



Sub-Study

Non-linear respiratory system mechanics during low versus high positive end-expiratory pressure during surgery in obese patients

proposed by

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Corresponding documents

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Background and Hypothesis

Respiratory system mechanical parameters such as airway resistance and respiratory system compliance are frequently used to titrate levels of positive end-expiratory pressure (PEEP) and to guide ventilator settings during mechanical ventilation especially in injured lungs, e.g. during therapy of acute respiratory distress syndrome (ARDS)¹. The role of PEEP and the predictive information contained in mechanical parameters of the respiratory system have been studied in a representative study population on participants with BMI up to 40kg/m² during open-abdominal surgery in the light of post-operative pulmonary complications (PPCs) in the multi-centre high versus low PEEP PROVHILO trial².

However, especially in obese patients increased body weight and thus increased gravity dependent effects lead to potentially pronounced collapse of dependent lung areas (atelectrauma). Theoretically, respiratory system mechanics worsen, leading to over-distension in the remaining open lung regions (volutrauma in baby lung) with concordant cell injury and inflammation potentially leading to an increased number of post-operative pulmonary complications.

As part of the multi-centre randomized controlled trial PROBESE, this sub-study aims to relate (non-) linear respiratory system mechanical parameters with PPCs in order to quantify and qualify the predictive power of these parameters in the light of PPCs and their dependence on the perioperative PEEP strategy. Thus the sub-study aims to shed light on the relation between perioperative respiratory system mechanical properties and the development of PPCs.

Primary end-point of this sub-study is the non-linear index of overdistension %E₂, quantifying incidence of over-distension and intra-tidal recruitment/de-recruitment (R/D) based on dynamic airway pressure volume curves. It is hypothesized that intra-tidal R/D occurs more frequently in the low PEEP PROBESE group and is associated with respective PPCs, while intra-tidal overdistension occurs more frequently in the high PEEP group and is associated primarily with intra-operative cardiovascular complications (ICCs).

Methods

Measurements as part of this sub-study do not interfere with the originally described methods of the PROBESE multicentre controlled randomized trial. Additionally, airway pressure and airway flow

are measured with a sampling rate >50 Hz for 5 minutes after induction in supine position and sequentially every hour during surgery, including the recruitment manoeuvre and further 5 minutes in the group with higher PEEP. For each measurement body position (supine, Trendelenburg, anti-Trendelenburg, lithotomy, seated), existence of laparotomy (yes/no) and pneumoperitoneum (yes/no) is collected. After wound closure, but before initiation of spontaneous breathing a final measurement is performed in supine position.

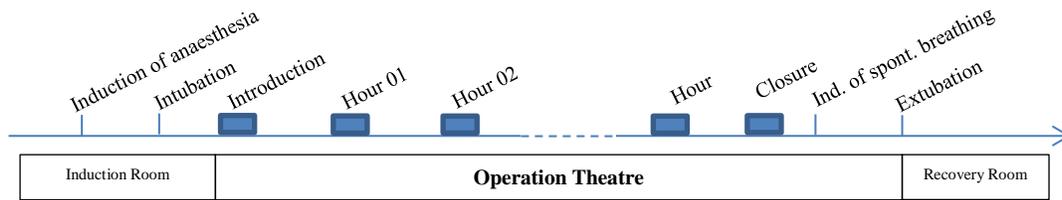


Figure 1 - Time line of respiratory signal measurements.

Airway pressure and flow waveform are post-processed and fitted using a non-linear elastance extension of the equation of motion and the index of overdistension %E₂ is determined as³:

$$\%E_2 = \frac{E_2 \cdot V_T}{E_1 + E_2 \cdot V_T} \quad \text{Eq. 1}$$

Primary End Point

- Index of overdistension %E₂

Secondary End Points

- Respiratory system elastance and resistance.
- Relation between perioperative respiratory system mechanics and formation of PPCs in this patient cohort.

Sample Size Calculation

Sample size estimation was performed based on the values of %E₂ in the sub-study of PROVHILO determined just before extubation. In this data between PEEP group variance was 9.9 % (standard



deviation) and error variance within groups was 19.2 %. This yielded a medium to large effect size of $f=0.37$. The probability of a type I error was set to 5 % (level of significance) and 1-probability of a Type II error was set to 80 % (power). This conceded in a required sample size of **30** patients per group. Sample size calculation was performed using the statistical software R.

References

1. ART Investigators. Rationale, study design, and analysis plan of the Alveolar Recruitment for ARDS Trial (ART): study protocol for a randomized controlled trial. *Trials* 2012;13:153.
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3. Carvalho AR, Spieth PM, Pelosi P, et al. Ability of dynamic airway pressure curve profile and elastance for positive end-expiratory pressure titration. *Intensive Care Med* 2008;34:2291–9.