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ORIGINAL PAPER

Lung mechanics - airway resistance in the dynamic elastance model

B. Laufer[1] · **J. Kretschmer**[1] · **P. D. Docherty**[2] · **Y. S. Chiew**[3] · **K. Möller**[1]

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Abstract The selection of optimal positive end-expiratory pressure (PEEP) levels during mechanical ventilation therapy of patients with acute respiratory distress syndrome (ARDS) remains a problem for clinicians. A particular mooted strategy states that minimizing the energy transferred to the lung during mechanical ventilation could potentially be used to determine the optimal, patient-specific PEEP levels. Furthermore, the dynamic elastance model of pulmonary mechanics could possibly be applied to minimize the energy by localization of the patients' minimum dynamic elastance range. The sensitivity of the dynamic elastance model to variance in the airway resistance was analyzed. Additionally, the airway resistance was determined by using three other established identification methods and was compared to the constant resistance obtained by the dynamic elastance model. For increasing PEEP, the alternative identification methods showed similar decreasing trends of the resistance during inspiration. This declining trend is apparently an exponential decrease. Results showed that the constant airway resistance, presumed by the dynamic elastance model, has to be rechecked and investigated.

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✉ B. Laufer
b.laufer@hs-furtwangen.de

[1] Institute of Technical Medicine (ITeM), Furtwangen University, Jakob Kienzle Str. 17, 78054 Villingen-Schwenningen, Germany

[2] Department of Mechanical Engineering, University of Canterbury, Christchurch, New Zealand

[3] School of Engineering, Monash University Malaysia, Bandar Sunway, Malaysia

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1 Introduction

Many studies have been carried out to determine optimal lung protective ventilation settings and improvements to patient outcomes have been achieved [1–4]. However, the selection of the optimal positive end-expiratory pressure (PEEP) level is still a challenge in treating patients with acute respiratory distress syndrome (ARDS) [5–8]. One approach to support the clinicians in managing mechanical ventilation setting is via physiological modelling of the pulmonary pressure-flow mechanics. The simplest known physiological model to describe the behaviour of the respiratory system is a first order model (FOM) [9]. The FOM models the airway resistance and pulmonary elastance as constant terms and its equation is as shown in Eq. (1).

$$P = EV + R\dot{V} + P_0 \tag{1}$$

where: P is the airway pressure, P_0 is the offset pressure, V is the tidal volume, $\dot{V}$ is the airway flow, R is the respiratory system resistance and E is the respiratory system elastance.

A FOM offers simplicity of modelling at the cost of descriptive ability and thus it cannot capture all pressure-flow characteristics of the breathing process. Bates et al. [10] referred to two different strategies to counter that problem – either increase model complexity or introduce non-linear parameters in the model. This study is based on the work of Chiew et al. [11, 12], who modified the FOM to include non-linear pressure-variant dynamic elastance *E(P)* but constant resistance *R*. *E(P)* was determined after an initial linear

regression identification of a constant R value over a single inspiratory period via evaluating Eq. (2).

$$E(P) = \frac{P - P_0 - R\dot{V}}{V} \tag{2}$$

Suter et al. proposed to set the pressure range of mechanical ventilation into the range of maximum compliance (the reciprocal of the elastance) [13]. They recommended a concept of reducing the incidence of ventilator induced lung injury (VILI) through minimizing energy transferred into the lung of the patient by mechanical ventilation. They showed that this energy is correlated to the compliance of the lung. Therefore, Chiew et al. made a well-supported assumption that the optimal PEEP level can be set in the region of the tidal pressure where the minimum of the dynamic pressure-dependent elastance curve appears [14]. The overall goal of the dynamic elastance model is to support the clinicians in the selection of the optimal PEEP level and mechanical ventilation in the range of minimal elastance is a worthwhile trial to prevent VILI. Aspects of energy represented by the dynamic elastance model can be split into two parts: the energy related to the airways (resistance to flow); and the energy related to the tissue elastance (resistance to expansion). Obviously, lung protective ventilation should use the minimization of the elastance energy, which is linked to tissue strain, stress, perhaps over distension and VILI. Thus, the approach of Chiew et al. [11] is an auspicious trail but unfortunately, the dynamic elastance approach generated dissimilar elastance curves for the same patient at different PEEP levels. This is exemplary shown in Fig. 1 by means of the McREM72 dataset, which will be introduced later. Consequently, the chances to predict the curve progression or determine the overall minimal elastance point ($\mathrm{argmin}_P(E(P))$) were low.

Subsequent studies mitigated this problem by introducing various correction terms [16–18]. For example, Knörzer et al. [16] introduced the α-method (3) to improve the dynamic elastance model in order to obtain the desired continuous prediction curve of $E(P)$.

$$E(P) = \frac{P - P_{0,i} - R\dot{V}}{\propto_i V} \tag{3}$$

where: α_i is the correction factor at a given PEEP level ($P_{0,i}$) with $i = 1 \ldots n$, n is the number of PEEP levels and $\alpha_1 = 1$.

This method used multiplicative correction terms α_i to $E(P)$ according to the PEEP levels $P_{0,i}$ and will be explained more detailed in the method section. By minimizing the deviation between the $E(P)$ curves (Fig. 1), the optimal values of R and α_i were identified.

The overall goal of Knörzer et al. and Chiew et al. was to find the point of minimal elastance $\mathrm{argmin}_P(E(P))$ and therefore, the presumed pressure point of minimal energy transfer, which simultaneously is a precondition to find the presumed pressure point of optimal PEEP settings (Fig. 2). However, the assumption of constant resistance in the dynamic elastance model contradicts the physiology of the airways. The airways are not comprised of rigid tubes but consist of various biological tissues with diverse properties [19]. Pressure changes during mechanical ventilation are accompanied by changes in diameter of the airways [20]. The Hagen-Poiseuille law links this change in diameter to changes in airway resistance [10] according to (4).

