogeneous per the White test. Results are summarized in table 3.

In the AVM-2 mode: there was a very strong collective significant effect between the DP, VT, RR, PEEP, and Power, $P < 0.001$, $R^2 = 0.98$). The individual predictors were examined further and indicated that DP ($P = 0.004$), VT ($P < 0.001$), RR ($P = 0.011$) and PEEP ($P < 0.001$) were significant predictors in the model.

In the VCV mode, the results of the multiple linear regression indicated that there was a very strong collective significant effect between the RR, PEEP, DP, and Power, ($P 0< .001$, $R^2= 0.98$. The individual predictors were examined further and indicated that RR ($P < .001$) and PEEP ($P < 0.001$) were significant predictors in the model, but the DP was a non-significant predictor in the model ($P = 0.08$). Effect of VT could not be examined as it was kept constant throughout the experiments.

In the PRVC mode, the results of the multiple linear regression indicated that there was a very strong collective significant effect between the RR, PEEP, DP, and Power, ($P < .001$, $R^2 = 0.98$.
The individual predictors were examined further and indicated that RR ($P < 0.001$) and PEEP ($P < 0.001$) and DP ($P < 0.001$) were significant predictors in the model. Effect of VT could not be examined as it was kept constant throughout the experiments.

	AVM-2	VCV	PRVC	P value
MV 100% (100 ml/kg/min: 7 l/min)				
Mild (C=40)				
• **PEEP 10**	13.71 ± 0.17 (0.342)	14.45 ± 0.23 (0.361)	14.92 ± 0.16 (0.373)	< 0.001
• **PEEP 15**	17.53 ± 0.21 (0.438)	18.17 ± 0.14 (0.454)	18.45 ± 0.11 (0.461)	< 0.001
• **PEEP 20**	20.79 ± 0.13 (0.52)	21.96 ± 0.25 (0.549)	22.06 ± 0.25 (0.551)	< 0.001
Moderate (C=30)				
• **PEEP 10**	15.24 ± 0.14 (0.508)	16.33 ± 0.11 (0.544)	16.79 ± 0.11 (0.559)	< 0.001
• **PEEP 15**	18.84 ± 0.11 (0.628)	19.51 ± 0.28 (0.651)	19.88 ± 0.37 (0.662)	< 0.001
• **PEEP 20**	22.71 ± 0.11 (0.757)	23.21 ± 0.09 (0.773)	23.61 ± 0.17 (0.787)	< 0.001
Severe (C=20)				
• **PEEP 10**	18.02 ± 0.14 (0.901)	18.73 ± 0.18 (0.936)	21.91 ± 0.22 (1.095)	< 0.001
• **PEEP 15**	21.47 ± 0.12 (1.073)	22.11 ± 0.15 (1.105)	25.01 ± 0.18 (1.251)	< 0.001
• **PEEP 20**	24.41 ± 0.21 (1.221)	25.81 ± 0.11 (1.291)	28.55 ± 0.15 (1.427)	< 0.001

