



Research

Comparison of Mechanical Power Calculations of Volume Control and Pressure Regulated Volume Control Modes: A Prospective Observational Study

Volüm Kontrollü ve Basınç Regüle Volüm Kontrol Modlarının Mekanik Güçlerinin Karşılaştırılması: Prospektif Gözlemsel Çalışma

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ABSTRACT

Objective: Mechanical ventilation is a life-saving practice in acute respiratory distress syndrome (ARDS) patients. However, if not used properly, it causes ventilator-induced lung injury (VILI). Therefore, mechanical power (MP), which combines different variables associated with VILI in a single parameter and is affects mortality, is important in the management of patients with ARDS. In this study, MP values calculated over pressure-volume loops of volume control (VCV) and pressure regulated volume control (PRVC) modes were compared.

Methods: While 36 patients received controlled mechanical ventilation support (VCV and PRVC) under deep sedation, in the supine position on the second day of their intensive care unit hospitalization, MP values were calculated from minute respiratory mechanics. After calculating the 60-minute MP of the patients in the VCV mode with the (MP_{vcv}) (simpl) formula, they were switched to the PRVC mode and the 60-minute MP values were calculated with the (MP_{prvc}) (simpl) formula. The opposite was done for patients initially ventilated in the PRVC mode. In this way, two dependent groups were formed. All data of 36 patients registered in the 'Metasivionback server' were transferred to Excel with Structured Query Language, and then the patient averages were obtained and compared with the paired t-test.

Results: MP ($p<0.0001$), work of breathing ventilatory ($p<0.0001$) mean values were found to be statistically significantly higher in the PRVC group than in the VCV group. Peak airway pressure ($p<0.0001$) mean values in the VCV group were found to be statistically significantly higher than those in the PRVC group. No significant difference was found between other respiratory parameters.

Conclusion: Although the respiratory parameters (tidal volume, drive pressure and respiratory rate) that contribute to the calculation of MP are similar, lower power values are calculated in VCV mode compared to PRVC.

Keywords: Volume control, pressure control, mechanical power, ventilation, driving pressure

Öz

Amaç: Mekanik ventilasyon akut respiratuvar distres sendromu (ARDS) hastalarında hayat kurtarıcı bir uygulamadır. Ancak doğru kullanılmadığında ventilatörün indüklediği akciğer hasarına (VİLİ) neden olmaktadır. Bu nedenle, VİLİ ile ilişkisi saptanan farklı değişkenleri tek bir parametrede birleştiren ve mortalite üzerinde de etkili olduğu düşünülen mekanik güç (MG) kavramı, ARDS hastalarının yönetiminde önem taşımaktadır. Bu çalışmada, volüm kontrol (VCV) ve basınç regüle volüm kontrol (PRVC) modlarının basınç-volüm döngüleri üzerinden hesaplanan MG değerleri karşılaştırılmıştır.

Gereç ve Yöntem: Yoğun bakım yatışlarının 2. gününde derin sedasyon altında, sırt üstü yatar pozisyonda ve kontrole modlarda (VCV ve PRVC) ventilasyon desteği alan 36 hastanın dakikalık solunum mekaniklerinden MG değerleri hesaplanmıştır. Başlangıçta VCV modundaki hastaların 60 dakikalık mekanik güçleri (basitleştirilmiş) formülü ile hesaplandıktan sonra hastalar PRVC moduna alınmış ve 60 dakikalık mekanik güç değerleri (basitleştirilmiş) formülü ile hesaplanmıştır. Başlangıçta PRVC modunda ventile edilen hastalar için ise tam tersi yapılmıştır. Bu şekilde bağımlı

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2 grup oluşturulmuştur. "Metasivion sunucusu"na kayıtlı 36 hastanın tüm verileri yapılandırılmış sorgu dili sorgulama dili ile elde edilip Excel programına aktarıldıktan sonra hasta ortalamaları alınarak paired t-testi ile karşılaştırılmıştır.

Bulgular: PRVC grubunda MG ($p<0,0001$) ve ventilatör tarafından hesaplanan solunum işi ($p<0,0001$) ortalama değerleri VCV grubuna göre istatistiksel olarak anlamlı yüksek bulunmuştur. VCV grubunda tepe hava yolu basıncı ($p<0,0001$) ortalama değerleri PRVC grubuna göre istatistiksel olarak anlamlı yüksek bulunmuştur. Diğer solunum parametreleri arasında anlamlı fark saptanmamıştır.