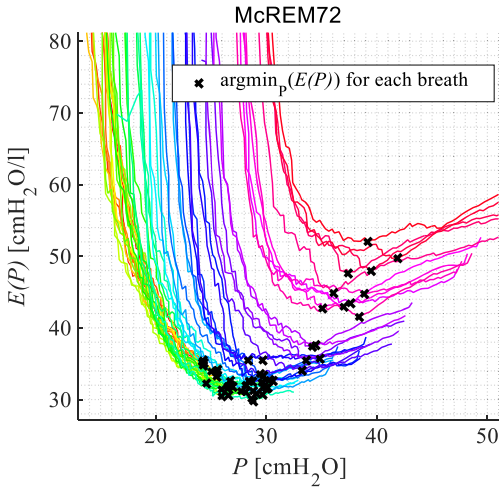

Fig. 1 The outcome of the dynamic Elastance model applied on the data of a mechanical ventilated patient (McREM72). The coloured curves are the $E(P)$ curves of different breaths at 11 different PEEP levels (5 breaths per PEEP level) [15]

$$R \sim \frac{1}{d^4} \tag{4}$$

where R is the resistance in a tube, while d is the diameter of the tube in case of laminar flow.

Thus, at higher pressure ranges, when the diameters of the tube system are increased, the resistance of the airways decreases - provided that the flow remains laminar. Consequently, the assumption of a constant airway resistance must be reviewed. The pressure dependence of the airway resistance R has been thoroughly analyzed in this study.

The identification of $R(P)$ determines resistance values across a range of pressure. In contrast, most existing lumped parameter methods use constant R values to represent resistance over the entirety of the pressure range. Unfortunately, direct measurement of airway resistance [21] via spirometry or the body plethysmography [22, 23] cannot be used for narcotized patients. During spirometry, the patients have to interact and the usage of body plethysmograph in the intensive care unit is not practicable. Other methods like airflow perturbation techniques [24] including the forced oscillation technique might be used, but none of the available datasets on which this study is based on delivers this additional information. Thus, analysing the airway resistance based on existing

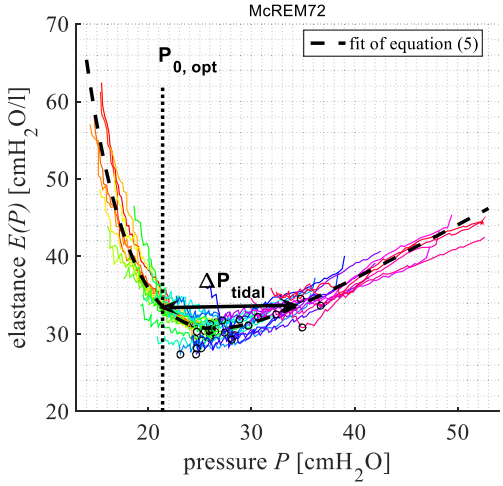

Fig. 2 Illustration of the identification of the optimal PEEP level $P_{0,opt}$ based on a mechanically ventilated patient (McREM072). The coloured curves are the *E(P)* curves of 5 different breaths at 11 different PEEP levels after the identification respectively the correction by α_i. The black dashed line shows the fit of Eq. (6) to the data. By ensuring the mean tidal pressure interval ΔP_{tidal} in the range of minimal elastance, $P_{0,opt}$ was identified

ventilation data is the easiest way during mechanical ventilation. In addition, this method is advantageous because the patients are not affected by any additional invasive measurement.

2 Methods

2.1 Patient data:

This study uses the Bersten et al. [25] and McREM [26] datasets:

- In the Bersten et al. dataset [25], ten acute lung injury (ALI) patients, eight with ARDS and two at risk, were studied. Multiple studies on separate days were conducted on patients' numbers 8, 9 and 10. Patients were ventilated using a Puritan-Bennett 7200ae ventilator (Puritan-Bennett Corp., Carlsbad, CA, USA) with a tidal volume (V_T) of 8–10 ml/kg, a square-wave inspiratory flow (V) pattern and an inspiratory: expiratory ratio *(I:E)* exceeding 1:1. PEEP trials were initially performed at the current, clinically set level of PEEP (baseline) and then repeated at 30 min intervals following random PEEP changes (5–15cmH_2O) with V, V_T and *I:E* ratio kept constant. Equipment and procedure: Flow was measured with a heated, Fleisch-type pneumotachograph (HP-47034A, Hewlett-Packard, Palo Alto, CA, USA) and transducer (21072A; Hewlett-Packard), which had been calibrated over the range 0–300 l/min with a flow calibration set (18987–1; Gould Godard VB, Bilthoven, The Netherlands). The pneumotachograph was connected between the Y-piece of the ventilator tubing and the endotracheal tube. P_{aw} was measured proximal to the endotracheal tube by a precalibrated (water manometer) strain gauge transducer (Bell and Howell 4–327-I; Trans-America Delaval, Pasadena, CA, USA). Flow and P_{aw} were recorded on a personal computer via a 12-bit analogue-to-digital converter (DT2801; Data Translation, Marlboro, MA, USA) at 100 Hz for later data analysis (ANADAT 5.1; RHT-InfoDAT, Montreal, Canada). After 30 min at each PEEP level, 60s of data were collected.
- The McREM dataset consists of 28 patients ventilated in square wave profile volume controlled mode and underwent an incremental PEEP trial amongst other respiratory or recruitment manoeuvres. This study was limited to the mentioned incremental PEEP trial - Starting at ZEEP, the PEEP-level was increased in steps of 2cmH_2O until a plateau pressure of 45cmH_2O was reached. Each PEEP level was maintained for about ten breaths. During the collection of the data [26], all patients were ventilated with identical Evita4Lab systems (Draeger Medical, Lübeck, Germany). The systems consisted of a standard patient ventilator (Draeger Evita4), a notebook computer, and measurement hardware. Gas flow was measured with a calibrated, nonheated Fleisch No. 2 pneumotachograph (F_G GmbH, Hechingen, Germany) connected to a differential pressure transducer (PC100 SDSF, Hoffrichter, Schwerin, Germany). A heat–moisture exchanger (Aqua_ FH, Hudson, Temecula, CA) was placed between the tube connector and the pneumotachograph to prevent moisture from affecting the flow measurement. Airway opening pressure was measured by a piezoresistive pressure transducer (1790, SI-special instruments, Nördlingen, Germany). Signals were digitized at 125 Hz using an analog-to-digital converter board (DAQCard- AI-16E-4, National Instruments, Austin, TX) and stored on the laptop controlling the ventilator (LabView 5.1.1, National Instruments). A noncompliant, single-patient tubing system was used in all patients (Intersurgical, Berkshire, UK).