MV 150% (150 ml/kg/min: 10.5 l/min)				
Mild (C=40)				
• **PEEP 10**	22.95 ± 0.16 (0.573)	23.08 ± 0.26 (0.596)	25.48 ± 0.13 (0.637)	< 0.001
• **PEEP 15**	27.77 ± 0.16 (0.639)	28.71 ± 0.12 (0.717)	30.49 ± 0.13 (0.762)	< 0.001
• **PEEP 20**	32.98 ± 0.24 (0.824)	34.05 ± 0.21 (0.851)	35.54 ± 0.16 (0.888)	< 0.001
Moderate (C=30)				
• **PEEP 10**	24.77 ± 0.15 (0.825)	27.05 ± 0.0.22 (0.901)	27.26 ± 0.17 (0.908)	< 0.001
• **PEEP 15**	30.11 ± 0.25 (1.003)	31.02 ± 0.22 (1.034)	32.11 ± 0.27 (1.075)	< 0.001
• **PEEP 20**	35.73 ± 0.17 (1.191)	36.49 ± 0.26 (1.216)	37.23 ± 0.11 (1.241)	< 0.001
Severe (C=20)				
• **PEEP 10**	29.94 ± 0.13 (1.381)	31.67 ± 0.11 (1.581)	31.76 ± 0.13 (1.589)	< 0.001
• **PEEP 15**	33.51 ± 0.37 (1.675)	37.04 ± 0.11 (1.849)	37.11 ± 0.19 (1.855)	< 0.001
• **PEEP 20**	37.79 ± 0.26 (1.911)	40.38 ± 0.21 (2.044)	42.34 ± 0.12 (2.117)	< 0.001
MV 200% (200 ml/kg/min: 14 l/min)				
Mild (C=40)				
• **PEEP 10**	34.89 ± 0.32 (0.872)	36.52 ± 0.23 (0.917)	41.17 ± 0.21 (1.039)	< 0.001
• **PEEP 15**	39.05 ± 0.65 (0.977)	41.73 ± 0.17 (1.043)	46.62 ± 0.17 (1.165)	< 0.001
• **PEEP 20**	46.03 ± 0.75 (1.15)	47.75 ± 0.23 (1.194)	48.76 ± 0.36 (1.219)	< 0.001
Moderate (C=30)				
• **PEEP 10**	35.56 ± 0.31 (1.185)	37.13 ± 0.51 (1.237)	41.56 ± 0.19 (1.385)	< 0.001
• **PEEP 15**	41.91 ± 0.41 (1.397)	43.65 ± 0.16 (1.455)	43.72 ± 0.11 (1.459)	< 0.001
• **PEEP 20**	49.65 ± 0.29 (1.655)	55.19 ± 0.22 (1.703)	59.29 ± 0.21 (1.839)	< 0.001
Severe (C=20)				
• **PEEP 10**	40.24 ± 0.19 (2.012)	44.66 ± 0.21 (2.233)	48.28 ± 0.15 (2.414)	< 0.001
• **PEEP 15**	47.61 ± 0.21 (2.381)	50.84 ± 0.13 (2.542)	55.24 ± 0.22 (2.762)	< 0.001
• **PEEP 20**	54.71 ± 0.35 (2.735)	58.33 ± 0.12 (2.916)	62.15 ± 0.59 (3.107)	< 0.001

Table 1: Mechanical power in J/min and Power Compliance Index between brackets under between the three tested modes in all experiments according to the severity, PEEP levels in cmH_2O. AVM-2: Adaptive Ventilation Mode-2, C: Compliance in ml/cmH_2O, PRVC: Pressure Regulated Volume Control, VCV: Volume Controlled Ventilation. Data presented in mean ± SD

	Mild ARDS (C=40)	Moderate (C=30)	Severe (C=20)	P value
MV 100% (100 ml/kg/min: 7 l/min)				
PEEP 10	6.1 ± 0.11 (16)	5.8 ± 0.12 (17)	5.07 ± 0.08 (19)	< 0.001
PEEP 15	6.28 ± 0.12 (16)	5.72 ± 0.13 (17)	5.06 ± 0.09 (19)	< 0.001
PEEP 20	6.3 ± 0.12 (16)	5.85 ± 0.11 (17)	5.06 ± 0.08 (19)	< 0.001
MV 150% (150 ml/kg/min: 10.5 l/min)				
PEEP 10	7.32 ± 0.15 (21)	6.81 ± 0.11 (21)	5.82 ± 0.09 (25)	< 0.001
PEEP 15	7.41 ± 0.14 (20)	6.8 ± 0.13 (21)	5.64 ± 0.08 (26)	< 0.001
PEEP 20	7.43 ± 0.15 (20)	6.84 ± 0.12 (20)	5.61 ± 0.09 (26)	< 0.001
MV 200% (200 ml/kg/min: 14 l/min)				
PEEP 10	8.4 ± 0.21 (23)	7.48 ± 0.13 (26)	6.62 ± 0.11 (30)	< 0.001
PEEP 15	8.17 ± 0.19 (24)	7.58 ± 0.13 (25)	6.55 ± 0.12 (30)	< 0.001
PEEP 20	8.38 ± 0.18 (23)	7.58 ± 0.11 (25)	6.67 ± 0.12 (30)	< 0.001

