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Model based prediction of plateau pressure in mechanically ventilated patients

Abstract: The risk of ventilator induced lung injury in mechanically ventilated (MV) critically ill patients can be mitigated by patient-specific optimisation of ventilator settings. Recent studies have shown that driving pressure, i.e. the difference between plateau pressure (P_{plat}) and PEEP, is a strong indicator for survival in MV patients suffering from ARDS. However, to measure P_{plat} , an extended end-inspiratory pause (EIP) has to be applied, possibly interrupting ventilation therapy. This study presents a method for predicting P_{plat} from normal breaths in MV patients.

A total of 859 MV breaths with a 5 second EIP were recorded in 27 MV patients with ARDS. Two methods for determining P_{plat} were tested, one using an exponential fit of the pressure data and the other using a four-parameter viscoelastic model (VEM). Each method was identified using various lengths of data after the peak inspiratory pressure (PIP). Using the identified parameters, both methods were then used to predict the P_{plat} recorded at 5 seconds.

The exponential method showed a median coefficient of variation (CV) from the real P_{plat} of 42.9% using data from PIP to 0.5 seconds after PIP, 24.9% using 1 second of data and 15.2% using 1.5 seconds of data. The respective VEM prediction median CVs were of 17.2%, 9.7% and 8.4%. Therefore, the VEM showed a better prediction than the non-physiological exponential model, allowing it to be used to reduce the clinical burden of determining P_{plat} by reducing the required length of the EIP to 1.5 seconds.

Keywords: Mechanical ventilation, decision support, mathematical model, plateau pressure.

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1 Introduction

The application of mechanical ventilation (MV) is a common treatment to support patients that suffer from respiratory failure in the intensive care unit (ICU). It provides sufficient oxygenation and carbon dioxide removal to the patient to allow recovery from the underlying disease. However, due to heterogeneous disease states in those patients the response to MV is diverse. Thus, it is mandatory that clinicians manage MV based on patient-specific needs. In particular, specific patient disease states trigger specific responses to ventilation and thus require individualized therapy settings.

Excessive airway pressures can lead to barotrauma of the alveoli [1], which can result in ventilator induced lung injuries (VILI). In patients suffering from Acute Respiratory Distress Syndrome (ARDS), VILI can occur more frequently, especially with ventilation settings that have not been adjusted based on patient-specific requirements [2]. The current clinical strategy to avoid VILI in ARDS patients is a ventilation with low tidal volumes (6ml/kg predicted body weight) and high end-expiratory pressures (PEEP) [3]. Recent studies have shown that because of the reduced lung compliance in ARDS patients the tidal volume should not be scaled to body weight but normalized to the lung compliance [4]. That ratio, termed “driving pressure”, was stated to be routinely calculable from the difference between plateau pressure (P_{plat}), i.e. the pressure at the end of the end-inspiratory pause, and PEEP. Determining the true P_{plat} however requires an extended end-inspiratory pause (EIP) is required, possibly interrupting ventilation therapy. The aim of the presented study therefore is to test two different approaches to predict P_{plat} from shorter EIPs.

2 Methods

2.1 Data

This study used retrospective clinical data of a multicentre study [18], where different respiratory manoeuvres were performed on 28 mechanically ventilated patients suffering

from ARDS. The studied patients were 50.8 ± 14.9 (SD) years old, 25 male, 3 female, height was 175.6 ± 8.6 cm, weight was 84.9 ± 15.7 kg, tidal volume 7.5 ± 1.5 ml kg^{-1} , PaO₂/FiO₂-ratio 210.2 ± 53.6 mmHg, 8.8 ± 4.9 days on MV before study inclusion. All patients were ventilated in volume controlled mode using identical Evita4Lab systems (Dräger Medical, Lübeck, Germany). The systems consisted of a standard patient ventilator (Dräger Evita4), a notebook computer, and measurement hardware. A calibrated, non-heated Fleisch No. 2 pneumotachograph (F+G GmbH, Hechingen, Germany) connected to a differential pressure transducer (PC100SDSF, Hoffrichter, Schwerin, Germany) was used for gas flow was measured.