2.2 'α-method'

The pressure-variant dynamic elastance model in combination with the α-method (3) rests upon a constant airway resistance [16]. Due to the lack of the dynamic elastance model to get a continuous prediction curve of *E(P)* (Fig. 1), the α-method introduces for each PEEP level i a multiplicative correction factor α_i to the model. The overall goal was to get a continuous prediction curve of *E(P)* and thus the ability to determine the desired optimal PEEP level. Together with this correction factors α_i, the constant resistance R_α is obtained by reducing

the disagreement in $E(P)$ curves of all the analyzed breathing cycles and PEEP levels (5), obtained by the dynamic elastance model.

$$[R_\alpha, \alpha_1, \ldots, \alpha_n]_{opt} = \operatorname{argmin}\left(\sum_{i=1}^{nm}\sum_{j=i+1}^{nm}\sum_{P=P_{ij,\min},\ 0.1}^{P_{ij,\max}}\left(E(P)_i - E(P)_j\right)^2\right) \quad (5)$$

where: R_α is the constant airway resistance obtained by this optimisation, α_i is the correction factor at a given PEEP level ($P_{0,i}$) and $\alpha_1 = 1$. The method was used for all pressures $P \in [P_{ij,\min}, P_{ij,\max}]$, which was given by the overlapping area of the different curves $E(P)_i$ and $E(P)_j$, where $P_{ij,\min}$ and $P_{ij,\max}$ are defined as $P_{ij,\min} = \max(\min(P_i), \min(P_j))$ and $P_{ij,\max} = \min(\max(P_i), \max(P_j))$, n was the number of PEEP levels and m was the number of analyzed breaths per PEEP level.

This optimization had the aim to get a continuous prediction curve for $E(P)$ across all PEEP levels and was done using the *lsqnonlin.m* function in MATLAB (R2015a, The MathWorks, Natick, USA).

The α-method effectively ignores the changes in resistance that occur at different pressure levels. The sensitivity of the dynamic elastance model on the airway resistance has to be analyzed. Thus, the resistance was excluded from the optimization routine (5) and was varied from 1 to 20cmH_2Osec/l in steps of 1cmH_2Osec/l. When possible, the pressure point of minimal dynamic elastance ($\operatorname{argmin}_P(E(P))$) was identified by fitting a curve (6) to the data.

$$E(P) = x_1 e^{x_2 P} + x_3 P + x_4 \quad (6)$$

where x_1 has units of cmH_2O/l, x_2 of 1/cmH_2O, x_3 of 1/l, and x_4 of cmH_2O/l.

The minimum of this curve was determined via (7), which is an algebraic manipulation of Eq. (6).

$$\operatorname{argmin}_P(E(P)) = \frac{ln\left(\frac{-x_3}{x_1 x_2}\right)}{x_2} \quad (7)$$

Subsequently, the optimal PEEP level $P_{0,opt}$ was calculated via (8a), ensuring mechanical ventilation (mean tidal pressure ΔP_{tidal}) in the pressure range of minimal elastance (see Fig. 2).

$$E\left(P_{0,opt}\right) = E\left(P_{0,opt} + \Delta P_{\text{tidal}}\right) \quad (8)$$

$$P_{0,opt} = \frac{\ln\left(\frac{\Delta P_{tidal}\, x_3}{x_1\left(1 - e^{\Delta P_{tidal}\, x_2}\right)}\right)}{x_2} \quad (8a)$$

where: ΔP_{tidal} is the mean tidal pressure interval of all analyzed breaths and PEEP levels and x_i are the parameters of (6) obtained by the fitting process.

2.3 Alternative methods to determine the airway resistance

After the examination of the sensitivity of the dynamic elastance model in view of the airway resistance, the airway resistance R_α (5) obtained by the α-method was compared to the airway resistances, identified by three alternative models on the same ventilation data. In consideration of the fact that the dynamic elastance model is restricted to the inspiratory sections of the breathing cycles, the resistance-analysis in this study was also limited to the inspiratory parts of the patient data. The following alternative identification methods were used to evaluate the airway resistance.

2.3.1 The initial step method

One of these established identification methods, which will hereinafter be referred to as the *'initial step method'*, uses the inspiratory pressure step $\Delta P_{step,up}$ to determine the resistance as shown in Fig. 3. In this segment of the breathing cycle, the inspired volume was still close to 0 and thus it leads to the ability to neglect the elastance term in (1). Consequently, (1) can be reduced to (9).

$$\overline{R}_{\text{step}} = \frac{\Delta P_{\text{step},up}}{\Delta \dot{V}_{\text{step},up}} \quad (9)$$

It is important to note that $\overline{R}_{\text{step}}$ is a mean value of the airway resistance and represents the values of the pressure step.