Table 2: Comparison of tidal volume (ml/kg/breath) and respiratory rate/min (brackets under) in AVM-2 according to the percent minute ventilation (MV), compliance (C) in ml/cmH_2O and Positive end expiratory pressure (PEEP) in cmH_2O. Data presented in mean ± SD

	AVM-2	VCV	PRVC	P value
MV 100% (100 ml/kg/min: 7 l/min)				
Mild (C=40)	10.4 ± 0.15	11 ± 0.24	10.9 ± 0.22	< 0.001
Moderate (C=30)	13.3 ± 0.36	13.7 ± 0.42	13.9 ± 0.41	< 0.001
Severe (C=20)	17.2 ± 0.48	21.6 ± 0.33	20.9 ± 0.46	< 0.001
MV 150% (150 ml/kg/min: 10.5 l/min)				
Mild (C=40)	11.9 ± 0.21	11.5 ± 0.31	12.7 ± 0.23	< 0.001
Moderate (C=30)	15.5 ± 0.32	15.2 ± 0.36	16.5 ± 0.42	< 0.001
Severe (C=20)	22.3 ± 0.28	22.1 ± 0.32	23.3 ± 0.34	< 0.001
MV 200% (200 ml/kg/min: 14 l/min)				
Mild (C=40)	14.2 ± 0.32	12.7 ± 0.29	16.8 ± 0.25	< 0.001
Moderate (C=30)	17.9 ± 0.34	15.7 ± 0.19	18.5 ± 0.38	< 0.001
Severe (C=20)	22.6 ± 0.42	22.3 ± 0.36	24.8 ± 0.42	< 0.001

Table 3: Driving Pressure (DP) between each mode in all experiments. PEEP values in each mode did not change the DP. Data presented in mean ± SD

	RR	PEEP	DP	TV
AVM-2	0.011	< 0.001	P 0.004	< 0.001
VCV	< 0.001	< 0.001	0.08	N/A
PRVC	< 0.001	< 0.001	< 0.001	N/A

Table 4: Multiple regression analysis of variables on mechanical power in each of the 3 modes

