

# Targeted Lateral Positioning Decreases Lung Collapse and Overdistension in COVID-19-Associated ARDS

**Mikuláš Mlček**

Institute of Physiology, First Faculty of Medicine, Charles University, Prague

**Michal Otáhal**

Department of Anaesthesiology, Resuscitation and Intensive Medicine, First Faculty of Medicine, Charles University and General University Hospital in Prague, Prague

**João Batista Borges** (✉ [joabatistaborges8@gmail.com](mailto:joabatistaborges8@gmail.com))

Institute of Physiology, First Faculty of Medicine, Charles University, Prague

**Glasiela Cristina Alcala**

Pulmonology Division, Cardiopulmonary Department, Heart Institute, University of Sao Paulo, São Paulo

**Dominik Hladík**

Department of Anaesthesiology, Resuscitation and Intensive Medicine, First Faculty of Medicine, Charles University and General University Hospital in Prague, Prague

**Eduard Kurišćák**

Institute of Physiology, First Faculty of Medicine, Charles University, Prague

**Leoš Tejkl**

Institute of Physiology, First Faculty of Medicine, Charles University, Prague

**Marcelo Amato**

Pulmonology Division, Cardiopulmonary Department, Heart Institute, University of Sao Paulo, São Paulo

**Otomar Kittnar**

Institute of Physiology, First Faculty of Medicine, Charles University, Prague

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## Research Article

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# Abstract

## Background

Among the challenges for personalizing the management of mechanically ventilated patients with coronavirus disease (COVID-19)-associated acute respiratory distress syndrome (ARDS) are the effects of different positive end-expiratory pressure (PEEP) levels and body positions in regional lung mechanics. Right-left lung aeration asymmetry and poorly recruitable lungs with increased recruitability with alternating body position between supine and prone have been reported. However, real-time effects of changing body position and PEEP on regional overdistension and collapse, in individual patients, remain largely unknown and not timely monitored.

## Methods

We here report a series of consecutive mechanically ventilated patients with COVID-19-associated ARDS. Aiming at to individualize PEEP and body positioning in order to reduce mechanisms of ventilator-induced lung injury, collapse and overdistension, sixteen decremental PEEP titrations were performed in the first days of mechanical ventilation (8 pairs supine vs. targeted lateral position): supine position immediately followed by 30° targeted lateral position. The choice of lateral tilt was based on X-Ray: the less aerated lung was positioned up. Maps and percentages of global and regional collapse and overdistension were measured for each PEEP level by electrical impedance tomography.

## Results

Targeted lateral position resulted in significantly smaller amounts of overdistension and collapse when compared with the supine one: less collapse along the PEEP titration was found within the left lung in targeted lateral; and less overdistension along the PEEP titration was found within the right lung in targeted lateral. Regarding collapse within the right lung and overdistension within the left lung: no differences were found for position.

## Conclusions

Targeted lateral positioning with bedside personalized PEEP provided a selective attenuation of overdistension and collapse in mechanically ventilated patients with COVID-19-associated ARDS and right-left lung aeration/ventilation asymmetry.

## Background

Most critically ill patients with coronavirus disease (COVID-19) [1] develops acute respiratory distress syndrome (ARDS), needs mechanical ventilation for prolonged time, and exhibits high mortality [2]. In a

large cohort study with critically ill patients with COVID-19 referred for intensive care unit (ICU) admission [2], positive end-expiratory pressure (PEEP) levels were higher than those reported for the management of moderate-to-severe ARDS in the pre-COVID-19 era; and, along with high fraction of inspired oxygen ( $F_{iO_2}$ ) and low partial pressure of arterial oxygen ratio ( $PaO_2/F_{iO_2}$ ) at ICU admission, were an independent factor associated with high mortality. Lung heterogeneity, hypoxemia disproportional to mechanics, right-left lung aeration/ventilation asymmetry [3], and poorly recruitable lungs with increased recruitability with alternating body position between supine and prone [4] have been reported. However, real-time effects of changing body position and PEEP on regional overdistension and collapse, in individual patients, remain largely unknown and not timely monitored.

Lung collapse usually predominates within the most dependent units where the transpulmonary pressure ( $P_L = \text{airways pressure} - \text{pleural pressure}$ ) is the lowest, while lung overdistension predominates within the most nondependent ones where the  $P_L$  is the highest. When there is right-left lung heterogeneity of collapse and overdistension, as in many patients with COVID-19-associated ARDS, a targeted lateral positioning strategy is conceivable: by one-sided lateral position, the lung with more collapsed units in supine position can be positioned gravity-nondependent (mostly) and, conversely, the lung with more overdistended units in supine position can be positioned gravity-dependent. Such targeted lateral position, by which  $P_L$  becomes larger in the nondependent units and smaller in the dependent ones, may afford simultaneous regional/selective recruitment and relief of overdistension effects.

