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# Continuous estimation of respiratory system compliance and airway resistance during pressure-controlled ventilation without end-inspiration occlusion

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## Abstract

**Background** Assessing mechanical properties of the respiratory system ( $C_{st}$ ) during mechanical ventilation necessitates an end-inspiration flow of zero, which requires an end-inspiratory occlusion maneuver. This lung model study aimed to observe the effect of airflow obstruction on the accuracy of respiratory mechanical properties during pressure-controlled ventilation (PCV) by analyzing dynamic signals.

**Methods** A Hamilton C3 ventilator was attached to a lung simulator that mimics lung mechanics in healthy, acute respiratory distress syndrome (ARDS) and chronic obstructive pulmonary disease (COPD) models. PCV and volume-controlled ventilation (VCV) were applied with tidal volume ( $V_T$ ) values of 5.0, 7.0, and 10.0 ml/kg. Performance characteristics and respiratory mechanics were assessed and were calibrated by virtual extrapolation using expiratory time constant ( $RC_{exp}$ ).

**Results** During PCV ventilation, drive pressure (DP) was significantly increased in the ARDS model. Peak inspiratory flow (PIF) and peak expiratory flow (PEF) gradually declined with increasing severity of airflow obstruction, while DP, end-inspiration flow (EIF), and inspiratory cycling ratio (EIF/PIF%) increased. Similar estimated values of  $C_{rs}$  and airway resistance ( $R_{aw}$ ) during PCV and VCV ventilation were obtained in healthy adult and mild obstructive models, and the calculated errors did not exceed 5%. An underestimation of  $C_{rs}$  and an overestimation of  $R_{aw}$  were observed in the severe obstruction model.

**Conclusion** Using the modified dynamic signal analysis approach, respiratory system properties ( $C_{rs}$  and  $R_{aw}$ ) could be accurately estimated in patients with non-severe airflow obstruction in the PCV mode.

**Keywords** Pressure-controlled ventilation, Compliance, Airway resistance, Simulation, Chronic obstructive pulmonary disease

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## Background

Mechanical ventilation is an important lifesaving procedure with wide clinical applications for various critical conditions. The adequate setting of ventilator parameters should be based on the patient's condition for optimal patient outcomes and to minimize ventilator-associated injury and complications [1, 2]. Pressure-controlled ventilation (PCV) is broadly used for cases of severe respiratory failure. PCV improves arterial oxygenation and decreases peak airway pressure because it decelerates inspiratory flow. However, PCV has some limitations, including insufficient ventilation and excessive ventilation [3–8].

Currently, the dynamic properties of the respiratory system and engineering models for various diseases are exploited in the diagnosis and treatment of pulmonary disorders [9, 10]. However, mechanical features cannot be assessed directly during mechanical ventilation and are commonly presented as lumped indicators, including airway resistance ( $R_{aw}$ ) and compliance ( $C_{rs}$ ) [11, 12]. Static compliance ( $C_{st}$ ) is an important physiological index for evaluating the elastic properties of the overall respiratory system in invasive cases and is calculated by the ratio of the tidal volume to driving pressure [13].  $C_{st}$  can be monitored by setting an end-inspiratory occlusion in the volume-controlled ventilation (VCV) mode. During PCV, an appropriate inspiratory time should be preset to acquire the approximate plateau pressure ( $P_{plat}$ ). Nevertheless, setting an appropriate inspiratory time may be challenging because the patient's condition may change quickly. In addition, end-inspiration occlusion necessitates ventilation to be discontinued. Furthermore, this maneuver can be influenced by strong, spontaneous breathing. Therefore, other methods that do not require end-inspiratory occlusion need to be developed [14, 15].

Recently, methods have been proposed for the assessment of respiratory system properties without end-inspiration occlusion. Multiple linear regression (MLR), considering the least-squares fitting (LSF) technique, constitutes the most applied tool in recent years. It approximates  $C_{st}$  and  $R_{aw}$  with high accuracy in case of negligible spontaneous breathing effort [16–18]. Further tools encompass the constrained optimization strategy [19], electrical impedance tomography (EIT) monitoring, linear fitting of the flow velocity waveform, short expiratory occlusions, repeated changes in pressure support level, and artificial neural networks [20–23]. Still, the above techniques have some limitations: some do not adapt to spontaneous breathing conditions [16–18], while others apply sophisticated medical information or specific manual maneuvers, and others use empirical parameters [20, 22]. More importantly, most of them have more accurate measurements during VCV with constant inspiratory flow, with reduced accuracy when inspiratory flow

is variable, such as in the PCV and PSV modes or spontaneous breathing effort. Secondly, the noise interference of ventilation waveforms exists in the real clinical setting, and noises encompass spontaneous breathing efforts, suction, and coughing. Selecting adequate breaths that are less affected by noise might enhance accuracy in  $C_{st}$  and  $R_{aw}$  estimations.