Sonuç: Mekanik güç hesaplanmasına katkısı olan solunum parametreleri (tidal volüm, sürücü basınç ve solunum sayısı) benzer olmasına rağmen VCV modunda PRVC'ye göre daha düşük mekanik güç değerleri hesaplanmıştır.

Anahtar Kelimeler: Volüm kontrol, basınç kontrol, mekanik güç, ventilasyon, sürücü basınç

INTRODUCTION

The management of acute respiratory distress syndrome (ARDS), which is one of the important problems in the intensive care unit (ICU), has been the subject of intense discussion in the pandemic (1). Commonly used modes in mechanically ventilated patients in the ICU are volume control ventilation (VCV) and pressure regulated volume control ventilation (PRVC).

Mechanical ventilation is life-saving in patients with ARDS (2). However, if not used properly, it can cause ventilator-induced lung injury (VILI), which has an undesirable outcome (3,4). Therefore, lung protective ventilation practices have been developed to minimize VILI in patients with ARDS (5,6). The protective mechanical ventilation strategy provides the necessary oxygenation that will not cause hypoventilation for the patient without causing trauma to the lung (barotrauma, volutrauma, atelectotrauma) (7). For this reason, the orientation to protective ventilation strategies has increased considering experience and scientific data from the past to the present (8). Today, the concept of 'less is more' has gained importance (5,8). Gattinoni et al. (8) combined different variables, such as tidal volume (TV), driving pressure (DP), gas flow, respiratory rate (RR), and positive end-expiratory pressure (PEEP), which were associated with VILI in various studies, into a single parameter and termed the damage caused by mechanical power MP as ergotrauma (9-13). MP has been associated with increased mortality in intensive care patients (14). It is recommended to keep MP below 12 J/min in patients with ARDS and below 17 J/min in non-ARDS patients (15). For this reason, in the future, MP measurements will be routinely calculated on mechanical ventilator screens and will guide current protective ventilation strategies (8). MP is calculated from the pressure-volume curve (P-V loop) (7). Since the P-V loops of the VCV and PRVC modes are different, it is thought that the formulas developed for the VCV cannot be used for PRVC in the calculation of MP (16). Therefore, different formulae are derived for the VCV and PRVC modes (4,9,17-23).

In this study, the simplified MP equation $[MP_{vcv(simpl)}]$ developed by Gattinoni et al. (9) was used for the VCV and the simplified MP equation $[MP_{prvc(simpl)}]$ developed by Becher et al. (19) was used for the PRVC mode in MP calculations. Thus, the MP applied to the lung in the VCV and PRVC modes were compared.

METHODS

Ethical committee approval was obtained from the Clinical Research Ethics Committee of the University of Health Sciences Türkiye Bakırköy Dr. Sadi Konuk Training and Research Hospital (decision no: 2019-02-23, date: 21.01.2019). Informing and consent forms of all patients that the patient data will be used in prospective scientific studies during the ICU admission were signed by the relatives of the patients. This study was registered at ClinicalTrials.gov (NCT05494554).

Inclusion Criterias

Patients with confirmed coronavirus disease-2019 (COVID-19) diagnosis in ICU admission and diagnosed with ARDS according to the Berlin criteria (24),

Intubated patients were followed up in the supine position on the second day of ICU hospitalization.

Exclusion Criteria

Patients with a known diagnosis of chronic obstructive pulmonary disease,

Patients with unstable hemodynamics during mechanical ventilation,

Patients receiving inotropic support,

Patients with missing data.