## Methods

We used electrical impedance tomography (EIT) [5] with decremental PEEP titration algorithm ( $PEEP_{\text{EIT-titration}}$ ), which provides information on regional overdistension and collapse [6], to individualize PEEP and body position aiming to minimize ventilator-induced lung injury (VILI) mechanisms, namely collapse and overdistension.

The design was a prospective study. The settings were the ICU of the Department of Anaesthesiology, Resuscitation and Intensive Medicine, First Faculty of Medicine, Charles University, General University Hospital in Prague, Czech Republic; and the ICU of the Pulmonology Division, Cardiopulmonary Department, Heart Institute, University of São Paulo, Brazil. All the experiment protocol for involving humans was in accordance to guidelines of national/international/institutional or Declaration of Helsinki.

Sixteen  $PEEP_{\text{EIT-titration}}$  were performed during the first days of mechanical ventilation in five consecutive patients with COVID-19-associated ARDS in supine immediately followed by targeted lateral position ( $30^\circ$ ). Thus 8  $PEEP_{\text{EIT-titration}}$  pairs were obtained. The choice of lateral tilt was based on X-Ray: the less aerated lung was positioned up. During all the procedures, the patients were deeply sedated and under muscle paralysis.

Immediately before all  $PEEP_{\text{EIT-titration}}$ , the same lung recruitment maneuver was performed both in supine position and the corresponding targeted lateral position: 2 minutes of PEEP 24 cmH<sub>2</sub>O and driving

pressure 15 cmH<sub>2</sub>O. PEEP<sub>EIT-titration</sub> were performed with decremental PEEP steps of 2 cmH<sub>2</sub>O until reaching a lower PEEP level set by the clinician.

The EIT data of all PEEP<sub>EIT-titration</sub> was analyzed in order to quantify the amounts of lung collapse and overdistension, for each lung, at each PEEP step.

## Results

All patients exhibited less aeration and ventilation in the left lung, thus the right (down) lateral tilt was decided.

**Collapse-Left Lung:** There was a statistically significant two-way interaction between position (supine vs. targeted lateral) and PEEP ( $P= 0.014$ ; two-way repeated measures ANOVA) in the % of collapse within the left lung: less collapse along the PEEP titration was found within the left lung in targeted lateral (right down) than supine position (Fig. 1). Additionally, when the simple main effects were tested, the following significant differences were found: PEEP 14 ( $P= 0.034$ ), PEEP 10 ( $P= 0.028$ ), PEEP 8 ( $P= 0.019$ ), and PEEP 6 cmH<sub>2</sub>O ( $P= 0.007$ ).

**Overdistension-Right Lung:** There was a marginal two-way interaction between position and PEEP ( $P= 0.073$ ; two-way repeated measures ANOVA). The main effect of position showed a statistically significant difference in the % of overdistension within the right lung: less overdistension along the PEEP titration in targeted lateral (right down) than supine position ( $P= 0.005$ ; Fig. 2). The main effect of PEEP on right lung overdistension showed a statistically significant difference ( $P< 0.0005$ ). Additionally, for many PEEP levels significant  $P$  values were found in the pairwise comparisons with adjustment for multiple comparisons (Bonferroni).

### **Collapse-Right Lung and Overdistension-Left Lung**

No statistically significant differences were found for position.

Hemodynamic compromise was not detected for any patients during all procedures of the study.

## Discussion

A major focus of mechanical ventilation for COVID-19 is the avoidance of VILI while facilitating gas exchange via lung-protective ventilation. This is the first description of using EIT with targeted lateral positioning to personalize PEEP in adult patients with COVID-19-associated ARDS. A randomized and controlled trial demonstrated the feasibility and efficacy of a postural recruitment maneuver in children with anesthesia-induced atelectasis [7]. Besides being applied in children with healthy lungs, another difference between the Acosta et al. and our study is the lack of PEEP titrations. Very recently, Zhao et al. reported the use of EIT for individualized ventilation strategy in one patient with COVID-19 [8]. Similarly to

the study in children with anesthesia-induced atelectasis [7], a key difference between the Zhao et al. case report and our case series is the lack of a strategy to personalize PEEP during the lateral positioning.