In mechanically ventilated cases, expiration is a passive process depending on the expiratory time constant ( $RC_{exp}$ ) of the respiratory system.  $RC_{exp}$  reflects the mechanical features of the respiratory system [elastance and resistance ( $RC_{exp} = R_{aw} \times C_{rs}$ )] and reveals the changes in the features of the pneumatic respiratory system [24].  $C_{rs}$  and  $R_{aw}$  might be obtained from the passive deflation of lungs by using  $RC_{exp}$  and specific equations. In a previous bench study by the authors, the  $C_{rs}$  value was generally overestimated in the active breathing patient and underestimated in severe obstructive conditions, and the estimated error of  $R_{aw}$  by the  $RC_{exp}$  technique was minimal during passive breathing [15]. Recently, respiratory mechanics were estimated by modifying ventilation waveforms in the PCV mode to assess  $C_{st}$  and  $R_{aw}$  obtained by the end-inspiratory occlusion maneuver in the VCV mode. The continuous ventilation waveforms were examined, and an extra virtual tidal volume ( $V_T$ ) was calculated using  $RC_{exp}$  and an appropriate equation. Then, respiratory mechanics were estimated by analyzing the dynamic signals, which considerably improved static measurements. Such an approach improves estimation precision in respiratory system mechanics via real-time collection of respiratory data from the inspiration and expiration phases by applying specific Eqs. [25, 26].  $C_{st}$  and  $R_{aw}$  measurements based on the end-inspiratory occlusion maneuver in the real clinical setting were considered the gold standard for the validation of the proposed approach. The present study aimed to assess the accuracy of respiratory mechanical properties by the extra virtual  $V_T$  in the PCV mode.

## Methods

### Lung models

The ASL 5000 Breathing Simulator (IngMar Medical, Pittsburgh, PA, USA) features a computerized lung simulator with a piston that moves in a cylinder. This simulator was set to a single compartment based on a work by Beloncle et al. and previous bench studies by the authors [15, 27]. The applied respiratory mechanics parameters simulated an adult patient (65 to 70 kg body weight) placed in the semi-recumbent position. Six clinical scenarios with/without expiratory flow limitation (EFL) were constructed as follows [10, 28, 29]: healthy adult [inspiratory resistance ( $R_{insp}$ ) and expiratory resistance ( $R_{exp}$ ) of 5.0 cmH<sub>2</sub>O/L/s], mildly, moderate-to-severe obstruction [ $R_{insp}=R_{exp}=10.0, 15.0, \text{ and } 20.0$  cmH<sub>2</sub>O/L/s],

severe obstruction with EFL [ $R_{\text{insp}}=10.0 \text{ cmH}_2\text{O}/(\text{L}/\text{s})$ ,  $R_{\text{exp}}=20.0 \text{ cmH}_2\text{O}/(\text{L}/\text{s})$ ], and ARDS [ $R_{\text{insp}}=R_{\text{exp}}=10 \text{ cmH}_2\text{O}/(\text{L}/\text{s})$ ].  $C_{\text{st}}$  was set at 30 (ARDS) and 60 (COPD) mL/cmH<sub>2</sub>O, and inspiratory time at 0.8 s (ARDS) and 1.6 s (COPD). Inspired oxygen fraction ( $F_{\text{I}}\text{O}_2$ ) was 0.21 for all measurements.

### Ventilator settings

A dry circuit was used for the bench work, simulating a passive condition with both breathing frequency and  $P_{\text{mus}}$  of zero. A Hamilton C3 ventilator (Hamilton Medical AG, Bonaduz, Switzerland) was attached to the lung simulator calibrated by the end-inspiratory occlusion maneuver in the VCV mode utilizing a constant flow. The Hamilton C3 device was used in the VCV mode. Positive end-expiratory pressure (PEEP) was 5.0 cmH<sub>2</sub>O, and the backup breathing rate was 10 breaths/min. During VCV and PCV, respiratory mechanics setting was performed to maintain the output tidal volume ( $V_{\text{T}}$ ) at 5.0, 7.0, and 10.0 ml/kg. A reduced inspiratory rise time was applied to prevent overshooting in the PCV mode.

### Data collection

After baseline pressure stabilization, typical breaths were selected and recorded at 1-min intervals. Data were obtained for a total of six times after inspiratory pressure levels were adjusted in each lung model. All breaths were assessed offline using the ASL 5000 breathing simulator software.

Peak inspiratory flow (PIF), end-inspiratory flow (EIF), end-inspiratory pressure (EIP), and actual inspiratory time ( $T_{\text{I}}$ ) were determined using the simulator. Expiratory  $V_{\text{T}}$  was also evaluated. Peak expiratory flow (PEF) and total PEEP were collected in the expiration phase (Figure S1).