2.3.2 The fitting method

Another established identification of the airway resistance method is the *'fitting method'*. This identification method fits a FOM (1) to the ventilation data using a least square fit method in MATLAB. By fitting a FOM to the inspiration data of each PEEP level, values for resistance and elastance, $\overline{R}_{\text{fitting}}$ and $\overline{E}_{\text{fitting}}$ were obtained for each PEEP level. To evaluate differences, we used two different regions of the inspiration data. One region limited the inspiration data until the maximum of the airway pressure – the peak inspiratory pressure (PIP) was reached, while the other one also included the end-inspiratory pause (EIP).

These methods will hereinafter be referred to as *'fitting method P_{max}'* and *'fitting method EIP'*. The resistance values obtained by these methods are mean values of R in the corresponding pressure range of the inspiration phase. As the corresponding points of pressure the mean values of all the pressures in the specified pressure ranges are used.

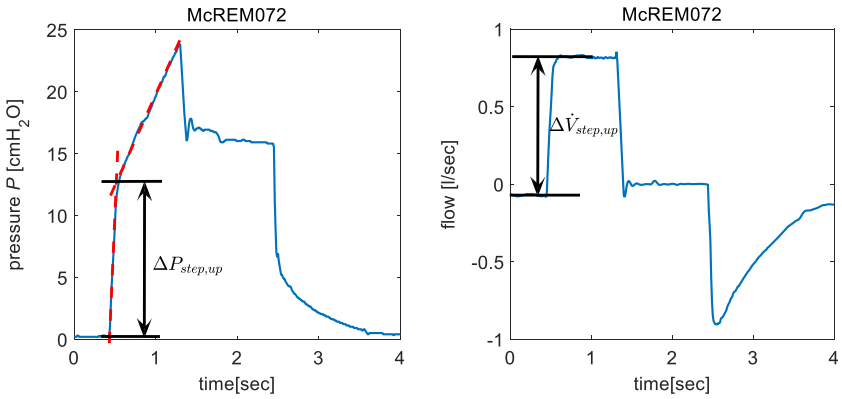

Fig. 3 Identification of $\overline{R}_{\text{step}}$ based on a mechanically ventilated patient, the step of the pressure curve $\Delta P_{step,up}$ (left) is caused by the step of the flow $\Delta V_{\text{step},up}$ (right)

2.3.3 Static resistance

Lastly, for comparison reasons, the *'static resistance'* value was determined: The zero-flow phase at the end of inspiration (during end inspiratory pause (EIP)) can be used to calculate the static resistance R_{static} [27], which is defined as the pressure difference between the peak inspiratory pressure (PIP) and the plateau pressure P_{plat} of the EIP divided by the flow step $\Delta V_{\text{step,down}}$ (see Fig. 4 and (10)).

$$R_{\text{static}} = \frac{PIP - P_{\text{plat}}}{\Delta \dot{V}_{\text{step,down}}} \tag{10}$$

As no end inspiratory pause was used in the ventilation mode of the Bersten dataset, the static resistance couldn't be identified.

3 Results

The sensitivity of the dynamic elastance model on the airway resistance (influence of R on $\text{argmin}_P(E(P))$) showed that small changes in R can result in crucial changes of $\text{argmin}_P(E(P))$. Consequently, the assumption that variance in R does not significantly affect the identified optimal PEEP level $P_{0,opt}$ is false. Figure 5 shows the sensitivity of the dynamic elastance model on the airway resistance of three datasets (AB11, McREM009 and McREM023). Small changes in R reveal maximal shifts in $\text{argmin}_P(E(P))$ up to 5cmH_2O for small changes in R of 1cmH_2Osec/l, which is highly relevant to clinical practice.

Table 1 shows the optimized R_α value from the α-method and in case of its existence the pressure point of minimal elastance $\text{argmin}_P(E(P))$ at different values of R (from 1 to 20cmH_2Osec/l) for the Bersten dataset. Table 2 shows the analogous values of the McREM dataset.

The results of the different methods of identifying the airway resistance are shown in Fig. 6. While the α-method yields a constant value of the airway resistance R_α at all PEEP levels (black dashed line), the identification of $\overline{R}_{\text{fitting, Pmax}}$ respectively $\overline{R}_{\text{fitting, EIP}}$ via the *'fitting method'* (full inspiration) and the determination of $\overline{R}_{\text{step}}$ via the *'initial step method'* have shown the expected decrease of the resistance with increasing pressures. This trend can be seen across all patients of the McREM dataset and is illustrated in Fig. 6 by means of McREM009, McREM072 and McREM088. Furthermore, Fig. 7 and Table 3 demonstrated that the pressure dependent decreasing trend of the airway resistance could potentially be exponential.

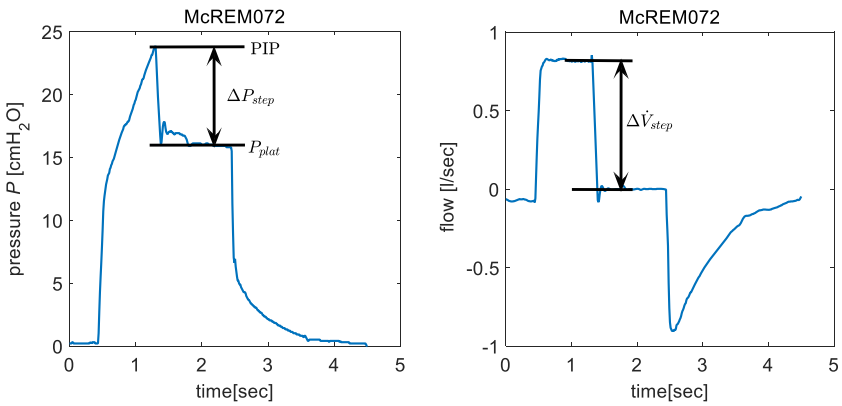

Fig. 4 Identification of R_{static} based on a mechanically ventilated patient, the step in the pressure curve after the peak inspiratoy pressure $\Delta P_{step,down} = PIP - P_{plat}$ (left) is caused by the step down in the flow $\Delta V_{\text{step,down}}$ before the EIP (right)