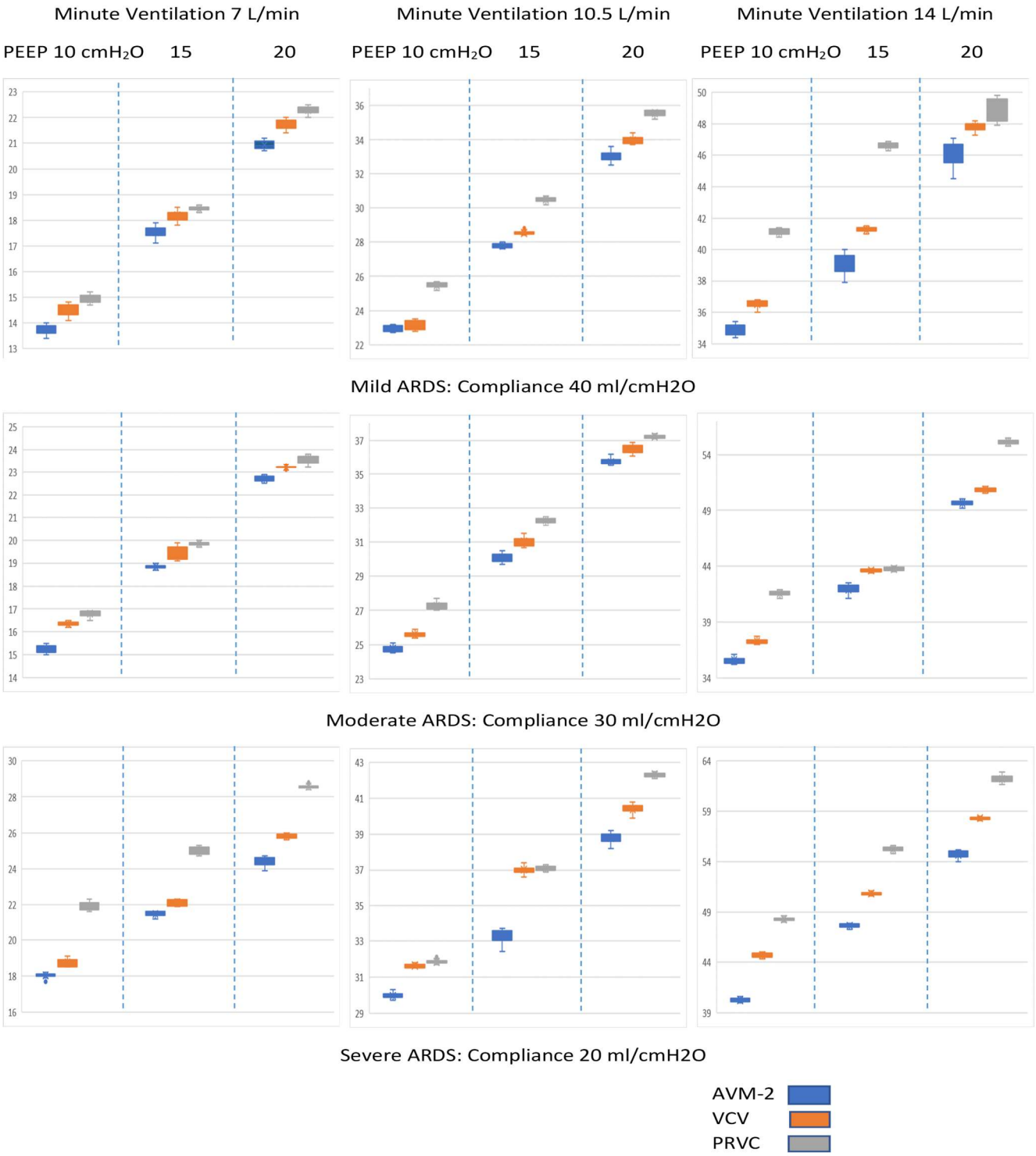

Figure 1: Mechanical power in all the experiments.