Respiratory mechanics indexes were considered the main determinants of the interaction between the patient and the ventilator. During PCV, the quasi-static two-point compliance of the respiratory system ( $C_{\text{rs}}$ ) was determined as  $V_{\text{T}}$  by driving pressure (DP). DP was the difference between EIP and total PEEP obtained at end-inspiration and end-expiration, respectively.  $RC_{\text{exp}}$  was the  $V_{\text{T}}$ /flow ratio at 75% of expiratory  $V_{\text{T}}$  [30]. The equations representing these relationships are:

Extra virtual tidal volume:

$$V_{\text{T virtual}} = RC_{\text{exp}} \times \text{EIF} \quad (1)$$

$$C_{\text{rs}} = (V_{\text{TE}} + V_{\text{T virtual}}) / (\text{EIP} - \text{PEEP}) \quad (2)$$

Inspiratory resistance ( $R_{\text{insp}}$ ) was derived from the following equations considering dynamic signals:

$$P_{\text{Ers insp}} = (V_{\text{TE}} - V_{\text{PIF}}) / C_{\text{rs}} \quad (3)$$

$$R_{\text{insp}} = [P_{\text{PIF}} - (\text{EIP} - P_{\text{Ers insp}})] / \text{PIF} \quad (4)$$

Expiratory resistance ( $R_{\text{exp}}$ ) was assessed with Eqs. 5 and 6:

$$P_{\text{Ers exp}} = (V_{\text{TE}} - V_{\text{PEF}}) / C_{\text{rs}} \quad (5)$$

$$R_{\text{exp}} = [P_{\text{PEF}} - (\text{EIP} - P_{\text{Ers exp}})] / \text{PEF} \quad (6)$$

The percentages of measurement errors for compliance or resistance (%error  $C_{\text{rs}}$  and %error  $R_{\text{aw}}$ ) were calculated as follows [27]:

$$\% \text{ error } C_{\text{rs}} = (C_{\text{rs-estimate}} - C_{\text{rs-VCV}}) / C_{\text{rs-VCV}} \times 100\% \quad (7)$$

$$\% \text{ error } R_{\text{aw}} = (R_{\text{aw-estimate}} - R_{\text{aw-VCV}}) / R_{\text{aw-VCV}} \times 100\% \quad (8)$$

### Statistical analysis

All analyses were performed using SPSS 19.0 (IBM, Armonk, NY, USA). Data were shown as means  $\pm$  standard deviations (SDs). The Shapiro-Wilk test was used for normality assessment. One-way ANOVA was used for comparisons in different settings.  $C_{\text{rs}}$ ,  $R_{\text{insp}}$ , and  $R_{\text{exp}}$  were calculated in the VCV mode using the end-inspiration occlusion approach and the dynamic signal analysis method with extra virtual  $V_{\text{T}}$  in the PCV mode, with a two-tailed  $t$ -test for comparisons. Absolute differences between the extra virtual  $V_{\text{T}}$  and occlusion methods were determined, and  $P < 0.01$  indicated statistical significance. Differences between PCV and VCV were determined as absolute percentages of values measured in the VCV mode.

### Results

#### EIF and extra virtual $V_{\text{T}}$ in the PCV mode under passive breathing

In PCV, EIF/PIF% was not above 5% in the non-severe obstructive lung models [ $R_{\text{aw}} \leq 10.0 \text{ cmH}_2\text{O}/(\text{L}/\text{s})$ ] and close to 0 in the ARDS lung model. EIF/PIF% was increased with the aggravation of airflow obstruction, i.e., about 10% at a  $R_{\text{aw}}$  of 20.0 cmH<sub>2</sub>O/L/s ( $P < 0.001$ ). Extra virtual  $V_{\text{T}}$  and the percentage of extra virtual  $V_{\text{T}}$  and  $V_{\text{TE}}$  ( $\Delta V_{\text{T}}\%$ ) were also increased (all  $P < 0.05$ ). Compared with the normal adult lung model, there were significant differences in EIF/PIF% and  $\Delta V_{\text{T}}\%$  under moderate to severe obstructive conditions (Table 1).

#### Estimation of $C_{\text{rs}}$ in various models in the VCV and PCV modes

Inspiratory  $V_{\text{T}}$  in the PCV mode was corrected by  $RC_{\text{exp}}$  and EIF. The estimated value of  $C_{\text{rs}}$  was larger than the value without extra virtual  $V_{\text{T}}$  calibration and close to the value obtained in the VCV mode with end-inspiratory

