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SHORT COMMUNICATION

The endotracheal tube biases the estimates of pulmonary recruitment and overdistension

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Abstract To assess the impact of the endotracheal tube (ETT) and of different flow waveforms on estimates of alveolar cyclic recruitment (CR) and overdistension (AO). Numerical simulation of the respiratory system plus ETT (inertance L plus a flow-dependent resistance, K_1 and K_2), with the following non-linear equation of motion

$$P_{\mathrm{AW}}(\mathrm{t}) = \left(\left(K_1 + K_2 \cdot \left|\dot{V}(\mathrm{t})\right|\right) \cdot \dot{V}(\mathrm{t}) + L \cdot \ddot{V}(\mathrm{t})\right) + \mathrm{Rrs} \cdot \dot{V}(\mathrm{t}) + (E_1 + E_2 \cdot V(\mathrm{t})) \cdot V(\mathrm{t}) + P_0$$

(P_{AW} pressure at the airways opening, V volume), under volume-controlled mechanical ventilation. An index $\%E_2 = 100 \cdot (E_2 \cdot V_{\mathrm{T}})/(E_1 + E_2 \cdot V_{\mathrm{T}})$ can be calculated where $\%E_2 > 30\%$ represents AO and $\%E_2 < 0\%$ represents CR. Parameters were estimated by the least-squares method, either with the complete equation or supressing L, K_2 or both. $\%E_2$ is always underestimated (down to –152 percent points) with incomplete equations of motion. The estimation of $\%E_2$ may be strongly biased in the presence of an ETT excluded from the estimation model.

Keywords Respiratory mechanics · Alveolar overdistension · Tidal recruitment · Model identification · Non-linear models

List of symbols

ALI	Acute lung injury
AO	Alveolar overdistension
CR	Cyclic recruitment
E_1	Linear elastance
$E_2.V$	Volume-dependent elastance
$\%E_2$	Contribution of the volume-dependent elastance to the total elastance
ETT	Endotracheal tube
K_1	Linear resistance of the ETT
$K_2\left\|\dot{V}(\mathrm{t})\right\|$	Flow-dependent resistance of the ETT
L	Inertance
P_0	Airways pressure when volume and respective derivatives are zero
P_{AW}	Pressure at the airways opening
Pel	Elastic component of the airways pressure
Pel-V	Elastic pressure–volume relationship
PEEP	Positive end-expiratory pressure
Pinf	Mathematical inflection point of the Pel-V curve
Pmcd	Point of maximal decrease of compliance
Pmci	Point of maximal increase of compliance
Rrs	Resistance of the respiratory system
RS	Respiratory system
VCV	Volume-controlled ventilation
V_{T}	Tidal volume
V(t)	Volume
$\dot{V}(\mathrm{t})$	Flow
$\ddot{V}(\mathrm{t})$	Time-derivative of the flow

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1 Introduction

The mathematical modeling of the mechanical properties of the respiratory system (RS) constitutes a valuable tool to monitor RS disorders. In the last years, extensions of the classical resistance-plus-elastance model of the RS have been proposed to describe changes in the shape of the elastic component of the airway pressure versus volume curve (Pel-V) during mechanical ventilation. These changes have been associated with tidal alveolar overdistension (AO, characterized by an upward concavity in Pel-V) and cyclic (or tidal) recruitment (CR, reflected as a downward concavity in Pel-V). Ranieri et al. [10] showed that avoiding AO and CR during volume-controlled mandatory ventilation (VCV) with constant inspiratory flow, achieved by keeping the time course of airway pressure (P_{AW}) during inspiration close to a straight line, reduced the lung mechanical stress and inflammation and probably constitutes a protective ventilatory approach.