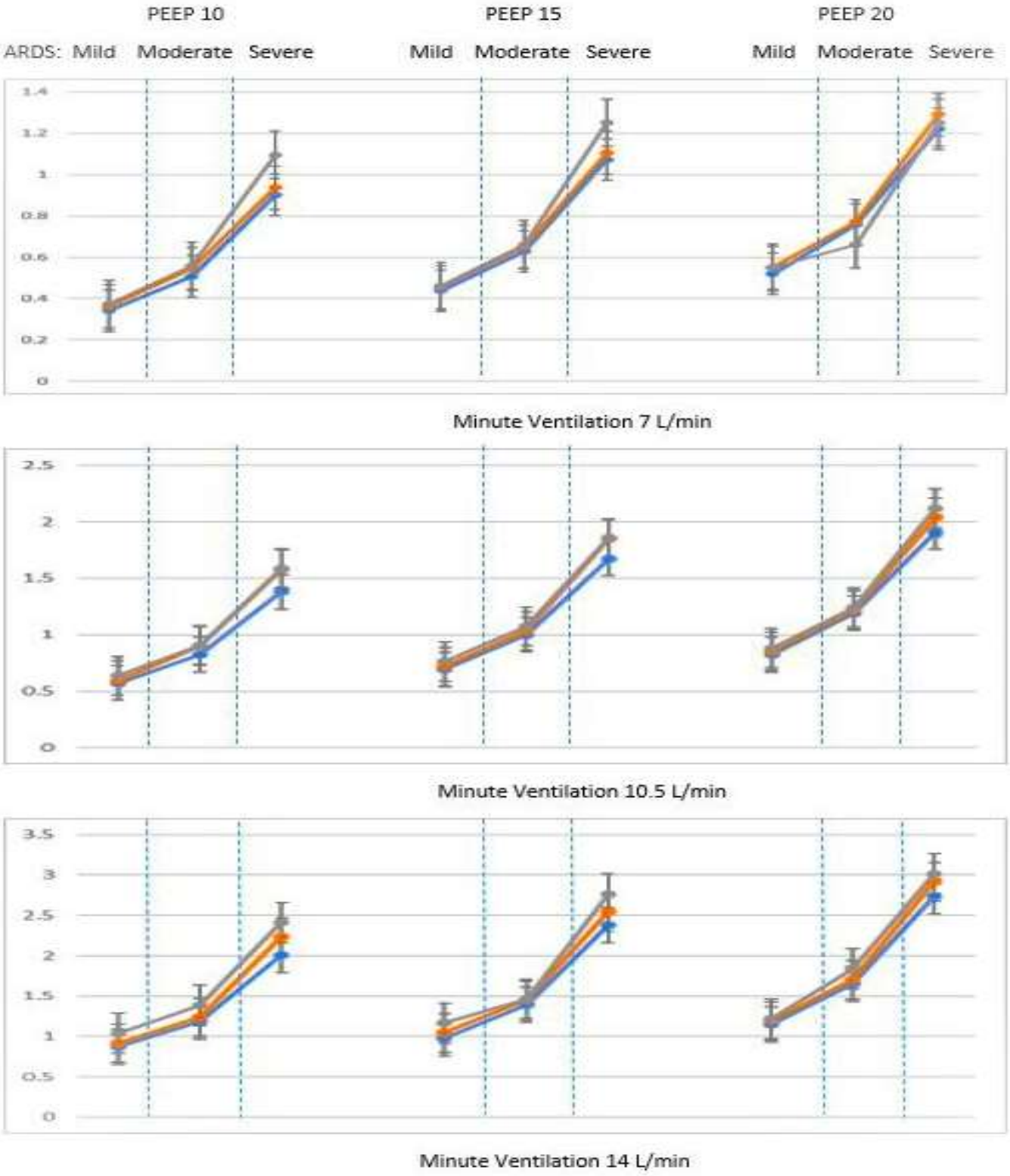

Figure 2: Power Compliance Index in all the experiments.

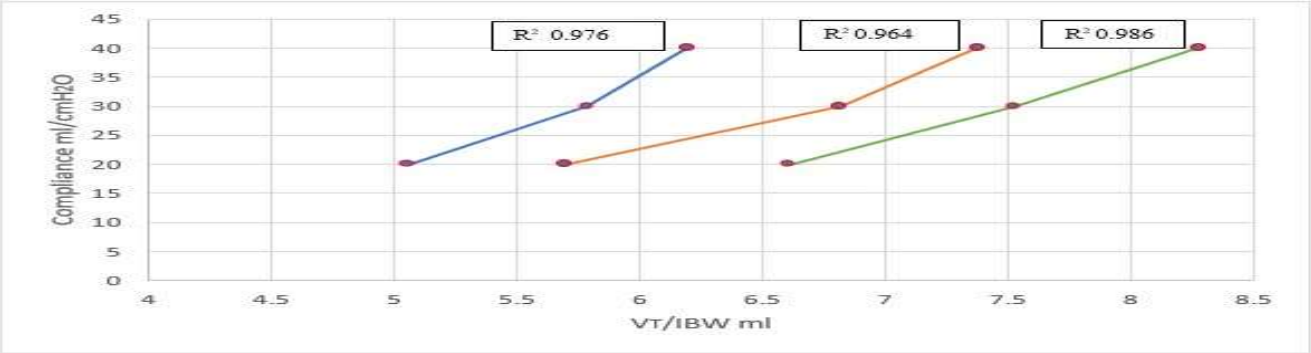

Figure 3: Pearson correlation between tidal volume/IBW versus compliance in AVM-2