**Table 1** EIF/PIF% and  $\Delta V_T$ % in various lung models in the PCV mode

	<b>Normal adult</b> ( $C_{rs}=60$ , $R_{insp}=R_{exp}=5.0$ )	<b>Mild obstructive</b> ( $C_{rs}=60$ , $R_{insp}=R_{exp}=10.0$ )	<b>Moderate obstructive</b> ( $C_{rs}=60$ , $R_{insp}=R_{exp}=15.0$ )	<b>Severe obstructive</b> ( $C_{rs}=60$ , $R_{insp}=R_{exp}=20.0$ )	<b>Obstructive with EFL</b> ( $C_{rs}=60$ , $R_{insp}=10.0$ , $R_{exp}=20.0$ )	<b>ARDS</b> ( $C_{rs}=30$ , $R_{insp}=R_{exp}=10.0$ )
EIF/PIF%	1.34 ± 0.42	1.74 ± 0.86 ( $t=1.7732$ ) ( $P=0.0426$ )	5.55 ± 0.65* ( $t=23.0803$ ) ( $P<0.001$ )	10.86 ± 0.41* ( $t=68.8143$ ) ( $P<0.001$ )	1.80 ± 0.48* ( $t=3.0599$ ) ( $P=0.0022$ )	0.16 ± 0.20* ( $t=10.7619$ ) ( $P<0.001$ )
$\Delta V_T$ >%	1.12 ± 0.33	1.58 ± 0.75 ( $t=2.3818$ ) ( $P=0.0115$ )	4.66 ± 0.61* ( $t=21.6554$ ) ( $P<0.001$ )	10.07 ± 0.61* ( $t=54.7503$ ) ( $P<0.001$ )	1.67 ± 0.77* ( $t=2.7854$ ) ( $P=0.0043$ )	0.13 ± 0.16* ( $t=11.4528$ ) ( $P<0.001$ )

\* $P$  value (Student's  $t$ -test) for comparing normal adult and airflow obstruction lung models. Data are mean ± standard deviation, from 18 measurements/cases

**Table 2** System compliance ( $C_{rs}$ ) among lung models in different ventilatory modes

	<b>Normal adult</b> ( $C_{rs}=60$ , $R_{insp}=R_{exp}=5.0$ )	<b>Mild obstructive</b> ( $C_{rs}=60$ , $R_{insp}=R_{exp}=10.0$ )	<b>Moderate obstructive</b> ( $C_{rs}=60$ , $R_{insp}=R_{exp}=15.0$ )	<b>Severe obstructive</b> ( $C_{rs}=60$ , $R_{insp}=R_{exp}=20.0$ )	<b>Obstructive with EFL</b> ( $C_{rs}=60$ , $R_{insp}=10.0$ , $R_{exp}=20.0$ )	<b>ARDS</b> ( $C_{rs}=30$ , $R_{insp}=R_{exp}=10.0$ )
VCV	60.37 ± 0.65	59.93 ± 0.74	59.24 ± 2.06	57.38 ± 1.00	56.17 ± 1.23	30.16 ± 0.24
PCV	58.99 ± 0.60	58.37 ± 0.83	54.62 ± 1.15	49.28 ± 0.34	52.79 ± 1.02	29.97 ± 0.20
PCV-cal	59.92 ± 0.66* ( $t=2.0610$ ) ( $P=0.047$ )	59.03 ± 0.84	57.16 ± 1.25	54.24 ± 0.30	53.67 ± 1.04	30.01 ± 0.19* ( $t=2.0790$ ) ( $P=0.045$ )
$F$	21.96	17.05	40.56	747.05	45.68	18.59
$P$	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01

occlusion. The estimated  $C_{rs}$  decreased significantly with increasing severity of airflow obstruction in either ventilatory mode, and uncalibrated  $C_{rs}$  values were only 49.28 ± 0.34 mL/cmH<sub>2</sub>O (PCV mode) and 57.38 ± 1.00 mL/cmH<sub>2</sub>O (VCV mode) ( $P<0.01$ ) in the severe obstructive lung model [ $R_{aw}=20.0$  cmH<sub>2</sub>O/L/s]. After the correction of extra virtual  $V_T$ , the calculated errors were <5% in all four lung models [ $R_{aw} \leq 15.0$  cmH<sub>2</sub>O/L/s], which showed no significant differences compared with estimated values in the VCV mode (Table 2; Fig. 1A).

### Estimation of $R_{aw}$ in various models in the VCV and PCV modes

There were similar estimated  $R_{insp}$  and  $R_{exp}$  in the PCV and VCV modes with  $R_{aw} \leq 10.0$  cmH<sub>2</sub>O/L/s, and calculated errors were  $\leq 10.0\%$ . After  $V_T$  calibration, the estimated errors of  $R_{insp}$  and  $R_{exp}$  were reduced to <5%. In severe obstructive and obstructive with EFL models, the estimated errors of  $R_{insp}$  and  $R_{exp}$  were significantly reduced and were below 10% after  $V_T$  calibration (Tables 3 and 4; Fig. 1B and C).