To prevent moisture from affecting the flow measurement, a heat-moisture exchanger (Aqua_FH, Hudson, Temecula, CA) was placed between the tube connector and the pneumotachograph. Airway opening pressure was measured by a piezoresistive pressure transducer (1790, SI - special instruments, Nördlingen, Germany). Signals were digitized at 125 Hz using an analogue-to-digital converter board (DAQCard-AI-16E-4, National Instruments, Austin, TX) and stored on the laptop that was controlling the ventilator (LabView 5.1.1, National Instruments). A non-compliant, single-patient tubing system was used in all patients (Intersurgical, Berkshire, UK). Measurements of the SCASS (Static compliance by automated single steps) manoeuvres in 27 patients were analysed in this study, while data of one patient did not contain the respective manoeuvre. During the SCASS manoeuvre a randomised tidal volume (in increments of 50 ml) and a randomised inspiration time were applied with a constant flow. Inspiration was followed by an occlusion of the airways for 5 seconds to obtain a quasi-static pressure/volume relationship. P_{plat} did not exceed 45 mbar.

2.2 Models

2.2.1 Exponential method

The first method tested used an equation of double exponential decay (DED) of the following form to reproduce the pressure drop during the end-inspiratory pause:

$$P_{aw}(t) = x_1 e^{-x_2 t} + x_3 e^{-x_4 t} \quad (1)$$

Here, $P_{aw}(t)$ is airway pressure at time t , and parameters x_{1-4} are tuned to the measured recorded pressure decay during the end-inspiratory pause (EIP).

2.2.2 Viscoelastic model

The viscoelastic model of respiratory mechanics is a model of second order comprising two capacitances and two resistances. It is based on the assumption that the nonlinear pressure decay during the EIP is caused by the viscoelastic behaviour of the lung tissue. **Figure 1** shows the equivalent circuit diagram, where R_1 describes the sum all respiratory resistances, while C_1 describes the static compliance of the respiratory system, Elements R_2 and C_2 then describe the viscoelastic properties of the tissue [5].

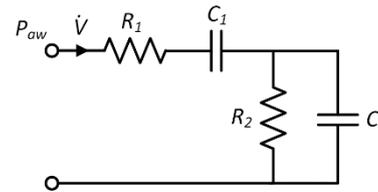


Figure 1: Electrical analogue of the viscoelastic model.

The behaviour of the model can be described by the state-space representation in time domain as:

$$\begin{bmatrix} \dot{P}_{c1}(t) \\ \dot{P}_{c2}(t) \end{bmatrix} = \begin{bmatrix} 1/C_1 \\ 1/C_2 \end{bmatrix} \dot{V}(t) - \begin{bmatrix} 0 & 0 \\ 0 & (R_2 C_2)^{-1} \end{bmatrix} \begin{bmatrix} P_{c1}(t) \\ P_{c2}(t) \end{bmatrix}$$

$$P_{aw}(t) = \begin{bmatrix} 1 & 1 \end{bmatrix} \begin{bmatrix} P_{c1}(t) \\ P_{c2}(t) \end{bmatrix} + R_1 \dot{V}(t) \quad (2)$$

Here, $\dot{V}(t)$ is the air flow supplied by the ventilator.

2.3 Calibration

To determine the influence of the length of the inspiratory pause on the prediction of P_{plat} , both models were identified over different lengths of post peak inspiratory pressure (PIP) data. Three sets of data were used for each patient, model and breath and began at PIP and ended at 0.5, 1 and 1.5 seconds, respectively. The exponential method was calibrated using only the data from PIP to 0.5, 1 and 1.5 seconds after PIP, while the data used to calibrate the VEM also included the pressure data recorded during inspiration (PEEP to PIP). **Figure 2** shows the different data sets. This difference in data used to identify each model allows identification over the range of data that the models were designed to capture.