Discussion

In this study we compared AVM-2 with the traditional modes of ventilation using a lung simulator simulating ARDS lungs. This study is a follow up to a study by our group on the performance of AVM-2 against conventional modes of mechanical ventilation with normal respiratory mechanics where we found that AVM-2 resulted in lower mechanical power compared VCV and PRVC (AVM-2 < VCV < PRVC). [21]

In this current study, we found that AVM-2 delivered a lower mechanical power compared with traditional modes of ventilation like VCV and PRVC in an ARDS model regardless of the severity of compliance tested, the PEEP levels, or the amount of minute ventilation. A recent study confirms our findings that VCV with no inspiratory pause delivered less power than VCV with a pause, and both less than PCV. [23]

To our knowledge, this is the first study that compares AVM-2 to conventional modes of ventilation in ARDS scenarios.

Mechanical power can be calculated using the geometric method which measures the dynamic inspiratory area in the airway pressure-volume curve during the respiratory cycle. [24] In volume-controlled ventilation (VCV) there is a linear increase in airway pressure during inspiration [25] and inspiratory flow remains constant. While in pressure-controlled ventilation modes like PRVC, the flow decelerates while the pressure in the airways remains constant. This generates variation in inspiratory (driving or tidal) pressure which is dependent on the resistance and the compliance of the respiratory system and patient effort. The different shapes of the pressure-volume curve under VCV and PCV explains the lower mechanical power in VCV compared to PCV despite the same tidal volume, inspiratory time, and PEEP levels (Figure 4). Though AVM-2 is a pressure-controlled mode that uses the decelerating inspiratory flow waveform, the manipulation of the respiratory rate, tidal volume, inspiratory flow, and I:E ratio according to its algorithm resulted in lower total mechanical power. [20]

As summarized in Table 3 and Figure 3, our current study shows that AVM-2 maintained low tidal volume ventilation (4-8 ml/kg) as recommended by some guidelines. [26] A lower tidal volume with a higher respiratory rate was applied as the compliance decreased regardless of the percent minute ventilation dialed. It is important to keep in mind that AVM-2 optimizes the respiratory rate and I:E in terms of alveolar minute ventilation and the expected dead space, not the proximal minute volume. We did not compare the tidal volumes between AVM-2 and the conventional modes as the tidal volumes were fixed at 6ml/kg in VCV and PRVC.

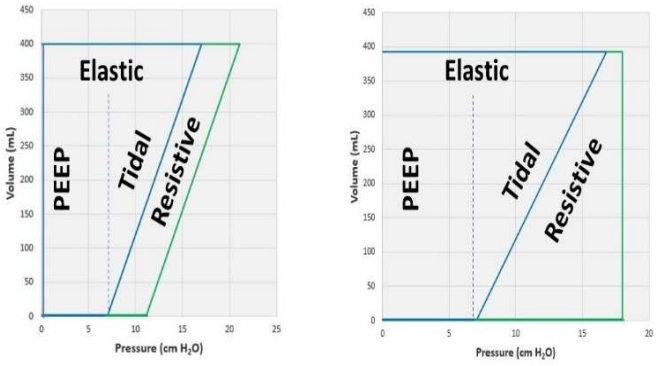

Figure 4: components of mechanical power according to the pressure volume curve in Volume Controlled Ventilation (left) and Pressure Controlled Ventilation (right)

Regarding the DP, an interesting finding that the DP applied by AVM-2 was lower compared to VCV and

PRVC in the 100% MV (7 L/min), but as the MV increased to 150% and 200% the DP was lower with VCV than AVM-2 as the tidal volume increased in AVM-2 but kept constant in the other modes. However, the trans-pulmonary DP rather than the airway DP appears to be more relevant in the development of VILI. [27] Giosa and colleagues [28] found that the actual Stress in the lung units can be up to 4 times greater than that measured in the upper airways.