### Bland-Altman analysis of differences between the PCV and VCV modes

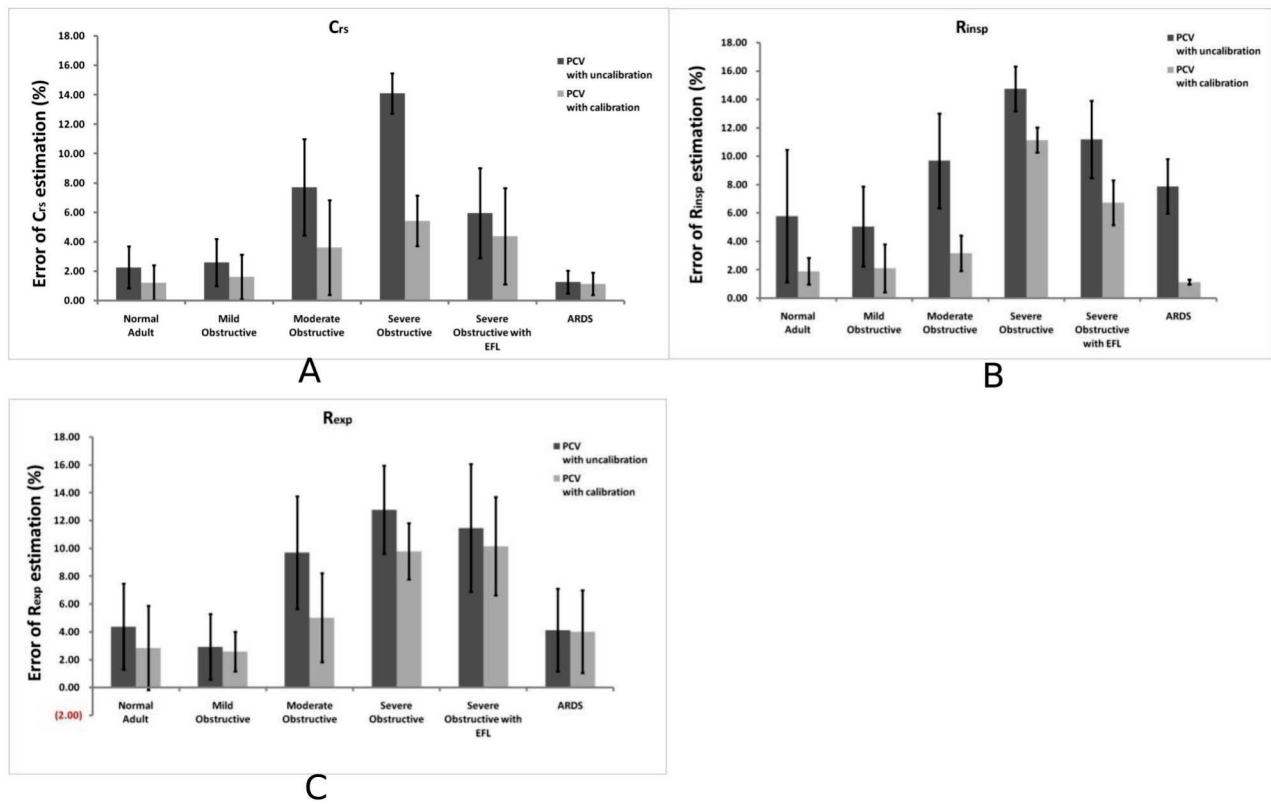
In all five lung profiles with normal system compliance (60.0 mL/cmH<sub>2</sub>O), the difference in  $C_{rs}$  between the  $V_T$  calibration and end-inspiration occlusion approaches was 1.82 ± 1.43 mL/cmH<sub>2</sub>O; the weighted correlation coefficient of  $C_{rs}$  equaled 0.549 after  $V_T$  calibration ( $P<0.001$ ). The differences of  $R_{insp}$  and  $R_{exp}$  values in all lung models

were 0.79 ± 1.96 × 0.89 and 0.38 ± 1.96 × 0.69 cmH<sub>2</sub>O/L/s, and the weighted correlation coefficients of  $R_{insp}$  and  $R_{exp}$  were equal to 0.954 and 0.969, respectively (all  $P<0.001$ ) (Figs. 2 and 3).

### Discussion

This bench study mostly revealed the following. (1) During PCV under the passive breathing condition, the estimated error was affected by the severity of airway obstruction, significantly underestimated in  $C_{rs}$ , and significantly overestimated in  $R_{aw}$  without  $V_T$  calibration. (2) In the non-severe obstructive condition [ $R_{aw} \leq 10.0$  cmH<sub>2</sub>O/L/s], estimated errors were  $\leq 10\%$  in calculated  $C_{rs}$  and  $R_{aw}$ . (3) The estimated accuracies of  $C_{rs}$ ,  $R_{insp}$ , and  $R_{exp}$  were improved by  $V_T$  calibration with extra virtual inspiratory volume.