The parameters of both methods were identified using a Nelder-Mead Simplex-Search method [6] implemented in MATLAB (R2015a, The MathWorks, Natick, USA) as *fminsearch*. The initial guesses for the VEM parameters were calculated using a hierarchical approach [7], to ensure a robust identification of parameters.

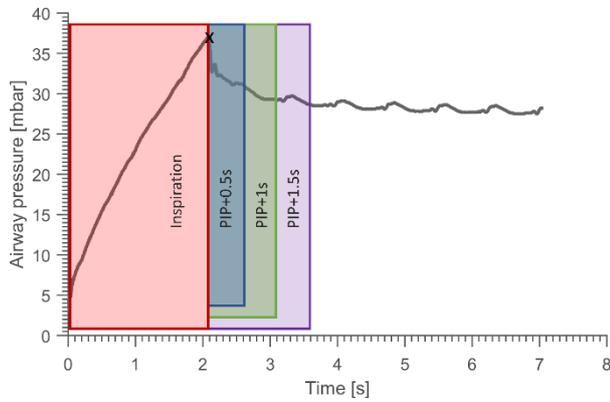


Figure 2: Different data sets used for calibrating the proposed methods. The DED was calibrated using P_{aw} data from PIP to 0.5s, 1s and 1.5s respectively, while the VEM was calibrated also using the data recorded during inspiration. The black cross denotes PIP.

2.4 Evaluation

Both methods were evaluated by comparing their prediction of P_{plat} after calibration with the recorded P_{plat} in the patient. Because the recorded EIP data showed significant cardiogenic oscillations, i.e. periodic pressure changes in the thoracic cavity caused by the contraction and relaxation of the heart muscles, the real P_{plat} could not be determined directly. Instead, a double exponential decay function as shown in Eq. 1 was fitted to the recorded EIP data, using the last data point of the fitted function as the assumed P_{plat} . **Figure 3** shows the recorded EIP data, the fitted double exponential decay function and the assumed P_{plat} .

3 Results

Figure 4 shows exemplary results for the predictive quality of the two methods in relation to the data used for calibration.

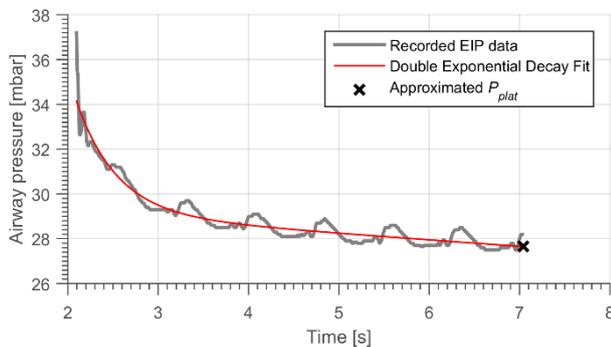


Figure 3: Approximation of the true P_{plat} by fitting a double exponential decay function to the recorded P_{aw} data during EIP.

The median coefficient of determination (R^2) between the true P_{plat} values and the values predicted by the DED were $R^2_{DED} = [0.95 \ 0.95 \ 0.94]$ for 0.5, 1 and 1.5 seconds of data after PIP, respectively. The results of the VEM calibration were $R^2_{VEM} = [0.85 \ 0.85 \ 0.84]$ for 0.5, 1 and 1.5 seconds of data after PIP, respectively. **Table 1** shows the quartiles of the mean coefficient of variation (CV) of the P_{plat} predicted by both models in relation to the length of data after PIP used for calibration.

Table 1: [1st quartile, median and 3rd quartile] of the CV [%] of the P_{plat} predicted by both methods with respect to the length of data after PIP used for calibration.