Obtaining Patient Data

This study was conducted prospectively with 36 COVID-19 related patients with ARDS who were intubated and diagnosed with ARDS according to the Berlin criteria, in the ICU of University of Health Sciences Türkiye, Bakırköy Dr. Sadi Konuk Training and Research Hospital (24). The definite COVID-19 diagnosis was confirmed by PCR (Bio-

Speedy Covid-19 RT-Qpcr detection Kit-Bioeksen, Türkiye) obtained from the nasal swab sample and chest computed tomography images. All patients were ventilated with Maquet Servo-i (Sweden) ventilators. The ventilator parameters of the patients are MP, work of breathing ventilatory (WOBv, automatically measured by the ventilator), inspiratory airway pressure (ΔP_{insp}), [DP, plateau pressure (P_{plato})-PEEP for VCV and fixed ΔP_{insp} preset for PRVC], PEEP, mean airway pressure [(P_{mean}, calculated by ventilator: [(peak airway pressure (P_{peak}) - PEEP) \times (T_{insp}/T_{total}) + PEEP] for PRVC and [(P_{peak} - PEEP) \times 1/2 \times (T_{insp}/T_{total}) + PEEP] for VCV], P_{peak}, P_{plato}, expiratory tidal volume (T_{Ve}), PEEP, RR, expiratory minute volume (M_{Ve}), end-expiratory gas flow (V_{ee}), inspiration/expiration ratio (I:E ratio), inspiratory rise time (T_{slope}) were recorded instantly in ImdSoft-Metavision/ QlinICU Clinical Decision Support Software (Canada). Later, these data were obtained from 'Metavision back server' with Structured Query Language queries and transferred to an Excel file.

While 36 patients received controlled mechanical ventilation support (VCV and PRVC) under deep sedation, in the supine position on the second day of their ICU hospitalization, MP values were calculated from minute respiratory mechanics. If the patient is ventilated in VCV mode, after 60 min of respiratory mechanics and MP values were obtained, it is switched to PRVC mode for 60 min without changing the ventilator settings (RR, PEEP, I:E ratio). Likewise, if the patient is ventilated in PRVC mode, it is switched to VCV mode for 60 min after 60 min of MP calculation in PRVC. Thus, two dependent groups were formed. MP values were calculated from the minute respiratory parameters of all patients with the MP formulas defined in the software. Statistical analyses were performed after taking the patient averages of the 60-minute respiratory parameters (including MP) of both groups.

Calculation of Mechanical Power

This power applied by the ventilator is calculated from the P-V loop area between the airway pressure measured in inspiration and the volume axis (9). Since the P-V loop areas of the VCV and PRVC are not the same, the equations used to calculate the MP are also different (4,9,17-23).

In this study, a simplified volume control power equation [$MP_{\text{vcv(simpl)}}$] developed by Gattinoni et al. (9) was used to calculate MP in VCV mode (9). For the PRVC mode, the simplified pressure control power equation [$MP_{\text{prvc(simpl)}}$] developed by Becher et al. (19), which assumes that the pressure wave is in the form of an ideal square, was used (16).

Calculation of MP for VCV:

$$MP_{\text{vcv(simpl)}} = 0.098 \times \Delta V \times RR \times (P_{\text{peak}} - DP/2) \quad (9)$$

Calculation of MP for PRVC:

$$MP_{\text{prvc(simpl)}} = 0.098 \times RR \times \Delta V \times (\Delta P_{\text{insp}} + PEEP) \quad (19)$$

(MP: mechanical power, 0.098= conversion factor, RR: respiratory rate, ΔV : tidal volume, P_{peak}: peak airway pressure, P_{plato}: plato pressure, DP: driving pressure, ΔP_{insp} : pressure above PEEP during pressure-controlled ventilation)

Statistical Analysis

Descriptive statistical methods [mean, standard deviation (SD), percentage] were used while evaluating the demographic data. The homogeneity of the data was evaluated with the Shapiro-Wilk test. The sample size was calculated as 36 patients based on a pilot study (power=95%; α =0.05) (G*Power version 3.1.9.4, Germany). Respiratory mechanics and MP values of both dependent groups were distributed homogeneously and were compared with the paired t-test. A p-value <0.05 was considered significant. Graphpad Prism 9 (San Diego, USA) was used for statistical analysis.

RESULTS

This study was conducted with 36 patients. The characteristics of the patients included in the study are shown in Table 1.

Mean/SD and p-values of all parameters are shown in Table 2.

Mean values of MP (<0.0001) and WOBv (p<0.0001) were significantly higher in the PRVC group than in the VCV group (Table 2).

Mean values of P_{peak} (p<0.0001) were significantly higher in the VCV group than in the PRVC group (Table 2).