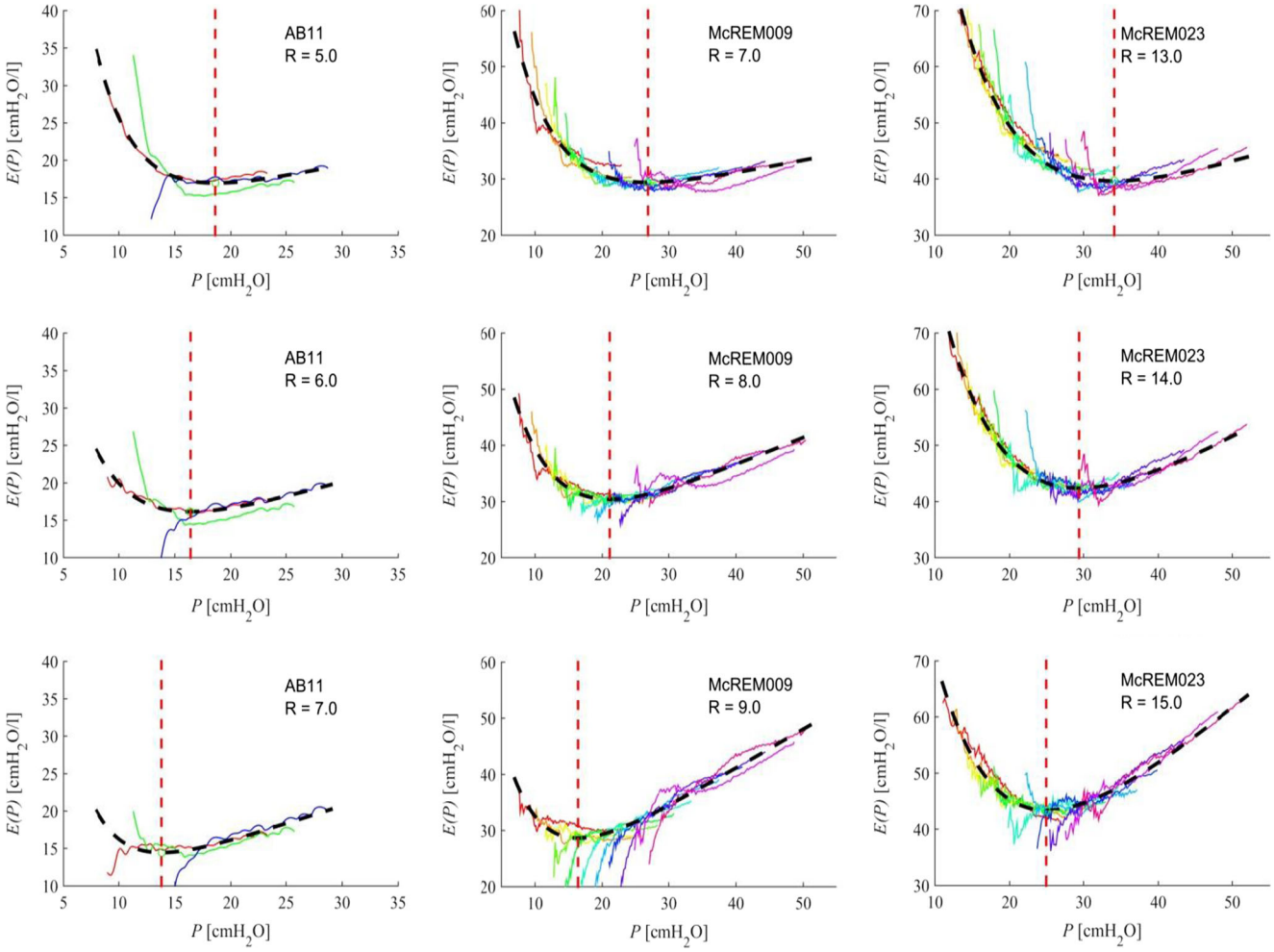

Fig. 5 Influence of small changes in *R / [cmH₂Osec/l]* on *argmin$_P$(E(P))* with data Patient Bersten AB11 (left), McREM009 (middle) and McREM023 (right) – the red dashed line shows the location of *argmin$_P$(E(P))*. The *E(P)* curves of different PEEP levels are displayed in different colours and the black dashed line shows the curve fitting result to (6)

4 Discussion

Analyzing the influence of the constant airway resistance on the outcome of the dynamic elastance model, which was an objective of this study, shows that the sensitivity of argmin$_P$(*E(P)*) to changes in *R* is high. Table 1, Table 2 and Fig. 5 illustrate this sensitivity. Hence, the influence of the airway resistance on the point of minimal elastance argmin$_P$(*E(P)*) cannot be ignored. Small variations in *R* can lead to outcomes for the suggested optimal PEEP level on a scale that is highly relevant to clinical practice. Table 2 shows that patients McREM009, McREM023 and McREM072 reveal maximal shifts in argmin$_P$(*E(P)*) up to 5cmH$_2$O for small changes in *R* of 1cmH$_2$Osec/l. Some patients showed less sensitivity but the influence of small changes in *R* can be observed for nearly all datasets. The optimal PEEP level defined by the α-method is highly sensitive to the identified value of R_α. Figure 6 shows that variance in *R* should be expected across PEEP steps and that changes of such magnitude have the potential to alter the PEEP level defined by the α-method. Hence, it is imperative that the α-method is updated with some *R(P)* function. However, there is significant potential for two profiles for *E(P)* and *R(P)* to tradeoff and thus limit the uniqueness and robustness of the outcomes.