Also seeking to identify AO, Kano et al. [7] proposed the use of a non-linear unicompartmental model to fit the respiratory mechanics, in which the elastance has a volume-independent and a volume-dependent term. Those authors suggested that an index derived from this model could detect AO by quantifying the weight of the non-linearity of the Pel in patients under VCV. Bersten [1], using the same model, showed that AO was a common finding in patients with acute lung injury (ALI) and that this model may be useful to guide the mechanical ventilator settings. Edibam et al. [3], in their turn, found that the flow pattern and respiratory timings of the mechanical ventilation influenced the estimates of the volume-dependent model, in ALI patients in either pressure-controlled or VCV, further supporting the use of such a model to assess the status of the respiratory system in disease conditions.

Nevertheless, the numerical computational estimation of mechanical model parameters may be susceptible to various sources of errors. Sullivan et al. [12] demonstrated that the estimates of elastance and resistance of the classical unicompartmental mechanical model can be distorted if the inertance and flow-dependent resistance of the endotracheal tube (ETT) are not included in the fitted model. This and other studies, applied to different areas of physiology such as cardiovascular mechanics (Spaan [11]) indicate that neglecting the non-linearities present in the resistive component may considerably bias the elastic estimates.

However, to clinically evaluate the ability of the index proposed by Kano et al. [7] to effectively indicate AO as well as CR, its sources of biases must be known and compensated for, in order to avoid misdirecting ventilatory settings by erroneous interpretations of the patient's status and of the effects of ventilatory strategies. In view of the potential bias generated in elastance estimates by the presence of an inertive and non-linearly resistive ETT, this work aims to assess, through numerical simulation, the impact of neglecting the ETT characteristics and also the effects of different flow waveforms on parameter estimates of the RS mechanics, particularly on Kano's index applied to detect AO and CR.

2 Materials and methods

2.1 Model

The numerically simulated model features a linear resistance, representing the resistive behavior of the RS (Rrs, set to 5 $cmH_2O.s.L^{-1}$), in series with a linear (K_1) plus a flow-dependent (K_2) resistance and an inertance (L), to model the characteristics of the ETT. Three value sets for K_1, K_2 and L, as given by Sullivan et al. [12], corresponding to ETTs with internal diameters of 6, 7 and 8 mm were used.

The elastic component of the RS was modeled as in Eq. 1

$$\mathrm{Pel}(V(\mathrm{t})) = (E_1 + E_2 \cdot V(\mathrm{t})) \cdot V(\mathrm{t}) \tag{1}$$

where V(t) is the time course of the tidal volume, E_1 is the volume-independent elastic term and ($E_2.V$(t)) is the volume-dependent term. The elastic pressure fitted a quasi-static Pel-V curve obtained from a patient with acute respiratory distress syndrome (ARDS) [5]. In brief, the expiratory limb of the Pel-V curve of the patient was non-linearly fitted by the Levenberg-Marquardt algorithm [5] to the sigmoidal model proposed by Venegas et al. [14]:

$$V(\mathrm{Pel_V}) = a + \left[\frac{b}{1 + e^{\frac{-(\mathrm{Pel_V} - c)}{d}}}\right] \tag{2}$$

where Pel is the elastic pressure, V is the expiratory volume and a, b, c, and d are the coefficients to be adjusted. From these parameters, three fiducial points of the curve were obtained, the points of maximal increase/decrease of compliance (respectively, Pmci and Pmcd) and the mathematical inflection point (Pinf) [5]. Then, three pressure–volume point sets were calculated around each of the fiducial points of the fitted curve, spanning 0.6 l with increments of 1 ml. Finally, three pairs of E_1 and E_2 were obtained by fitting second-degree polynomials to each of the point sets. Each set of E_1 and E_2 corresponds to regions of the Pel-V curve which, according to Kano et al. [7] and Bersten [1], suggest recruitment ($\%E_2 < 0$), a linear behavior ($\%E_2 \approx 0$), and overdistension ($\%E_2 > 30\%$) (see Fig. 1).

