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Research Article

Comparison of Pulmonary Compliance Measured by Multiple Linear Regression Versus Traditional Methods in Mechanically Ventilated Patients

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ABSTRACT

Background: Pulmonary compliance measurement is a critical component of monitoring mechanically ventilated patients with respiratory failure. The traditional method calculates compliance by dividing delivered tidal volume by the resultant airway pressure (plateau pressure minus positive end-expiratory pressure [PEEP]). However, this approach requires intermittent ventilator disconnection, limiting its frequency. A novel method using multiple linear regression (MLR) analysis of continuous pressure and flow waveforms enables breath-to-breath compliance measurement without disrupting ventilation. This study compares pulmonary compliance values obtained by MLR and traditional methods.

Methods: In this clinical study, pulmonary compliance was measured and compared in consecutive mechanically ventilated patients using both traditional and MLR methods. MLR-derived compliance was obtained using the ventilator's integrated monitoring function, while traditional compliance was calculated as tidal volume divided by (plateau pressure – PEEP).

Results: Among 200 enrolled patients, the two methods showed strong correlation (*r* = 0.9, *p* < 0.01). However, MLR-derived compliance values were consistently lower than those from the traditional method (44.74 ± 21.78 mL/cmH_2 O vs. 57.95 ± 26.64 mL/cmH_2 O, *p* < 0.01).

Conclusion: MLR is a reliable alternative for continuous pulmonary compliance monitoring, though its systematically lower values—likely reflecting dynamic rather than static compliance—may necessitate a correction factor. The method's ability to provide breath-to-breath measurements offers significant clinical advantages over traditional intermittent assessments.

Introduction

Mechanical ventilation is a life-saving intervention for patients with acute respiratory failure, but its non-physiological delivery of positive pressure can lead to ventilator-induced lung injury (VILI) [1]. Pulmonary compliance, a key metric of respiratory mechanics, reflects lung distensibility and guides ventilator optimization to mitigate VILI risk [2].

While pulmonary compliance may decrease when the elasticity or total amount of lung tissue decreases, like for example in pneumothorax, endobronchial intubation, acute respiratory distress syndrome, lung contusion, pneumonia, and aspiration pneumonitis, its increase may denote pulmonary function recovery, which signals for weaning from mechanical ventilation [3].

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Traditional Compliance Measurement: Limitations

The gold-standard static compliance (C_{stat}) requires an end-inspiratory hold to measure plateau pressure (P_{plat}):

$$C_{stat} = \frac{Vt}{(P_{plat} - PEEP)} \quad (1)$$

Where:

- C_{stat} = Static Compliance (ml / cmH_2O)
- Vt = Tidal Volume (ml)
- P_{plat} = Plateau Pressure (cmH_2O)
- PEEP = Positive End Expiratory Pressure

This method interrupts ventilation, necessitates sedation, and provides only intermittent snapshots [3].

MLR: A Dynamic Alternative

Multiple linear regression (MLR) analyzes continuous waveforms (pressure, flow, and volume) using the equation of motion:

$$P(t) = R \cdot \dot{V}(t) + \frac{1}{C} \cdot V(t) + P_0 \quad (2)$$

Where:

- P(t) = airway pressure at time t
- $\dot{V}(t)$ = airflow at time t
- V(t) = lung volume at time t
- R = respiratory resistance
- C = respiratory compliance

MLR estimates compliance, resistance, and auto-PEEP breath-by-breath without disrupting ventilation [4]. Its advantages include:

- Real-time monitoring for rapid clinical decisions [5].
- Robustness to noise via regression smoothing [6].

While MLR is embedded in modern ventilators (e.g., Hamilton C3), validation against traditional method remains limited, particularly in heterogeneous ICU populations. Systematic differences (e.g., dynamic vs. static compliance) may impact clinical interpretation [7].

We compared MLR-derived compliance (C_{MLR}) with the traditional method (C_{stat}) in a sample of mechanically ventilated adults to:

- Assess correlation and agreement.
- Quantify systematic bias.
- Propose correction factors if needed.

Methods

The study was approved by the Institutional Review Board (IR.MUI.MED.REC.1402.367). Waiver of informed consent granted for de-identified data collection.