The dynamic elastance model is limited to the inspiration phases of the breathing cycles and therefore the investigations of the resistance during inspiration were restricted the same way. To scrutinise the airway resistance during the inspiration phase of the breathing cycles, the *'fitting method'* and the *'step method'* were used to identify *R*. Both identification methods delivered a mean $\overline{R}$ value for different pressure ranges during the inspiration. While the *'fitting method'* was used on two different regions of the inspiration, the whole inspiratory pressure range contributed to the identification of the resistances. To get the corresponding pressure value, the mean pressures of the involved regions of inspiration were calculated and $\overline{R}_{\text{fitting,Pmax}}$ and $\overline{R}_{\text{fitting,}EIP}$ were related to these mean pressures.

Table 1 Bersten: $\text{argmin}_P(E(P))$ values (6 breaths per PEEP level)

Patient (Bersten)	R_α *(optimized) / [cmH₂Osec/l]*		*R / [cmH₂Osec/l]*											
			1	*2*	*3*	*4*	*5*	*6*	*7*	*8*	*9*	*10*	*12*	*14*
AB 1	7.6	$argmin_P E(P)$ / [cmH₂O]	-	-	29.7	28.3	27.2	26.3	24.1	22.4	20.4	18.0	-	-
AB 2	7.7		-	-	-	-	-	-	24.1	20.6	13.9	-	-	-
AB 3	2.0		35.8	35.4	33.4	33.7	34.0	32.8	31.7	30.6	-	30.4	29.3	24.0
AB 4	14.5		No minimum											
AB 5	5.4		-	-	-	-	29.4	28.3	-	-	26.1	-	-	-
AB 6	4.2		-	-	-	-	30.1	29.4	27.9	27.7	25.5	-	-	-
AB 7	5.1		-	28.7	28.3	23.4	18.3	15.8	-	-	-	-	-	-
AB 8	10.5		No minimum											
AB 9	9.3		-	-	41.5	38.3	41.6	41.3	-	-	29.2	-	-	-
AB 10	7.1		-	-	27.4	28.0	26.9	25.2	24.4	22.4	20.0	17.2	-	-
AB 11	5.3		-	23.8	20.7	21.4	19.5	16.6	13.4	-	-	-	-	-
AB 12	6.4		-	-	-	-	-	-	39.2	39.5	32.8	32.2	29.4	-

- method failed to determine $\text{argmin}_P(E(P))$ due to lack of convexity in E(P)

In contrast, the *'step method'* used just a small pressure band at the beginning of each breathing cycle to determine $\overline{R}_{\text{step}}$. These differences in size and range of the corresponding pressure interval impede the correlation of the resistance explicitly to specific pressure points. However, the trends of the analyzed mean values and the trend of *R(P)* are similar.

The static resistance R_{static} refer to the pressure range P_{plat} to *PIP*. Especially in higher PEEP levels the determination of these pressures showed higher variance and fluctuation, but doesn't show the expected decrease, obtained by the other methods - these will be specified thereinafter.

In Fig. 6, the results of the *'fitting method'* and the *'initial step method'* are illustrated for three datasets. The expected reduction of $\overline{R}$ as pressure increased was observed. This trend can be observed in all patient data of the McREM and the Bersten dataset. To quantify this decline, we checked the quotient of

$$\frac{\overline{R}_{\text{fitting,Pmax}}(\text{PEEP} = 10\ cmH_2O)}{\overline{R}_{\text{fitting,Pmax}}(ZEEP)} \tag{11}$$

The mean quotient regarding all patients of the McREM dataset is 62.5% - in case of patient McREM009, this quotient is 72% (see Fig. 6), while it is 48% for McREM011. One could argue that for some patients (e.g. McREM009 in Fig. 6), the resistance R_α, given by the α-method is close to the mean value of $\overline{R}_{\text{fitting,Pmax}}$ over all PEEP levels. This may

Table 2 McREM: $\text{argmin}_P(E(P))$ values (1 breath per PEEP level)

Patient (McREM)	R_α *(optimized) / [cmH₂Osec/l]*		*R / [cmH₂Osec/l]*																
			2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18
*McREM*009	7.9	$argmin_P E(P)$ / [cmH₂O]	-	-	-	38.1	35.1	28.9	21.4	16.7	14.3	-	-	-	-	-	-	-	-
*McREM*011	4.1		-	-	-	-	-	-	40.3	39.1	37.8	36.3	34.7	33	32.1	30.8	30.1	29.9	29.5
*McREM*012	10.7		-	-	-	-	-	-	-	-	-	26	22.2	21.6	20.6	21	21.6	-	-
*McREM*013	14.9		-	-	-	-	-	-	-	-	41.5	39.9	40.2	42.2	41.8	31.7	28.5	-	-
*McREM*023	14.4		-	-	-	-	-	-	-	-	-	-	39.2	34.1	29.5	25.1	21.7	19.8	-
*McREM*027	9.7		-	-	-	-	-	-	-	-	-	-	-	-	33.4	32.1	-	-	-
*McREM*035	5.5		-	40.7	39.7	37.5	35.6	34.4	32.9	31.3	29.9	28.4	27.2	28	26.9	24.2	25.2	-	-
*McREM*042	10.5		44.4	-	42.6	-	40.8	-	39	38.2	37.4	36.8	35.9	35	32.5	31.2	30.4	-	28.9
*McREM*063	10.1		-	-	-	-	-	-	-	-	42.2	39	34.9	29.6	30	28.7	28	-	-
*McREM*069	10.8		-	-	-	-	43.6	-	-	39	39.5	38.3	37.5	-	34	-	30.6	-	-
*McREM*072	8.7		-	-	-	-	40.1	35.1	30.1	24.9	21.6	20.1	-	-	-	-	-	-	-
*McREM*075	20.8		-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
*McREM*078	13.1		-	-	-	-	-	-	-	-	35.5	31.1	28	22.5	19	16.4	-	-	-
*McREM*088	5.7		-	28.5	30.4	34.5	27.8	25.3	23.0	21.2	-	-	-	-	-	-	-	-	-
*McREM*111	7.7		38.5	-	38.8	-	30.9	26.6	22.6	16.8	-	-	-	-	-	-	-	-	-