The equation of motion employed to simulate the complete model is:

$$\begin{aligned} P_{AW}(t) = &\left(\left(K_1 + K_2 \cdot \left|\dot{V}(\mathrm{t})\right|\right) \cdot \dot{V}(\mathrm{t}) + L \cdot \ddot{V}(\mathrm{t})\right) \\ &+ \mathrm{Rrs} \cdot \dot{V}(\mathrm{t}) + (E_1 + E_2 \cdot V(\mathrm{t})) \cdot V(\mathrm{t}) + P_0 \end{aligned} \tag{3}$$

where $P_{AW}(t)$ is the pressure measured at the airways opening at time t, $\dot{V}$(t) is flow, V(t) is volume and P_0 is the airways pressure when volume and respective derivatives are zero.

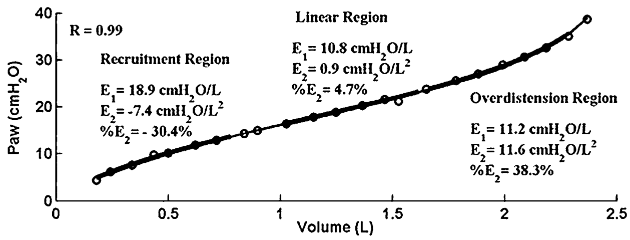

Fig. 1 Measured data points (*open circles*) and fitted sigmoidal curve (*thin line*) of the descendent Pel-V limb obtained from the patient. The *thick segments* represent the volume excursions that drove the model to render the different sets of E_1 and E_2. P_{AW} is the pressure at the airways opening

The ventilator was modeled as a flow source during inspiration and a pressure source (0 cmH_2O) during expiration, with its tubing modeled as a linear resistor (2 $cmH_2O.s.L^{-1}$), plus a compliance (2 ml cmH_2O^{-1}) representing the circuit's compressible volume. The ventilator was simulated in VCV with either constant or descendent inspiratory flow, at a respiratory rate of ten breaths per minute and P_0 was set to zero. The expiratory time was set to 4.5 s, sufficient to allow for complete expiration in every condition. The tidal volumes provided by the ventilator were adjusted in order to compensate the loss due to the tubing's compressible volume. Hence, the effective volume delivered to the RS was kept constant at 0.6 l in every case, with errors below 1 ml.

The simulations were performed in Simulink (MathWorks, USA) at a fixed rate of 1,000 samples per second, with the ODE5 algorithm. Four cycles were simulated in each condition. The trapezoidal integration of the simulated flow from each respiratory cycle rendered the volume signal.

2.2 Parameter estimation

In each condition, the mechanical parameters were estimated by the least-squares method from the third simulated cycle, to avoid transient effects. In addition to estimating the parameters with the complete model as in Eq. 3 (Model 0), three other sets of estimates for each simulation were calculated, removing from Model 0, respectively, the components K_2 (Model 1), L (Model 2) and both (Model 3).

Kano's index was calculated from all simulated sets according to Eq. 4:

$$\%E_2 = 100 \cdot \left(\frac{E_2 \cdot V_T}{E_1 + E_2 \cdot V_T} \right) \tag{4}$$

.

3 Results

The Pel-V curve employed in this work is shown in Fig. 1. The data points and the fitted sigmoidal curve are displayed, as well as the recruitment, linear and overdistension regions. Figure 2 depicts the fitting residuals for Models 0 and 3 for the case with an ETT of 7 mm and square flow waveform.

Table 1 shows the estimates of $\%E_2$ for each simulation with different ETT diameters and flow waveforms. Note that $\%E_2$ was always underestimated with Models 1–3, and that the underestimation tends to increase with the reduction in the ETT size. Note also that Model 3 always presents the highest bias, irrespective of flow waveform, ETT size or region of Pel-V curve.