During mechanical ventilation, assessing the respiratory mechanics by end-inspiratory occlusion with a constant inspiratory flow is a classic measurement method. However, the occlusion technique may be performed with no gas flow and fixed tidal volume. It is important for the patient to make no efforts during static measurements, whether related to disease, sedation, or paralysis, and special ventilatory settings are also required (such as constant inspiratory flow and end-inspiration pause) [31–33]. The most important concern is that measurement data are reflected by mechanical properties under static or quasi-static conditions. The occlusion method could neither be adapted to the PCV mode since inspiratory flow is always variable nor be used in assisted



**Fig. 1** (A) Errors of system compliance (Crs) in various lung models during PC ventilation. (B) Errors of Rinsp in different lung models during PC ventilation. (C) Errors of Rexp in different lung models during PC ventilation. Data are shown as mean ± SD

**Table 3** Comparison of R<sub>insp</sub> between lung models in different ventilatory modes

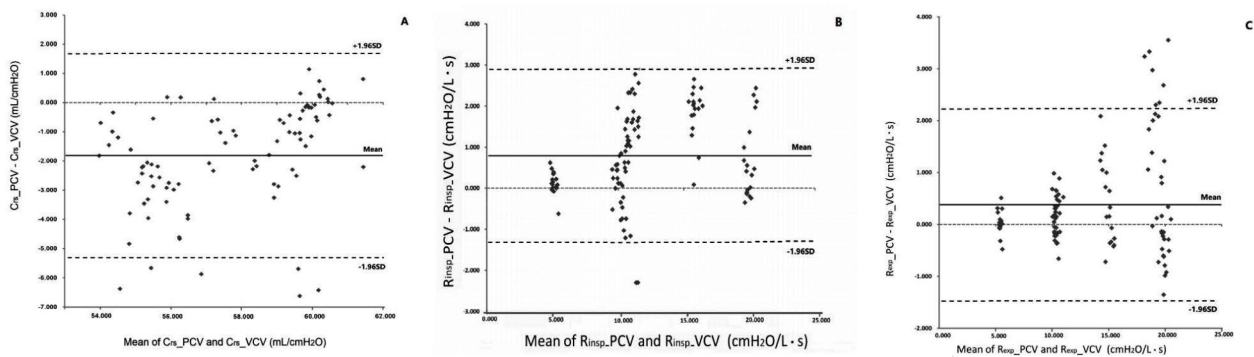
	Normal adult (C <sub>rs</sub> =60, R <sub>insp</sub> =R <sub>exp</sub> =5.0)	Mild obstructive (C <sub>rs</sub> =60, R <sub>insp</sub> =R <sub>exp</sub> =10.0)	Moderate obstructive (C <sub>rs</sub> =60, R <sub>insp</sub> =R <sub>exp</sub> =15.0)	Severe obstructive (C <sub>rs</sub> =60, R <sub>insp</sub> =R <sub>exp</sub> =20.0)	Obstructive with EFL (C <sub>rs</sub> =60, R <sub>insp</sub> =10.0, R <sub>exp</sub> =20.0)	ARDS (C <sub>rs</sub> =30, R <sub>insp</sub> =R <sub>exp</sub> =10.0)
VCV	5.05 ± 0.28	10.04 ± 0.25	14.93 ± 0.41	19.68 ± 0.37	10.25 ± 0.38	10.54 ± 1.02
PCV	5.27 ± 0.15	10.53 ± 0.39	16.31 ± 0.39	22.57 ± 0.81	11.38 ± 0.32	10.10 ± 0.33
PCV-cal	5.18 ± 0.14* (t = 1.7618) (P = 0.087)	10.72 ± 0.51	15.78 ± 0.43	22.38 ± 0.71	12.07 ± 0.43	10.09 ± 0.34* (t = 1.7757) (P = 0.085)
F	5.48	14.00	51.81	108.78	105.60	2.82
P	0.007	< 0.01	< 0.01	< 0.01	< 0.01	0.069

\*P-values (Student t-test) are for comparisons between the VCV and PCV modes. Data are shown as means ± standard deviations and are the results of 18 measurements/cases

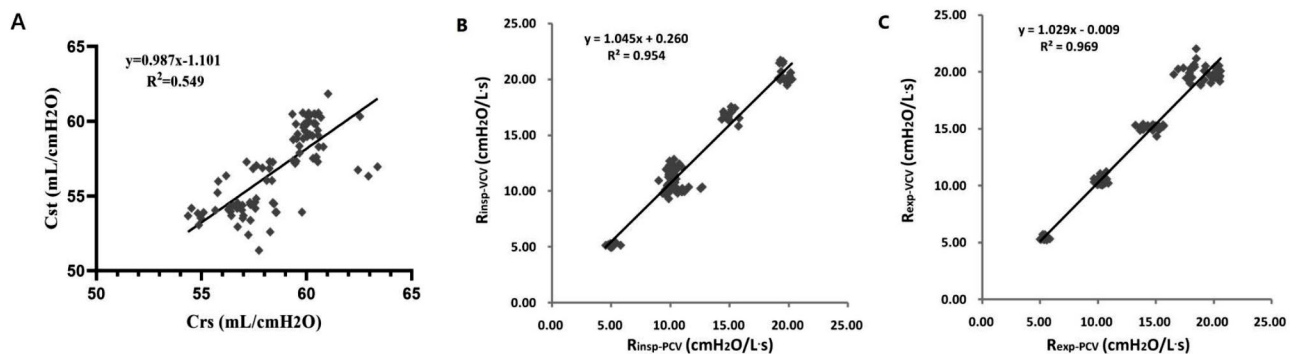
**Table 4** R<sub>exp</sub> values in lung models in different ventilatory modes