- method failed to determine $\text{argmin}_P(E(P))$ due to lack of convexity in E(P)

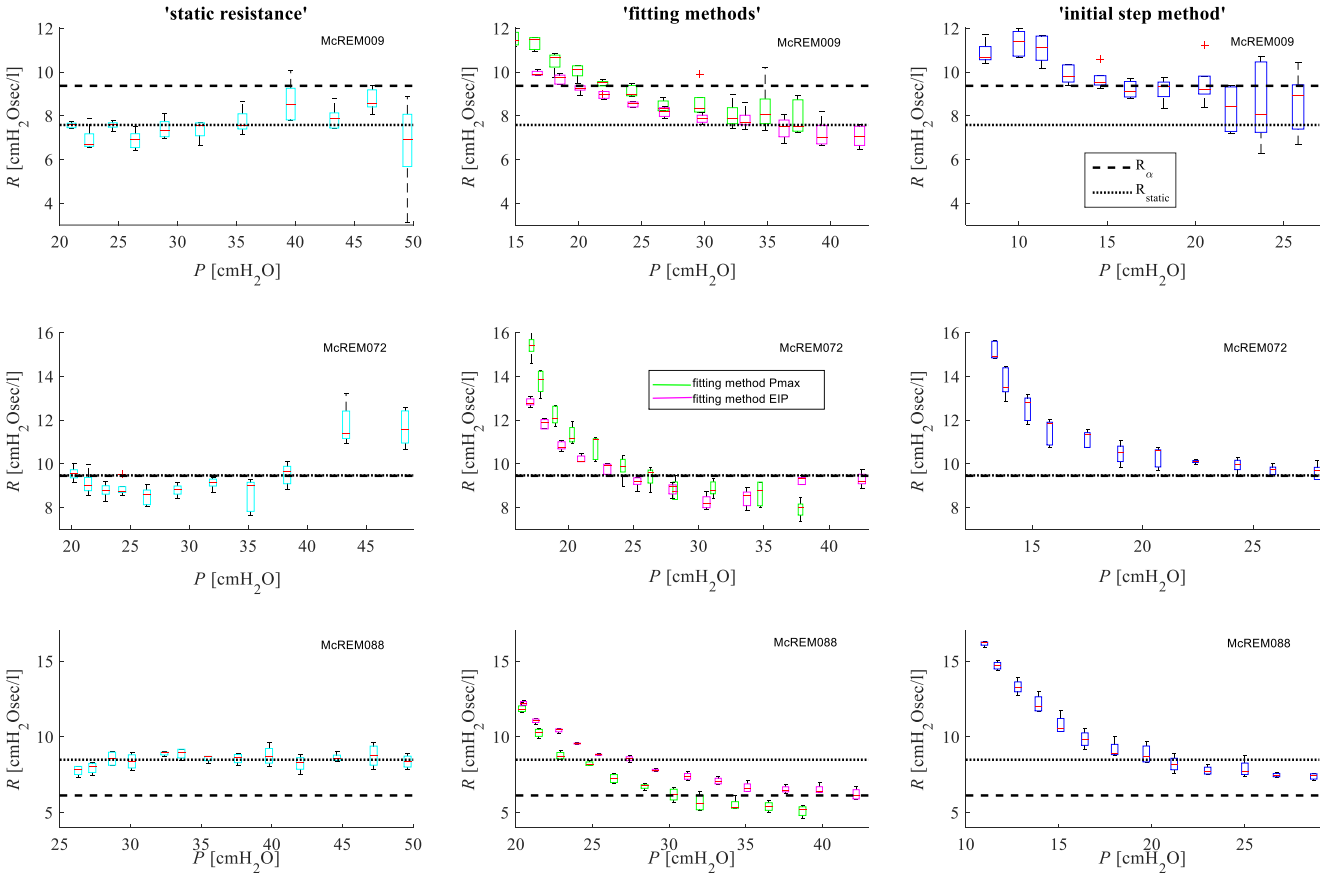

Fig. 6 Determination of R: (left) R_{stat} using the peak and plateau pressures and the step down in flow, (middle) $\overline{R}_{\text{insp}}$ - *'fitting methods'* using different ranges of the inspiratory part of the breathing cycle and (right) $\overline{R}_{\text{step}}$ - *'step method'*, using the initial step. The black dashed line shows the constant value of R_α gained by the α-method and the black dotted line the mean static resistance. 6 breaths in each PEEP level were analyzed

justify a constant R_α for this patient. However, a clear reduction of $\overline{R}_{\text{fitting,Pmax}}$ for increasing PEEP levels has been shown for all the patients. Thus, the Hagen-Poiseuille assumes a reduction in the resistance in case of increasing diameter of the tube, this behaviour can be seen and the disagreement between a constant R_α across PEEP levels and $\overline{R}_{\text{fitting,Pmax}}$ is proven.

Despite ambiguous results with higher variance and higher fluctuations, the initial slope method exhibit the expected declining trend of R. Therefore, the independency of the resistance on the size of the pressure interval leads to the hypothesis that $R(P)$ will follow the same trend.