It is also noteworthy that, whereas Model 0 is, as expected, practically insensitive to any change in simulation conditions, Model 3 is clearly the most sensitive to changing from square to descendent waveform, and this sensitivity seems to be importantly dependent on the ETT size. Notwithstanding the presence of bias in every condition, the other two models seem to behave somewhat erratically as to the effects of changing the conditions. This is especially true with Model 2 and descending waveform: in this case, ETT of 7 mm always presented the largest bias.

Further processing of the signal to simulate more realistic experimental conditions were performed by filtering the signals with a 4th-order lowpass Butterworth filter with cutoff frequency 33 Hz and downsampling the filtered signal to 200 Hz. The resulting estimates, however, did not differ significantly from those obtained from the original signals.

Fig. 2 Residuals between the simulated and estimated P_{AW} on the estimates with the Model 0 (*thin line*) and the Model 3 (*dashed line*), with respective coefficients of determination (R^2) and residual mean square differences (RMSD) (ETT of 7 mm, square flow waveform)

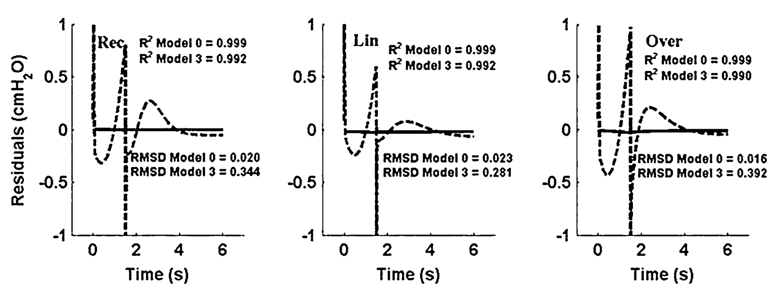

Table 1 Calculated $\%E_2$ with different ETT, flow waveforms and estimation models

		ETT (6 mm)			ETT (7 mm)			ETT (8 mm)		
		Simulated $\%E_2$			Simulated $\%E_2$			Simulated $\%E_2$		
		Rec	Lin	Over	Rec	Lin	Over	Rec	Lin	Over
Flow waveform	Estimation models	–30.4	4.7	38.3	–30.4	4.7	38.3	–30.4	4.7	38.3
Square	Model 0	–30.2	4.9	38.3	–30.2	4.9	38.3	–30.2	4.8	38.3
	Model 1	–61.0	–26.9	10.8	–48.4	–14.9	22.4	–42.6	–8.9	27.6
	Model 2	–47.1	–15.7	24.8	–46.6	–14.2	26.7	–44.4	–10.7	28.7
	Model 3	–71.4	–36.2	4.15	–59.7	–24.9	15.1	–53.1	–18.1	20.8
Descendent	Model 0	–30.3	4.7	38.2	–30.3	4.7	38.3	–30.3	4.7	38.3
	Model 1	–117.6	–90.4	–21.6	–67.9	–39.7	12.1	–50.6	–21.3	23.9
	Model 2	–40.3	–0.9	30.8	–42.7	–3.8	29.6	–40.7	–4.5	31.7
	Model 3	–121.7	–93.8	–23.8	–72.9	–43.1	9.4	–54.9	–24.5	21.2

4 Discussion

The estimation of lung stress from respiratory mechanics may be useful in reducing lung inflammation, as shown by Ranieri et al. [10]. The volume-dependent elastance model constitutes therefore a potential bedside monitor for lung stress, helping to titrate PEEP [1] and thus replacing demanding methods such as the quasistatic Pel-V curve [9]; moreover, it may be employed with any flow waveforms, differently from the stress index employed by Ranieri et al. [10].

Nevertheless, the present results suggest that the $\%E_2$ index may be rather sensitive to the ventilatory set-up and showed that the assumption of negligible inertance and non-linear resistive component may strongly influence the estimation of $\%E_2$. The data in Table 1 indicate that the estimated Pel-V concavity is biased downwards in these cases, which may result in an erroneous interpretation of the status of the respiratory mechanics. On the other hand, the technique proposed by Ranieri et al. [10] may be less sensitive to the presence of either an inertance or a non-linear resistance, provided that the stress index is calculated in a rather constant flow interval.