Study Design and Population

This cross-sectional study was conducted in the intensive care units (ICUs) of a university-affiliated teaching hospital. We enrolled 200 consecutive adult patients (aged ≥18 years) receiving invasive mechanical ventilation for acute respiratory failure. Inclusion criteria were:

- Mechanically ventilated via endotracheal tube or tracheostomy
- Volume-controlled ventilation mode (VCV) with constant flow.

Exclusion criteria were:

- Air leaks (e.g., bronchopleural fistula, uncuffed tracheostomy).
- Active patient-ventilator asynchrony (as assessed by waveform analysis).
- Hemodynamic instability during measurement periods.

Ventilator Specifications

All measurements were performed using the Hamilton C3 ventilator (Hamilton Medical AG, Switzerland) with the following configuration:

- Mode: Volume-controlled ventilation (VCV).
- Flow waveform: Square (constant flow).
- PEEP: Set per clinical protocol (range: 5–15 cmH_2O).
- FiO_2 : Adjusted to maintain SpO_2 ≥ 92%.
- Inspiratory pause: 0.5 sec for P_{plat} measurement.
- MLR algorithm: Embedded in ventilator software (firmware v4.1.2), sampling at 100 Hz.

Compliance Measurement Protocols

Traditional Static Compliance (C_{stat}):

- Measured during sedation-induced apnea (Richmond Agitation-Sedation Scale [RASS] ≤ −3) to ensure muscle relaxation.
- Vt, P_{plat}, and PEEP recorded after a 0.5-sec end-inspiratory hold.
- Calculated using equation 1.
- Triplicate measurements were averaged to minimize intra-observer variability.

MLR-Derived Compliance (C_{MLR}):

- Continuously estimated by the Hamilton C3's MLR algorithm (equation 2).
- Values logged every 10 breaths and averaged over 5 minutes preceding C_{stat} measurement.

Sample Size and Statistical Analysis

The primary outcome was the correlation between C_{stat} and C_{MLR}. Assuming an expected Pearson's $r = 0.8$ (based on pilot data), a value of $\alpha = 0.05$, and aiming for a power of 90%, the sample size was calculated to be 18 patients. A total of 200 patients accounted for subgroup analyses and potential exclusions. Data were analyzed using SPSS v27.0. Since the Shapiro-Wilk test confirmed the non-normal distribution of residuals, non-parametric tests were prioritized. Spearman's rank was used to correlate

C_{stat} vs C_{MLR}. Percent bias is calculated as (C_{stat} – C_{MLR}) / C_{stat}. The Wilcoxon signed-rank test (paired, non-parametric) is used to compare means of C_{stat} vs C_{MLR}.

Bland-Altman analysis was used to evaluate bias and limits of agreement between Cstat and C_{MLR}.

Results

A total of 200 patients enrolled in the study. (Table 1) shows different baseline and ventilatory parameters. The double histogram demonstrates the right-shifted distribution of C_{stat} values compared to C_{MLR}, reflecting higher absolute measurements (Figure 1).

Table 1- Baseline and ventilatory variables. Data are mean ± SD with range or n(%) with 95% confidence interval.

Age (year)	**56 ± 22.4**	**18 – 99**
Male	136 (68)	61 – 74
Female	64 (32)	25 – 38
Vt (ml)	467 ± 136	150 – 630
P_{plat}(cmH2O)	18 ± 5.2	12 – 35
PEEP (cmH2O)	6 ± 2.7	4 – 15
C_{stat} (ml/cmH2O)	58 ± 26.6	20 – 134
C_{MLR} (ml/cmH2O)	45 ± 22.4	11 – 136

Though C_{MLR} values were systematically lower than the C_{stat} values (mean difference 13 ml/cmH_2O, $p < 0.001$), Spearman correlation analysis showed a very strong correlation between them ($\rho = 0.9$, $p < 0.001$). The scatterplot confirmed the linearity of the relationship (slope = 0.82, $R^2 = 0.81$, Figure 2).