The vertical gradient of  $P_L$ , which is mainly due to gravity, changes with body mass and posture [9]. Agostoni and D'Angelo showed that the  $P_L$  gradient increased when body position was changed from supine to lateral position [10]. They demonstrated that lateral position leads to higher  $P_L$  in the most nondependent units and lower  $P_L$  in the most dependent ones. That is mainly because the thoracic right-to-left distance is longer than the anterior–posterior. Thus, generally, lateral positioning increases heterogeneity of  $P_L$  across the parenchyma, but this depends on PEEP and baseline lung conditions: recent reports in children have shown that an optimized PEEP after lateralization can minimize hyperdistension (maximizing ventilation) in a nondependent, sicker lung, while reasonably keeping functional residual capacity in dependent, healthier lung [11]. Our PEEP<sub>EIT-titration</sub> seems to be a promising tool to find such personalized PEEP at the bedside.

It is unclear what percentage of patients with COVID-19-associated ARDS is potentially suitable for the approach of our study by presenting sufficient right-left lung inequality. To address this issue, we measured the distribution of ventilation to right and left lung from additional 44 patients with COVID-19-associated ARDS. This distribution of ventilation was measured by EIT in supine position. All these patients were ventilated with PEEP set according to the PEEP– $F_{I}O_2$  table used in the original ARDS Network trial. The mean PEEP was  $11.4 \pm 3.1$  cmH<sub>2</sub>O. The mean of the % of ventilation of the right lung was  $54.9 \pm 8.2$  and the mean of the % of ventilation of the left lung was  $45.3 \pm 8.1$ . The right-left lung asymmetrical ventilation of  $> 65/35$  % was observed in 15 % of these patients.

Another potential beneficial effect of the targeted lateral positioning is an improved ventilation/perfusion matching due to: 1) attenuation of regional overdistension within the more aerated lung and, consequently, less diversion of pulmonary blood flow away from these units; 2) diminution of regional collapse within the less aerated lung. The consequent improvement of oxygenation may be important in these patients to manage their disproportional hypoxemia and “buy time” with minimum additional damage.

Our findings reinforce the importance of timely PEEP titrations [12] tackling the dynamically changing phases of this disease. They suggest the relevance of personalized PEEP adjustments every time body positions are changed. The recommendation of applying nonpersonalized low or high PEEP may lead to insufficient and/or excessive PEEP in terms of protection of VILI [13].

## Conclusions

Targeted lateral positioning with bedside personalized PEEP provided a selective attenuation of overdistension and collapse in mechanically ventilated patients with COVID-19-associated ARDS and right-left lung aeration/ventilation asymmetry.

# List Of Abbreviations

COVID-19

coronavirus disease

ARDS

Acute respiratory distress syndrome

ICU

Intensive care unit

PEEP

Positive end-expiratory pressure

$F_{I}O_2$

Fraction of inspired oxygen

$PaO_2$

Arterial oxygen partial pressure

$PaO_2/F_{I}O_2$

Partial pressure of arterial oxygen ratio

$P_L$

Transpulmonary pressure ( $P_L$  = airways pressure – pleural pressure)

EIT

Electrical impedance tomography

$PEEP_{EIT-titration}$

PEEP titration algorithm using EIT

VILI

ventilator-induced lung injury

## Declarations

### ***Ethics approval and consent to participate***

The study was approved by the Ethics Committee of the General University Hospital in Prague, Prague, Czech Republic.

Informed consent was obtained from all patients included in the study for  $PEEP_{EIT-titration}$ .

We confirm that all the experiment protocol for involving humans was in accordance to guidelines of national/international/institutional or Declaration of Helsinki.

### ***Consent for publication***

Not applicable. Our manuscript does not contain any individual person's data in any form (including individual details, images or videos).

### ***Availability of data and materials***

The data are with the authors and will be available upon reasonable request.

The data is available from the corresponding author: João Batista Borges.

### ***Competing interests***

The authors report no conflict of interests.

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### ***Authors' contributions***

MM, MO, JBB, GCA, DH, LT and MA collected the data.

JBB and GCA analyzed the patient data and drafted the manuscript.

MM, MO, GCA, EK, MA and OK developed the concept.

MM, MO, JBB, GCA, EK and MA interpreted the data.

All authors revised the manuscript critically.

All authors read and approved the final manuscript.