In our study, we indexed the mechanical power values to their relative compliance from all 81 experiments and coined the term

"*Power Compliance Index*" "*PCI*"

Given the marked heterogeneity of lung units especially in ARDS, normalizing or indexing the mechanical power to the compliance of the lung (Trans-pulmonary mechanical power) or the amount of aerated lung might be more meaningful than mechanical power alone, as it represents the amount of energy delivered to a specific injured unit. [8, 16] Theoretically, a well aerated lung with better compliance will require less mechanical power i.e. a lower Power Compliance Index versus a non-aerated lung with poorer compliance which requires a higher mechanical power i.e. higher Power Compliance Index to achieve targets of ventilation.
Van der Meijden and colleagues [29] noted that the mechanical power values for ARDS was higher than other clinical conditions of respiratory failure using the PCV mode. Similarly, Franck and colleagues [30] found higher values of mechanical power in patients with COVID-19 ARDS requiring mechanical ventilation with the VCV mode.

Some authors suggested that a well aerated compliant lung might be less vulnerable to develop VILI in response to mechanical power, [20] on the other hand some suggested that a healthy lung might be more vulnerable to injury versus an already injured lung. [31, 32] Logically, targeting one value of mechanical power regardless of severity of injury will be unreasonable and ill advised.

Gattinoni and colleagues tested the effects of each individual component (RR, DP, PEEP, Inspiratory flow) when other variables were kept constant. [12] They found linear relationships with each component but to a different extent. In our current study, we also attempted to study the effects of the different components of the mechanical power in each of the tested ventilator modes. Comparable to their findings, we found similar results except that the DP in the VCV did not reach statistical significance (P 0.08) as seen in table 4, however, we could not measure the effects of V_T in the VCV and PRVC as we intentionally kept them the same at 6 ml/kg. Similarly, recent finding of a study by Franck and colleagues [30] in SARS-CoV-2 with moderate ARDS showed a moderate positive correlation of mechanical power with RR and a weak positive correlation with DP, denoting that there is a tendency for the increase of the mechanical power is more due to the increase in RR and, consequently, in the minute ventilation, than to the variation in DP with fixed V_T.

Gattinoni and colleagues [12] found that each increase in the RR by 20% resulted in a 37% increase in mechanical power, and each increase in PEEP levels by 20% resulted in only an increase of 5.7% in mechanical power. In our study we found the strongest correlation with mechanical power was the respiratory rate but could not replicate the exact numbers as there was different weight of the variables depending on the mode, the minute ventilation, and compliance tested.
The differences between our findings and their findings could be related to the method of measuring the mechanical power. They measured the mechanical power according to their proposed equation, we measured it from computing the volume-pressure curve. Additionally, we tested three different modes of ventilation that already had different mechanical power results, while they tested only one mode of ventilation. We do not believe that the relationship of each component to the total mechanical power is linear and predictable in different modes and under different respiratory mechanics.

As explained above, the energy transferred from the ventilator in each breath can be divided into two components, the elastic component (Tidal plus PEEP), and the resistive component (Figure 4). While PEEP does increase total mechanical power, it is unclear what effect this has in application as it is considered a stored kinetic energy, while the tidal component might be more contributory to VILI but this is still unclear and debatable.

However, the PEEP level has some indirect complex interaction which might affect the elastic energy as a whole and indirectly the tidal energy including its effect on lung recruitability and by affecting transpulmonary pressure. For one, if the lung is

recruitable, PEEP will improve the compliance which in turn will increase the tidal volume and FRC thus altering the strain on lung units and at the same time reducing the driving pressure. And by altering the compliance, PEEP might also affect the trans-pulmonary pressure and result in reduction of stress on the alveolar units. These effects need to be investigated in more detail in future studies.

In our study, the higher respiratory rate in the high minute ventilation experiments (10.5 and 14 L/min) caused auto-PEEP (to various degrees higher in the compliance of 40 $cmH_2O/L/s$ and least in the compliance of 20 $cmH_2O/L/s$) in the VCV and PRVC modes but not in the AVM-2 mode.
It is worth noting that auto-PEEP increases total power in the same way as set PEEP does, however the equations used currently might not be 100% accurate because it assumes no auto-PEEP.