In accordance with Sullivan et al. [12], who pointed out the influence in the estimates of elastance if the inertance and the flow-dependent resistance of the endotracheal tube (ETT) were not considered, Lanteri et al. [8] showed that omitting the inertance term in a volume-dependent model model of elastance causes important effects on parameter estimates in mechanically ventilated puppies. In addition, regarding the signal processing, Jandre et al. [6] showed that interchannel sampling delays and heterogeneous filtering of the signals used in the estimation of the parameters of ventilatory mechanics may cause considerable bias in the estimates of the volume-dependent model [6].

The interactions between ETT characteristics and the flow waveforms may be the origin of the bias in $\%E_2$. As the peak inspiratory flow increases, so does the flow-dependent component of resistance; as the derivatives of flow grow larger, the inertial effects also increase. It seems as though these two effects take part in biasing $\%E_2$. Higher values of K_2 and inertance, with the reduction of the ETT size, magnify the bias of $\%E_2$, more prominently under descendent flow waveform, in which both the peak flow and the flow derivative are higher. However, possibly due to the complicated dynamics generated by the interactions between the elements of the model, less intuitive results also appear, as observed with Model 2 and descendent flow waveform.

The present results lead to the conjecture that, at least in part, previous findings, for instance those of Edibam et al. [3], could be explained by estimation artifacts similar to the ones shown in the present study, besides possible true changes in the underlying mechanics of the RS. Those authors reported that the $\%E_2$ estimated during pressure-controlled ventilation was significantly lower than that estimated during square flow VCV, although no difference in hyperinflated areas were found, as assessed by computed tomography. In the present study, the descendent flow waveform in VCV approaches that of pressure-controlled ventilation and further supports the conjecture.

Our results are paralleled by experimental findings, besides those of Sullivan et al. [12] and Lanteri et al. [8]. Some authors have shown that the estimated elastance may be flow- and volume-dependent [4, 13]. These entangled effects were pointed out by Dries and Marini [2] as one of the causes of the elusiveness of the "best PEEP" as a target to be pursued. The question arises whether these dependencies have come from true changes in elastic properties or from estimation artifacts, such as shown here. In the present study, the concept of avoidance of AO or CR, as identified by $\%E_2$, by changes in ventilatory settings (lowering the tidal volume or PEEP), is hindered by the resulting estimation artifacts, therefore blunting the efforts in seeking for a "best PEEP" defined by the estimated mechanical properties of the lungs, such as suggested by Ranieri et al. [10]. In taking $\%E_2$ as a guide to set mechanical ventilation, the kind of error reported here may encourage the therapist to apply higher levels of PEEP, higher volumes, or even to perform a recruitment maneuver in order to achieve the linear concavity of the dynamic Pel-V. The use of more complete models, however, may require enhanced attention to reduce estimation bias that may induce misinterpretations and potentially harmful ventilatory settings [6]. These effects may have particularly important implications in the study of pediatric respiratory mechanics, for instance, in which higher respiratory rates involve further increase in inertial pressures [8].

A limitation of this study lies in that the Pel-V data used in the simulation comes from a quasi-static inflation maneuver in a patient. Notwithstanding previous experimental findings, that show good agreement between the quasistatic and dynamic Pel-V estimated by non-linear elastic models [9], quasistatic curves are only partially representative of the dynamic Pel-V behavior of the lung of an injured patient during mechanical ventilation. Optimal ventilation of the injured lung is presumably a matter of minimizing the tissue stresses generated, regardless of the origin, and these stresses are best reflected in the nature of the dynamic Pel-V relationship. Nevertheless, this work intends to test the hypothesis that a known, fixed $\%E_2$ parameter, that remains independent of all other parameters and ventilatory settings, is differently estimated due to the chosen model. In any circumstance, it is interesting to have unbiased parameter estimation, in the interest of robustness and comparability, for instance when comparing among individuals or across different set-ups for the same individual.