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## Figures

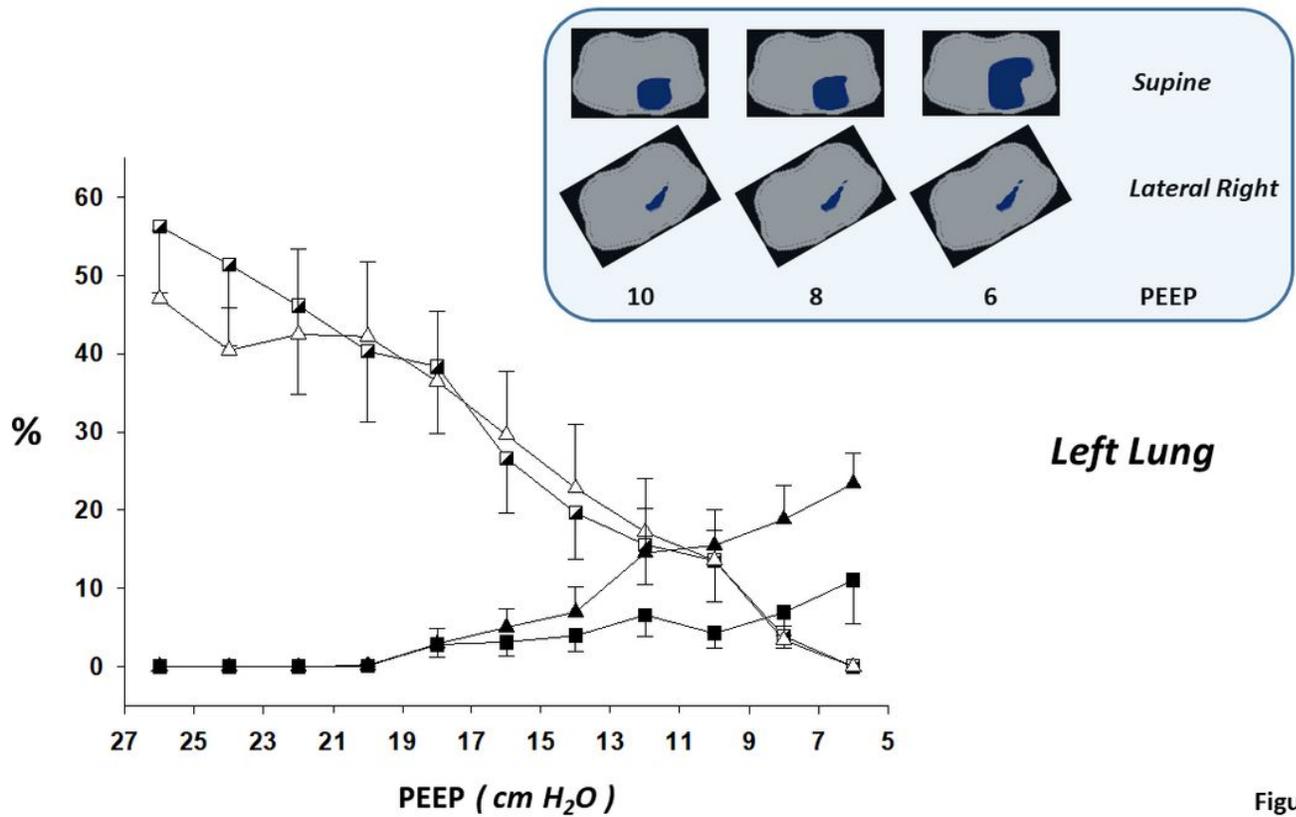


Figure 1

Figure 1

Lung collapse and overdistension by electrical impedance tomography in supine vs. targeted lateral body position within the left lung. Left-to-right lung asymmetry was present on initial X-Ray taken in supine body position: unequivocally more opacities within the left lung. Thus lateral right positioning (30°) was indicated (“targeted”) and performed with the platform-based rotation bed Multicare® (LINET). Line graphs of electrical impedance tomography (EIT)-based estimations of collapse and overdistension during decremental positive end-expiratory pressure (PEEP) titrations (supine vs. targeted lateral body position) are shown (mean ± SEM). Some illustrative and representative EIT images of collapse are also shown: collapsed pixels in purple. Note that the amount of collapsed units within the left lung present in the supine body position was minimized in the lateral right one. X axis: Decremental PEEP levels of the EIT-PEEP titrations. Y axis: Percent of overdistended and collapsed lung units out of the total lung imaged by EIT. Triangle: Supine body position. Square: Targeted lateral body position (lateral right). Black triangle and black square: Percent of collapsed lung units out of the total lung imaged by EIT. White triangle and white semi-filled square: Percent of overdistended lung units out of the total lung imaged by EIT.