Model	PIP+0.5s	PIP+1s	PIP+1.5s
DED	[27.1 42.9 64.1]	[17.7 24.9 33.5]	[10.3 15.2 19.8]
VEM	[7 17 41]	[4.3 9.7 22.9]	[3.4 8.4 20.3]

4 Discussion

Although mechanical ventilation is regularly used in patients on the ICU, the patient-specific optimization of the ventilator

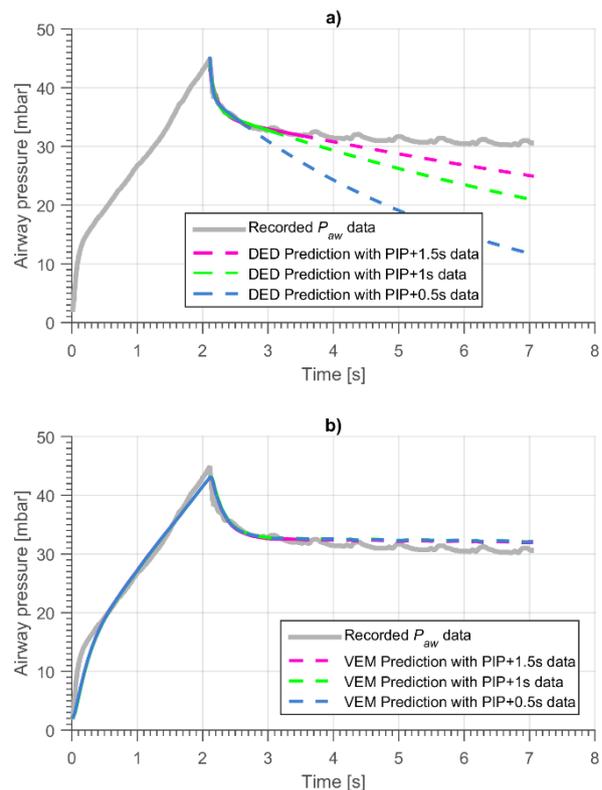


Figure 4: Calibration and prediction results for patient McREM042, SCASS breath 17. a) Calibration and prediction using DED, b) Calibration and prediction using VEM. Solid line show the data used for calibration, broken lines show the resulting prediction.

settings is a challenging task. For critically ill patients suffering from ARDS, avoiding further injury to the lung tissue by the application of ventilation therapy is difficult. However, improving the clinicians' access to information on the underlying patient state will ultimately improve therapeutic optimisation and reduce morbidity and mortality from ARDS. Mathematical models that are able to reproduce the physiological effects of therapies on patients can be used to predict the outcome of changes in the therapy settings on the patient as well as reveal otherwise hidden parameters of the individual patient.

The presented R^2 results show that both the DED and the VEM could reproduce the presented data when being calibrated to it. The resulting prediction of P_{plat} shows an increase in accuracy, when the length of the EIP data used for calibration is increased, visible as a decrease in CV. Both the DED and the VEM thus profit from an increase in information in the calibration data, thus with an increase in EIP length, the prediction of P_{plat} becomes more accurate. However, the goal of the presented study is to shorten the necessary EIP, where the VEM results showed that 1.5 seconds of EIP are sufficient for an acceptable prediction accuracy of P_{plat} . Here, the VEM showed a median CV between predicted and approximated real P_{plat} of 8.4% while the DED still deviates by a median of 15.2%.

The VEM is a physiologically descriptive model. However, the DED was designed to capture trends frequently observed in EIP pressure-volume plots and has limited relevance to physiology. Hence, the VEM was able to reproduce the pressure relaxation visible during EIP better than the DED. In addition, the VEM can extract vital information from the inspiration. The DED was not designed to capture inspiration data or characteristics. The increased accuracy of the VEM was not due to the parameterisation of the models as both models contained four identified parameters.

In summary, the VEM is able to predict P_{plat} from normal breath data, eliminating the necessity of a prolonged end-

inspiratory pause to identify the current disease state of the patient and to avoid ventilator-induced lung injury.

Author's Statement

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