Mean values of lung compliance (p=0.466), DP (p=0.772), P_{plato} (p=0.879), T_{Ve} (p=0.927), PEEP (p=0.442), RR (p=0.175), M_{Ve} (p=0.373), V_{ee} (p=0.497), I:E ratio (p=0.101), T_{slope} (p=0.621) did not differ between the VCV and PRVC groups (Table 2).

DISCUSSION

In the previous studies, the superiority of the VCV and PRVC modes to each other could not be demonstrated. There is still disagreement about which mode is better.

In this study, although all respiratory parameters contributing to the calculation of MP (RR, PEEP, P_{plato}, T_{Ve}, DP, I:E ratio) were equal between both ventilation modes (VCV

and PRVC), there was a statistically and clinically significant difference between mechanical power values. The lower MP calculation in the VCV group was attributed to the geometric difference in the P-V loops of both modes (16). In the study by Giosa et al. (17) in which they compared the VCV corrected surrogate MP formula ($MP_{surr,corr}$) with the VCV simplified power formula [$MP_{vcv(simpl)}$] at 5 and 15 cmH₂O values, they

Table 1. Demographic data of the patients

Patient characteristics (no=36)	Mean/SD
Female (%)	12 (33.3%)
Age (year)	52±16
Height (cm)	172±8
Predicted body weight (kg/m ²)	63±9
APACHE-II -first	21±7
APACHE-II -last	24±12
APACHE-II -mortality (%)	43±21
SOFA-first	11±4
SOFA-last	11±6
Length of stay in ICU (hours)	342±188
ICU mortality (%)	24 (63.2%)

SD: Standard deviation, APACHE-II: Acute physiology and chronic health evaluation-II, ICU: Intensive care unit, SOFA: Sequential organ failure assessment score

found that both formulas calculated power values very close to each other in VCV (17). Chiemello et al. (7), in their study comparing the $MP_{surr,corr}$ formula and the geometric method, compared VCV and PRVC modes at a constant gas flow of 30 L/min. MPs calculated by the geometric method were 7.91±1.98 J/min and 7.84±2.39 J/min in VCV and PRVC modes, respectively. In the same study, MPs calculated with $MP_{surr,corr}$ formula were 7.91±2.06 J/min and 8.64±2.62 J/min in VCV and PRVC modes, respectively (7). These differences were not considered clinically significant. That study suggests that a single formula can be used for both VCV and PRVC to calculate MP (7). In our study, calculated MP values (13.1±2.7 J/min vs 16.3±3.2 J/min for VCV and PRVC, respectively) are almost twice as large as the results of the above-mentioned study, and the power difference between the two modes is equally large. These differences were evaluated as statistically and clinically significant. Therefore, the idea of using the same formula for both modes suggested by Chiumello et al. (7) may not be correct as the difference between the VCV and PRVC modes becomes wider at high power values.

Recently, it has been pointed out that the flow pattern is as important as the flow rate (25). When evaluated in terms of MP, the decelerating gas flow pattern in PRVC causes higher power values compared to VCV even with

Table 2. Patient averages of respiratory parameters recorded in VCV (60 min) and PRVC (60 min) modes were compared with the paired t-test

Respiratory parameters	VCV (n=36) Mean/SD	PRVC (n=36) Mean/SD	p-value
Mechanical power (J/minute)	13.1±2.7	16.3±3.2	<0.0001
Work of breathing ventilatory (J)	1.15±0.19	1.37±0.21	<0.0001
Lung compliance (mL/cmH ₂ O)	30.61±9.14	29.83±9.369	0.466
Driving pressure (cmH ₂ O)	15.95±3.19	16.05±2.46	0.772
Peak airway pressure (cmH ₂ O)	28.69±3.37	24.80±2.81	<0.0001
Plato pressure (cmH ₂ O)	24.75±2.93	24.80±2.81	0.879
Expiratory tidal volume (mL)	429.7±55.85	428.6±74.55	0.927
Positive end-expiratory pressure (cmH ₂ O)	8.801±1.486	8.610±1.460	0.442
Respiratory rate (1/minute)	16.1±1.6	15.7±1.57	0.175
Expiratory minute volume (L/minute)	6.92±1.13	6.71±1.19	0.373
End-expiratory gas flow (L/second)	0.02±0.01	0.02±0.01	0.497
Inspiration/Expiration ratio	0.8±0.16	0.78±0.18	0.101
Inspiratory rise time (Ramp) (Tslope) (second)	0.2±0.11	0.19±0.06	0.621
Gas flow for VCV L/second	0.42±0.11	-	-