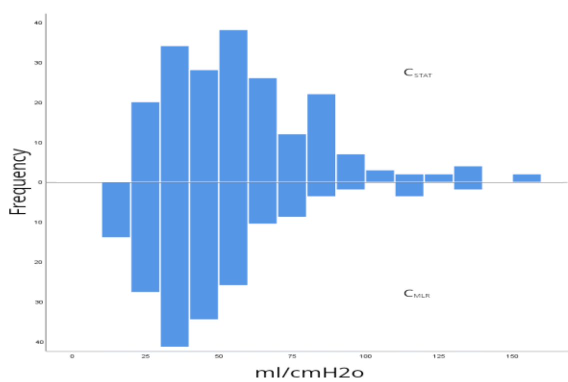

Figure 1- Shows a double histogram depicting frequency distribution for different values of compliances across two methods of measurement.

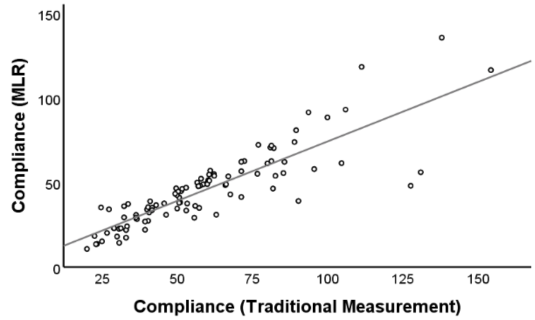

Figure 2- Scattergram showing the relationship between C_{stat} and C_{MLR}. Spearman $\rho = 0.9$, $p < 0.100$.

Bland-Altman analysis showed a bias of −13.2 mL/cmH_2 O, with 95% limits of agreement between C_{stat} and C_{MLR} ranging from −28.1 to +1.7 mL/cmH_2 O (Figure 3).

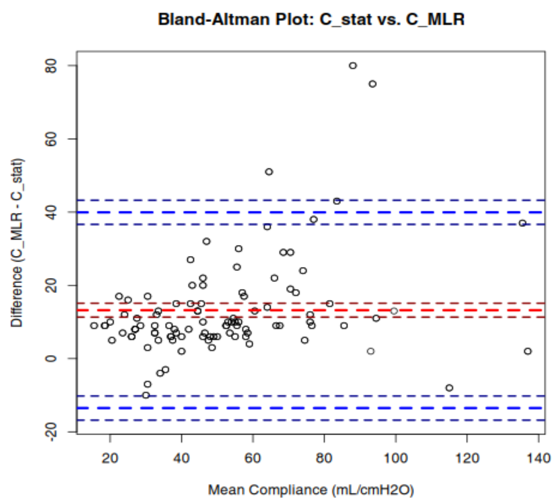

Figure 3- Bland-Altman analysis shows a strong correlation between C_{stat} and C_{MLR}.

Bias = −13.2 mL/cmH_2 O, 95% limits of agreement = −28.1 to +1.7 mL/cmH_2 O.

Discussion

This study demonstrated a strong correlation between MLR-derived and traditional static compliance measurements, supporting the utility of MLR for continuous monitoring. However, the systematic underestimation by MLR (−13.2 mL/cmH_2 O) highlights its reflection of dynamic compliance, which incorporates resistive and inertial forces absent in static measurements. MLR enables breath-to-breath compliance tracking without the need for extra sedation or ventilation disruption, ideal for guiding PEEP titration and recruitment maneuvers [8–12]. The consistent bias relative to traditional measurements suggests MLR values may require adjustment (e.g., +13 mL/cmH_2 O) when interpreting absolute compliance in protocols reliant on static thresholds (e.g., ARDS Network tables) [13]. The lower C_{MLR} values align with prior work showing dynamic compliance ≤ static compliance due to flow-resistive losses [14-15].

Our findings (ρ = 0.90) mirror validations of MLR in smaller cohorts [14–18]. The difference between two methods exceeds reports using older ventilators (e.g., −8 mL/cmH_2 O), possibly due to the higher sample size in the current study.

It must be noted the generalizability of the result of this study may vary with ventilator brands or patient populations. Another limitation in this study may be the escape of spontaneous breathing activity due to inadequate sedation, which tends to increase the measured value of Cstat. Also, heterogeneity of patients enrolled in this study (ARDS vs. non-ARDS subgroups) may further add to the limitation of the current study. Future direction to validate correction factors for MLR in protocolized settings (e.g., PEEP trials) is recommended.