	Normal adult (C <sub>rs</sub> =60, R <sub>insp</sub> =R <sub>exp</sub> =5.0)	Mild obstructive (C <sub>rs</sub> =60, R <sub>insp</sub> =R <sub>exp</sub> =10.0)	Moderate obstructive (C <sub>rs</sub> =60, R <sub>insp</sub> =R <sub>exp</sub> =15.0)	Severe obstructive (C <sub>rs</sub> =60, R <sub>insp</sub> =R <sub>exp</sub> =20.0)	Obstructive with EFL (C <sub>rs</sub> =60, R <sub>insp</sub> =10.0, R <sub>exp</sub> =20.0)	ARDS (C <sub>rs</sub> =30, R <sub>insp</sub> =R <sub>exp</sub> =10.0)
VCV	5.38 ± 0.18	10.35 ± 0.22	14.69 ± 0.77	19.93 ± 0.47	19.44 ± 1.13	10.18 ± 0.29
PCV	5.57 ± 0.13	10.59 ± 0.59	16.08 ± 0.31	22.47 ± 0.41	20.48 ± 0.84	10.48 ± 0.28
PCV-cal	5.41 ± 0.15* (t = 0.5432) (P = 0.587)	10.42 ± 0.29* (t = 0.8159) (P = 0.420)	15.12 ± 0.26* (t = 2.2448) (P = 0.0314)	21.77 ± 0.36	20.06 ± 0.80* (t = 1.8999) (P = 0.066)	10.36 ± 0.28* (t = 1.8944) (P = 0.0667)
F	7.85	1.71	36.15	179.22	5.64	5.11
P	0.0011	0.1908	< 0.01	< 0.01	0.0061	0.0095

\*P values (Student's t-test) are for comparisons between the VCV and PCV. Data are mean ± standard deviation from 18 measurements/cases



**Fig. 2** Bland-Altman plots depicting system compliance (A), inspiratory resistance (B) and expiratory resistance (C) by the  $V_T$  calibration and end-inspiration occlusion approaches. Data from 5 ( $C_{rs}$ ) and 6 ( $R_{aw}$ ) lung models, in totally 168 breaths. Each circle reflects one breath for a given model. Dashed lines in the middle depict mean differences between the  $V_T$  calibration and end-inspiration occlusion approaches. The remaining two dashed lines are mean  $\pm 1.96*SD$



**Fig. 3** Associations of estimated  $C_{rs}$  (A),  $R_{insp}$  (B) and  $R_{exp}$  (C) with gold standard obtained by the end-inspiration occlusion approach. Data from 5 ( $C_{rs}$ ) and 6 ( $R_{aw}$ ) lung models, totally 168 breaths were examined. Each circle reflects one breath for a given model

ventilation in which the spontaneous effort is always present and variable. Recently, several continuous respiratory mechanics measurement techniques, including LSF and expiratory time constant method ( $RC_{exp}$ ), have been developed. These newer approaches not only have good adaptability and anti-noise-interference performance but also could be applied during assisted mechanical ventilation with spontaneous breathing [34].

Volta et al. found that EFL substantially reduces the accuracy of resistance and compliance assessed by the LSF method; the determination of respiratory indexes during inspiration helps evaluate respiratory mechanics in flow-limited COPD cases, and the LSF technique could detect  $PEEP_{i,dyn}$  only using inspiratory data [18]. However, the estimated error of LSF was affected by the spontaneous breathing effort, and  $R_{aw}$  underestimation and  $C_{rs}$  overestimation were observed in the PSV mode [16, 35]. The other approaches have certain limitations. Some could not deal with significant spontaneous breathing, while others are based on sophisticated medical equipment or manual maneuvers, preventing their routine clinical use [18–22]. Recently, Pan et al. proposed

a tool measuring quasi-static respiratory system compliance ( $C_{q-stat}$ ) in the PCV mode without the need for the end-inspiratory occlusion maneuver, with a virtual assessment of flow-time waveforms with end-inspiration flow not equaling zero, to allow for  $C_{q-stat}$  determination [14]. In this bench study, the dynamic signal analysis approach was used to collect and calculate gas flow, airway pressure, and volume data at different time points during mechanical ventilation, and the estimated  $C_{rs}$ ,  $R_{insp}$ , and  $R_{exp}$  were calibrated by virtual extrapolation of  $V_T$  when end-inspiration flow was not zero. Dynamic signal analysis does not require special maneuvers such as long-time pauses at the inspiration or expiration phase [26]. In healthy adults and mild obstruction lung models, no significant differences were found in estimated  $C_{rs}$  and  $R_{aw}$  ( $R_{insp}$  and  $R_{exp}$ ) between the PCV and VCV modes with  $EIF < 2.0$  L/min and  $EIF/PIF\% < 5.0\%$ . The calculated error was increased when  $EIF/PIF\%$  was above 5% in the PCV mode. Due to the exacerbation of airflow obstruction, PIF was decreased, and EIF did not drop to zero at the end of inspiration.  $EIF/PIF\%$  was increased to about 10%, resulting in  $V_T$  decrease,  $C_{rs}$  underestimation, and

$R_{aw}$  overestimation. After  $V_T$  calibration with  $RC_{exp}$  and EIF, the accuracy of the estimation was improved significantly, and the values obtained were similar to those estimated in the VCV mode by the occlusion method.