VCV: Volume control ventilation, PRVC: Pressure regulated volume control ventilation, SD: Standard deviation

similar respiratory parameters. Because the high flow spikes in the PRVC mode, namely, the high gas flow applied in a short time, has a damaging effect (26,27). Additionally, the rapid transmission of cycle energy to the lungs in early inspiration may have an increasing effect on lung damage (25). This effect is more prominent in patients with ARDS than in patients with homogeneous lungs. It is an ongoing debate whether the decelerating flow pattern may put PRVC at a disadvantage (26).

The geometric method is the gold standard for MP calculation, but the measurement equipment was lacking.

CONCLUSION

Although respiratory parameters (TV, drive pressure and RR) that contribute to the calculation of mechanical power are similar, MP values in the VCV mode are both clinically and statistically lower than PRVC. Although the clinical superiority of the VCV and PRVC modes to each other has not been demonstrated, it is thought that VCV is more advantageous in terms of mechanical power values. Moreover, a single formula for calculating power at high power values will cause inaccurate measurements.

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ETHICS

Ethics Committee Approval: Ethical committee approval was obtained from the Clinical Research Ethics Committee of the University of Health Sciences Türkiye, Bakırköy Dr. Sadi Konuk Training and Research Hospital (decision no: 2019-02-23, date: 21.01.2019). The research conforms to the provisions of the Declaration of Helsinki in 1995 (as revised in Brazil 2013).

Informed Consent: Written consent was obtained from all patients or their relatives.

Authorship Contributions

Surgical and Medical Practices: F.T., S.A., İ.B., Z.Ç., Concept: F.T., S.A., İ.B., Z.Ç., Design: F.T., S.A., İ.B., Z.Ç., Data Collection or Processing: F.T., S.A., İ.B., Z.Ç., Analysis or Interpretation: F.T., S.A., İ.B., Z.Ç., Literature Search: F.T., S.A., İ.B., Z.Ç., Writing: F.T., S.A., İ.B., Z.Ç..