Conclusion

MLR is a reliable alternative for continuous pulmonary compliance monitoring, though its systematically lower values—likely reflecting dynamic rather than static compliance—may necessitate a correction factor. The method’s ability to provide breath-to-breath measurements offers significant clinical advantages over traditional intermittent assessments.

References

[1] Slutsky AS, Ranieri VM. Ventilator-induced lung injury. N Engl J Med 2013;369:2126-36.

[2] Tobin MJ. Advances in mechanical ventilation. N Engl J Med. 2001;344(26):1986-96.

[3] Harris RS. Pressure-volume curves of the respiratory system. Respir Care. 2005;50(1):78-98.

[4] Hess DR. Respiratory mechanics in mechanically ventilated patients. Respir Care. 2014;59(11):1773-94.

[5] Hezarjaribi N, Dutta R, Tao X, Murdoch GK, Mazrouee S, Mortazavi B, et al. Monitoring Lung Mechanics during Mechanical Ventilation using Machine Learning Algorithms, 2018 40th Annual International Conference of the IEEE Engineering in Medicine and Biology Society (EMBC), Honolulu, HI, USA, 2018; 1160-1163.

[6] Yi B, Wang C, Gao Y, Gong Y, Luo L, Yao R, et al. Continuous estimation of respiratory system compliance and airway resistance using multiple linear regression. BMC Pulm Med. 2024;24(1):106.

[7] Chen ZL, Yan YZ, Yu HY, Wang QB, Wang W, Zhong M. Influence of compliance and resistance of the test lung on the accuracy of the tidal volume delivered by the ventilator. BMC Pulm Med. 2024;24(1):498.

[8] Polak AG. Analysis of multiple linear regression algorithms used for respiratory mechanics monitoring during artificial ventilation. Comput Methods Programs Biomed. 2011;101(2):126-34.

[9] Nikischin W, Gerhardt T, Everett R, Bancalari E. A new method to analyze lung compliance when pressure-volume relationship is nonlinear. Am J Respir Crit Care Med. 1998;158(4):1052-60.

[10] Chen Y, Yuan Y, Chang Q, Zhang H, Li F, Chen Z. Continuous estimation of respiratory system compliance and airway resistance during pressure-controlled ventilation without end-inspiration occlusion. BMC Pulm Med. 2024; 24(1):249.

[11] Rousselot JM, Peslin R, Duvivier C. Evaluation of the multiple linear regression method to monitor respiratory mechanics in ventilated neonates and young children. Pediatr Pulmonol. 1992; 13(3):161-8.

[12] Kulkarni A, Sheela N. Methods to Evaluate Airway Resistance and Lung Compliance During Mechanical Ventilation: A Comparative Study. Int J Innov Sci Res Technol. 2020; 5(7):947-951.

[13] Acute Respiratory Distress Syndrome Network; Brower RG, Matthay MA, Morris A, Schoenfeld D, Thompson BT, Wheeler A. Ventilation with lower tidal volumes as compared with traditional tidal volumes for acute lung injury and the acute respiratory distress syndrome. N Engl J Med. 2000; 342(18):1301-8.

[14] Gutierrez, G. A novel method to calculate compliance and airway resistance in ventilated patients Intensive Care Med Exp. 2022; 10(1):55.

[15] Bradbrook CA, Clark L, Dugdale AH, Burford J, Mosing M. Measurement of respiratory system compliance and respiratory system resistance in healthy dogs undergoing general anaesthesia for elective orthopaedic procedures. Vet Anaesth Analg. 2013;40(4):382-9.

[16] Officer TM, Pellegrino R, Brusasco V, Rodarte JR. Measurement of pulmonary resistance and dynamic compliance with airway obstruction. J Appl Physiol (1985). 1998;85(5):1982-8.

[17] Stenqvist O., Practical assessment of respiratory mechanics, Br J Anaesth. 2003;91(1):92-105.

[18] Kamp L, Hunnekens B, Wouw N, Oomen T. An Estimation Perspective on Breathing Effort Disturbances in Mechanical Ventilation. IFAC-PapersOnLine. 2023; 56(2): 8215-8220.