In the classic system compliance ( $C_{rs}$ ) calculation equation,  $C_{rs}$  is the ratio of the monitored tidal volume ( $V_T$ ) to the driving pressure (DP) of the airway. The tidal volume is the sum of the gas output capacity of the ventilator during the inhalation phase. In the classic calculation scheme, the tidal volume is the gas output capacity value measured after the end-inspiratory flow rate reaches 0. On the other hand, in this study, due to the special nature of the PCV mode, the end-inspiratory flow rate does not always decrease to 0. Therefore, an additional parameter (i.e., the extra virtual tidal volume) was designed to simulate the gas capacity generated after the flow rate continued to decrease to 0. It was found that the addition of the extra virtual tidal volume was of great significance for calculating  $C_{rs}$  under the PCV ventilation state.

One of the limitations of the present bench study is the standardization of simulation indexes for the respiratory system's mechanics in the lung model. Although the mechanical lung simulator cannot completely replace animal experiments and real clinical practice, the ASL 5000 mechanical lung simulator also has its unique advantages. Firstly, it can simulate simple single-chamber linear models and complex lung mechanics models with dual-chamber nonlinearity. In this study, we attempted to explore a new respiratory mechanics calculation scheme that can be applied to non-interrupted breathing and non-constant inspiratory flow mechanical ventilation conditions and can accurately calculate the respiratory mechanics characteristics of patients with different respiratory system diseases. Therefore, a mechanical lung simulator was first used for the experiment because its output data is relatively stable, and this lung simulator is also often selected in many mechanical simulation experiments. Further animal experiments will be conducted in the future [36]. Secondly, the passive breathing condition was simulated during PCV since spontaneous breathing effort might affect  $V_T$  and  $C_{rs}$ . It is not clear whether this scheme could be applied to other assisted ventilatory modes such as PSV. Thirdly, airway resistance varies with gas flow through the trachea and bronchus. Therefore, the above data reflect maximal resistance in a patient during breathing, and whether they can be translated in the clinical setting is unknown. Therefore, further clinical trials are warranted.

## Conclusion

Using the modified dynamic signal analysis approach, respiratory system properties ( $C_{rs}$  and  $R_{aw}$ ) could be accurately estimated in patients with non-severe airflow obstruction in the PCV mode. Compared with the VCV

mode with constant flow, inspiratory flow decreased exponentially in the PCV mode. PIF and the deceleration rate of inspiratory flow were dependent upon the mechanical characteristics of the respiratory system, especially airflow obstruction.

## Abbreviations

PCV	Pressure-controlled ventilation
COPD	Chronic obstructive pulmonary disease
VCV	Volume-controlled ventilation
$V_T$	Tidal volume
DP	Drive pressure
PIF	Peak inspiratory flow
PEF	Peak expiratory flow
EIF	End-inspiration flow
EIF/PIF%	Inspiratory cycling ratio
$R_{aw}$	Airway resistance
$C_{st}$	Static compliance
$P_{plat}$	Plateau pressure
MLR	Multiple linear regression
LSF	Least-squares fitting
EIT	Electrical impedance tomography
$RC_{exp}$	Expiratory time constant
EFL	Expiratory flow limitation
PEEP	Positive end-expiratory pressure
EIP	End-inspiration pressure
$T_i$	Inspiratory time
$C_{rs}$	Respiratory system compliance
DP	Driving pressure
SD	Standard deviation
$C_{q-stat}$	Quasi-static respiratory system compliance

## Supplementary Information

The online version contains supplementary material available at <https://doi.org/10.1186/s12890-024-03061-2>.

Supplementary Material 1

Supplementary Material 2

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Not applicable.

## Author contributions

Yuqing Chen and Feng Li contributed to the concept and drafted the manuscript or substantively revised it. Yueyang Yuan contributed to the manuscript design. Qing Chang, Hai Zhang, and Zhaohui Chen contributed to data acquisition and analysis. FL contributed to the interpretation of the data. All authors read and approved the final manuscript.

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## Data availability

All data generated or analyzed during this study are included in this article.

## Declarations

### Ethics approval and consent to participate

This study does not involve humans and animals and is a purely mechanical simulation test with no ethical or consent required.

### Consent for publication

Not applicable.

**Competing interests**

The authors declare no competing interests.

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