In conclusion, the present work supports the knowledge that comparing estimates of mechanical properties under different ventilatory settings or employing different ETTs may be impaired by resulting biases; consequently, differences between individuals or groups may be concealed or artificially generated, impacting the interpretation of the results of a study and comparisons between studies. The evidences that ventilatory set-up may affect the estimates of the elastic characteristics of the respiratory system even in the absence of true changes, effect that is enhanced by model incompleteness, shall guide efforts around the instrumentation, modeling and algorithms employed in the analysis of the respiratory system mechanics. Further studies seeking to assess the clinical significance of the $\%E_2$ shall be aware of this potential source of bias to this index. The present study stresses the recommendations for keeping similar ventilatory conditions in experiments involving estimation of parameters of the respiratory mechanics, and for checking for possible non-linearities and higher order dynamics that should be included in the model employed in data analysis.

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References

1. Bersten AD (1998) Measurement of overinflation by multiple linear regression analysis in patients with acute lung injury. Eur Respir J 12:526–532
2. Dries DJ, Marini JJ (2002) Optimized positive end-expiratory pressure—an elusive target. Crit Care Med 30:1159–1160
3. Edibam C, Rutten AJ, Collins DV, Bersten AD (2003) Effect of inspiratory flow pattern and inspiratory to expiratory ratio on nonlinear elastic behavior in patients with acute lung injury. Am J Respir Crit Care Med 167:702
4. Fahy BG, Barnas GM, Flowers JL, Nagle SE, Agarwal M (1997) Effects of PEEP on respiratory mechanics are tidal volume and frequency dependent. Respir Physiol 109:53–64
5. Harris RS, Hess DR, Venegas JG (2000) An objective analysis of the pressure–volume curve in the acute respiratory distress syndrome. Am J Respir Crit Care Med 161:432–439
6. Jandre FC, Carvalho AR, Pino AV, Giannella-Neto A (2005) Effects of filtering and delays on the estimates of a nonlinear respiratory mechanics model. Respir Physiol Neurobiol 148:309–314
7. Kano S, Lanteri CJ, Duncan AW, Sly PD (1994) Influence of nonlinearities on estimates of respiratory mechanics using multilinear regression analysis. J Appl Physiol 77:1185–1197
8. Lanteri CJ, Petak F, Gurrin L, Sly PD (1999) Influence of inertance on respiratory mechanics measurements in mechanically ventilated puppies. Pediatr Pulmonol 28:130–138
9. Muramatsu K, Yukitake K, Nakamura M, Matsumoto I, Motohiro Y (2001) Monitoring of nonlinear respiratory elastance using a multiple linear regression analysis. Eur Respir J 17:1158–1166
10. Ranieri VM, Zhang H, Mascia L, Aubin M, Lin CY, Mullen JB, Grasso S, Binnie M, Volgyesi GA, Eng P, Slutsky AS (2000) Pressure–time curve predicts minimally injurious ventilatory strategy in an isolated rat lung model. Anesthesiology 93:1320–1328
11. Spaan JAE, Cornelissen AJM, Chan C, Dankelman J, Yin FCP (2000) Dynamics of flow, resistance, and intramural vascular volume in canine coronary circulation. Am J Physiol Heart Circ Physiol 278:383–403
12. Sullivan M, Paliotta J, Saklad M (1976) Endotracheal tube as a factor in measurement of respiratory mechanics. J Appl Physiol 41:590–592
13. Suter PM, Fairley HB, Isenberg MD (1978) Effect of tidal volume and positive end-expiratory pressure on compliance during mechanical ventilation. Chest 73:158–162
14. Venegas JG, Harris RS, Simon BA (1998) A comprehensive equation for the pulmonary pressure–volume curve. J Appl Physiol 84:389–395