Overall, due to the significant decrease of the airway resistance, obtained by the *'fitting method'* ($\overline{R}_{\text{fitting,Pmax}}$ and

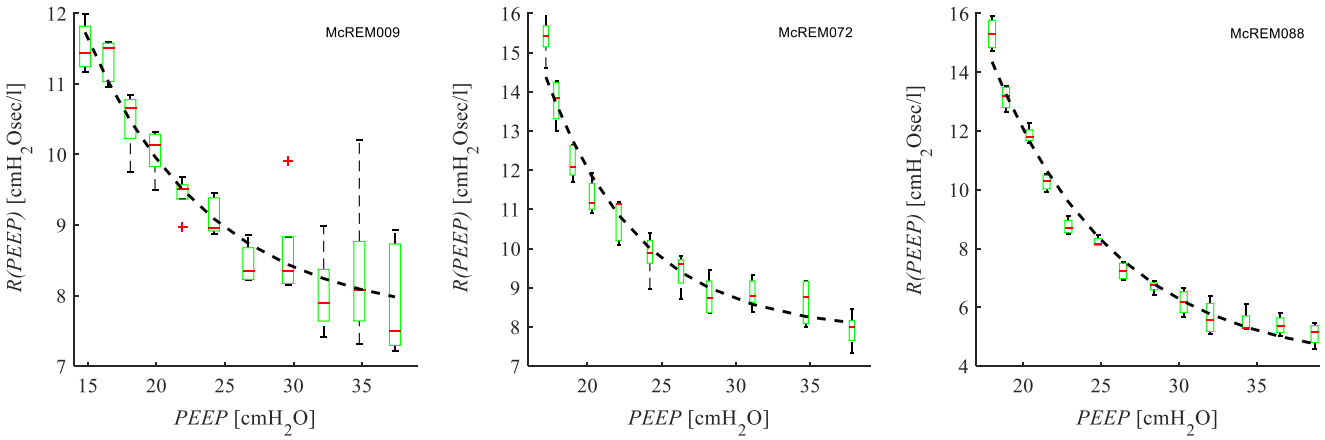

Fig. 7 Determination of $\overline{R}_{\text{fitting,Pmax}}$ - the black dashed line shows the fitting result to (12)

Table 3 McREM: Fitting-results to (12)

Patient McREM	Equation (12)
009	$R(P) = 6.63\ e^{-0.060P} + 3.96$
011	$R(P) = 30.99e^{-0.075P} + 0$
012	$R(P) = 9.189e^{-0.163P} + 10.04$
013	$R(P) = 6.34e^{-0.233P} + 14.83$
023	$R(P) = 17.99e^{-0.020P} + 0$
027	$R(P) = 17.93e^{-0.063P} + 7.49$
035	$R(P) = 21.47\ e^{-0.056P} + 0$
042	$R(P) = 25.90e^{-0.061P} + 0$
055	$R(P) = 1.54e^{-9.971P} + 18.85$
063	$R(P) = 10.31e^{-0.124P} + 10.10$
069	$R(P) = 37.17e^{-0.066P} + 4.22$
072	$R(P) = 9.04e^{-0.088P} + 5.65$
075	$R(P) = 8.44e^{-0.118P} + 11.89$
078	$R(P) = 15.33e^{-0.020P} + 3.72$
088	$R(P) = 10.68e^{-0.096P} + 3.72$
091	$R(P) = 9.16e^{-0153P} + 9.72$
092	$R(P) = 4.25e^{-0.417P} + 3.86$
093	$R(P) = 13.86e^{-0.107P} + 11.40$
108	$R(P) = 2.86e^{-0.159P} + 8.5$
117	$R(P) = 24.29\ e^{-0.132P} + 4.44$
119	$R(P) = 7.11\ e^{-0.154P} + 8.34$
120	$R(P) = 3.89\ e^{-0.086P} + 7.78$

$\overline{R}_{\text{fitting},EIP}$) or the *'initial step method'* ($\overline{R}_{\text{step}}$) and due to the lack in physiological conformability, the assumption of a constant airway resistance R_α seems false. A closer look at the trends of the resistances of both methods (*'fitting method'* as well as *'initial step method'*) leads to the presumption of an exponential nature of the decline across all patients of the McREM dataset. Despite the widespread expectation of polynomial behaviour (Hagen-Poiseuille) the non-linear bronchial elastance proves the exponential decreasing trend. Expressing the resistance values $\overline{R}_{\text{fitting,Pmax}}$ as an exponential decreasing function (12) confirms this supposition.

$$R(P) = x_1 e^{-x_2 P} + x_3 \tag{12}$$

where x_1 has units of cmH_2Osec/l, x_2 of $1/cmH_2O$ and x_3 of cmH_2Osec/l.

By a closer look at the changes in R_{stat}, which are negligible, reveals that these changes could be explained by the trend of this exponential decreasing function – in higher pressures the airway resistance converges to x_3 as the asymptote and the changes are minimal.

Figure 7 (McREM dataset) shows the graphical illustrations of the fitting results by means of McREM009, McREM072 and McREM088. It is remarkable that the exponential trend can be observed across all patients of the McREM dataset. Unfortunately, the limited number of PEEP steps (max. 4) in the Bersten dataset doesn't allow confirmation. Nevertheless in nearly all of the Bersten dataset an according decrease of the airway resistance over increases in PEEP can be seen.

5 Conclusion

The dynamic elastance model can potentially be used to support clinicians in finding the best possible settings for mechanical ventilation. The underlying principle of the dynamic elastance model is the minimization of energy transferred to the lung by mechanical ventilation. This study has shown that the sensitivity of the outcomes of the dynamic elastance model to the airway resistance is very high and in the region of clinical significance. Small changes in estimated resistance can cause large changes in the pressure at which minimal elastance occurs ($\text{argmin}_P(E(P))$) as well as the optimal PEEP level. Alternative determination methods of the airway resistance have shown that the resistance follows an exponential decreasing trend for an increasing pressure, which is conformable to physiological descriptions of the bronchial pathway.

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Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

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