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REFERENCES

1. Fan E, Beitler JR, Brochard L, Calfee CS, Ferguson ND, Slutsky AS, et al. COVID-19-associated acute respiratory distress syndrome: is a different approach to management warranted? *Lancet Respir Med* 2020;8:816-21.
2. Fan E, Needham DM, Stewart TE. Ventilatory management of acute lung injury and acute respiratory distress syndrome. *JAMA* 2005;294:2889-96.
3. Slutsky AS, Ranieri VM. Ventilator-induced lung injury. *N Engl J Med* 2014;370:980.
4. Paudel R, Trinkle CA, Waters CM, Robinson LE, Cassity E, Sturgill JL, et al. Mechanical Power: A New Concept in Mechanical Ventilation. *Am J Med Sci* 2021;362:537-45.
5. Cruz FF, Ball L, Rocco PRM, Pelosi P. Ventilator-induced lung injury during controlled ventilation in patients with acute respiratory distress syndrome: less is probably better. *Expert Rev Respir Med* 2018;12:403-14.
6. Villar J, Kacmarek RM, Pérez-Méndez L, Aguirre-Jaime A. A high positive end-expiratory pressure, low tidal volume ventilatory strategy improves outcome in persistent acute respiratory distress syndrome: a randomized, controlled trial. *Crit Care Med* 2006;34:1311-8.
7. Chiumello D, Gotti M, Guanziroli M, Formenti P, Umbrello M, Pasticci I, et al. Bedside calculation of mechanical power during volume- and pressure-controlled mechanical ventilation. *Crit Care* 2020;24:417.
8. Gattinoni L, Tonetti T, Quintel M. Intensive care medicine in 2050: ventilator-induced lung injury. *Intensive Care Med* 2018;44:76-8.
9. Gattinoni L, Tonetti T, Cressoni M, Cadringer P, Herrmann P, Moerer O, et al. Ventilator-related causes of lung injury: the mechanical power. *Intensive Care Med* 2016;42:1567-75.
10. Kumar A, Pontoppidan H, Falke KJ, Wilson RS, Laver MB. Pulmonary barotrauma during mechanical ventilation. *Crit Care Med* 1973;1:181-6.
11. Dreyfuss D, Soler P, Basset G, Saumon G. High inflation pressure pulmonary edema. Respective effects of high airway pressure, high tidal volume, and positive end-expiratory pressure. *Am Rev Respir Dis* 1988;137:1159-64.
12. Hotchkiss JR Jr, Blanch L, Murias G, Adams AB, Olson DA, Wangenstein OD, Leo PH, et al. Effects of decreased respiratory frequency on ventilator-induced lung injury. *Am J Respir Crit Care Med* 2000;161:463-8.
13. Cressoni M, Gotti M, Chiurazzi C, Massari D, Algieri I, Amini M, et al. Mechanical Power and Development of Ventilator-induced Lung Injury. *Anesthesiology* 2016;124:1100-8.
14. Serpa Neto A, Deliberato RO, Johnson AEW, Bos LD, Amorim P, Pereira SM, et al. Mechanical power of ventilation is associated with mortality in critically ill patients: an analysis of patients in two observational cohorts. *Intensive Care Med* 2018;44:1914-22.
15. Battaglini D, Sottano M, Ball L, Robba C, Rocco PR, Pelosi P. Ten golden rules for individualized mechanical ventilation in acute respiratory distress syndrome. *Journal of Intensive Medicine* 2021;1:42-51.
16. Zhao Z, Frerichs I, He H, Long Y, Möller K, Serpa Neto A, et al. The calculation of mechanical power is not suitable for intra-patient monitoring under pressure-controlled ventilation. *Intensive Care Med* 2019;45:749-50.
17. Giosa L, Busana M, Pasticci I, Bonifazi M, Macri MM, Romitti F, et al. Mechanical power at a glance: a simple surrogate for volume-controlled ventilation. *Intensive Care Med* 2019;7:61.

18. Aşar S, Acicbe Ö, Çukurova Z, Hergünel GO, Canan E, Çakar N. Bedside dynamic calculation of mechanical power: A validation study. *J Crit Care* 2020;56:167-70.
19. Becher T, van der Staay M, Schädler D, Frerichs I, Weiler N. Calculation of mechanical power for pressure-controlled ventilation. *Intensive Care Med* 2019;45:1321-3.
20. van der Meijden S, Molenaar M, Somhorst P, Schoe A. Calculating mechanical power for pressure-controlled ventilation. *Intensive Care Med* 2019;45:1495-7.
21. Aşar S, Acicbe Ö, Sabaz MS, Kucur Tülübaş E, Hergünel GO, Çukurova Z, et al. Simplified calculation of mechanical power for pressure controlled ventilation in Covid-19 ARDS patients. *Minerva Anesthesiol* 2022;88:42-50.
22. Chi Y, He H, Long Y. A simple method of mechanical power calculation: using mean airway pressure to replace plateau pressure. *J Clin Monit Comput* 2021;35:1139-47.
23. Trinkle CA, Broaddus RN, Sturgill JL, Waters CM, Morris PE. Simple, accurate calculation of mechanical power in pressure controlled ventilation (PCV). *Intensive Care Med Exp* 2022;10:22.
24. ARDS Definition Task Force, Ranieri VM, Rubenfeld GD, Thompson BT, Ferguson ND, Caldwell E, et al. Acute respiratory distress syndrome: the Berlin Definition. *JAMA* 2012;307:2526-33.
25. Gattinoni L, Marini JJ, Collino F, Maiolo G, Rapetti F, Tonetti T, et al. The future of mechanical ventilation: lessons from the present and the past. *Crit Care* 2017;21:183.
26. Marini JJ, Crooke PS, Gattinoni L. Intra-cycle power: is the flow profile a neglected component of lung protection? *Intensive Care Med* 2021;47:609-11.
27. Subirà C, de Haro C, Magrans R, Fernández R, Blanch L. Minimizing Asynchronies in Mechanical Ventilation: Current and Future Trends. *Respir Care* 2018;63:464-78.