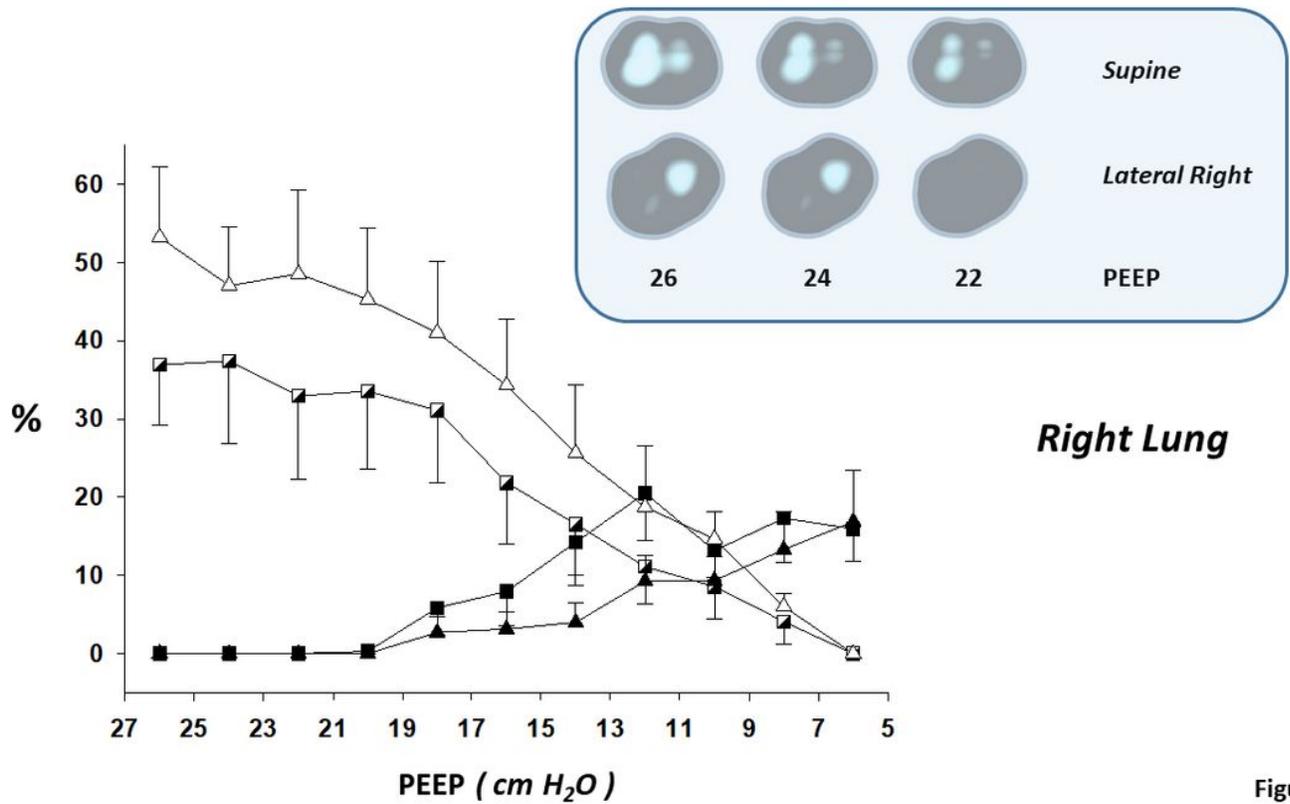


Figure 2

**Figure 2**

Lung collapse and overdistension by electrical impedance tomography in supine vs. targeted lateral body position within the right lung. Left-to-right lung asymmetry was present on initial X-Ray taken in supine body position: unequivocally more opacities within the left lung. Thus lateral right positioning (30°) was indicated (“targeted”) and performed with the platform-based rotation bed Multicare® (LINET). Line graphs of electrical impedance tomography (EIT)-based estimations of collapse and overdistension during decremental positive end-expiratory pressure (PEEP) titrations (supine vs. targeted lateral body position) are shown (mean ± SEM). Some illustrative and representative EIT images of overdistension are also shown: overdistended pixels in white. Note the asymmetric distribution of overdistension between the right and left lungs (concentration and predominance of overdistension within the right lung); and that the amount of overdistended units within the right lung in the supine body position was minimized in the lateral right one. Also note that the regional distribution of overdistension in the supine body position was much less gravitational-dependent than it is usually present in “typical” acute respiratory distress syndrome. X axis: Decremental PEEP levels of the EIT-PEEP titrations. Y axis: Percent of overdistended and collapsed lung units out of the total lung imaged by EIT. Triangle: Supine body position. Square: Targeted lateral body position (lateral right). Black triangle and black square: Percent of collapsed lung units out of the total lung imaged by EIT. White triangle and white semi-filled square: Percent of overdistended lung units out of the total lung imaged by EIT.