The effect of auto-PEEP on the P-V curve is complex and depends on the mode and the etiology of the auto-PEEP.

This interaction is explained by the Equation of Motion

$$\boldsymbol{Paw + Pmus = E \times V + R \times \dot{V} + PEEP\ Total}$$

Where Paw is airway pressure, Pmus is patient muscle pressure, E is the elastance of the respiratory system, V is the tidal volume, R is airway resistance, $\dot{V}$ is flow, PEEP total is set PEEP + auto-PEEP

In the VCV mode with constant flow, increasing the respiratory rate causing auto-PEEP would decrease the I time, the peak and plateau inspiratory pressure, with a fixed I:E ratio, the inspiratory flow, airway pressures will increase altering the shape of the P-V curve thus increasing the measured mechanical power. In the PCV mode, auto-PEEP would reduce the V_T and inspiratory flow and might reduce the calculated mechanical power. [33]

However, if the auto-PEEP is secondary to higher compliance, the mechanical power will be reduced in VCV due to reduced airway pressure, but increase in PCV due to increased V_T. If the auto-PEEP is secondary to worsening resistance, the opposite would happen, the mechanical power will be increased in VCV due to increased airway pressure but will be reduced in the PCV due to reduced V_T if the DP is unchanged. Those effects are secondary to the change in airway pressure and V_T in each mode respectively. [33]

We suggest including the total PEEP (set PEEP + auto-PEEP) in the equations used to calculate the mechanical power.

It is interesting to note that AVM-2 mode targets inspiratory power which is the sum of the resistive and tidal power, which should translate into decreases in tidal volume and driving pressure. [20] This is particularly notable in the context of ARDS Network trials that show mortality benefit with lower tidal volumes [6] as well as new observational data by Costa and colleagues [15] showing that respiratory rate and driving pressure were the only ventilator variables that were associated with mortality.

Our study noted that for a given minute ventilation, AVM-2 mode targeted a lower respiratory rate compared to VCV and PRVC modes while targeting a minimum inspiratory power.

Although DP was higher in the AVM-2 mode in M_E 150% and 200%, there is a balance between DP and RR that may provide the optimal benefit to reduction in VILI. [15] Tonna and colleagues [34] showed that driving pressure and mechanical power are complementary and are each independently associated with mortality.

In our study, mechanical power is reduced in all experiments compared to VCV and PRVC. Thus, the AVM-2 mode may optimize the variables that have most closely been associated with mortality since the ARDS Network trials, and theoretically could confer a mortality benefit in clinical practice, though this remains to be investigated.

There are no studies or guidelines on setting the minute ventilation AVM-2 in different clinical conditions, and we tested a wide range of minute ventilation from 100% (100 ml/kg/min) to 200% (200 ml/kg/min). The very high minute ventilation as expected resulted in very high mechanical power and might not be clinically indicated. Extrapolating from previous guidelines published for the closely related adaptive mode ASV, [35] setting the minute ventilation initially at 130% +/- 10% might be reasonable.

There are a few limitations to the present study. Due to the inherent limitations of lung simulation, we are unable to assess gas exchange, the hemodynamic effects our outcomes of AVM-2 ventilatory strategy would have in actual clinical practice. Lung simulators use a single compartment with linear resistance and compliance which is quite different

from the mammalian lungs. As well, we are only able to simulate passive conditions due to variations in total work in patients who are actively breathing due to differences in muscle work.

Our study highlights the importance of new closed loop ventilation modes in ARDS as our understanding of the role mechanical power plays in VILI. Additionally it highlights that careful manipulation of the ventilator settings should not only be pointing to parameters of oxygenation and ventilation but also to parameters of lung injury. Additionally, we point out the importance of normalizing or indexing the mechanical power to the severity of the lung injury. Our study needs to be validated by further clinical studies.

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