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Original Article

Effect of head-end of bed elevation on respiratory mechanics in mechanically ventilated patients with moderate-to-severe COVID-19 ARDS – A cohort study

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ABSTRACT

Background: Head-end elevation (HEE) is known to improve oxygenation and respiratory mechanics. In ARDS, poor lung compliance limits positive pressure ventilation causing delivery of inadequate minute ventilation (MVe). We observed that, in moderate-to-severe COVID-19 ARDS, the respiratory system compliance (Crs) reduces upon elevating the head-end of the bed, and vice-versa, which can be utilized to improve ventilation and avoid respiratory acidosis.
We hypothesized that increasing the degree of HEE reduces Crs.
Methods: We included 20 consecutive mechanically ventilated, moderate-to-severe COVID-19 ARDS patients in this pilot study (CTRI/2021/06/034,182). The Crs, Mve and Rinsp were recorded at 0°, 10°, 20° and 30° HEE. Repeated measures ANOVA was used to determine significant differences in measurements with increasing degrees and repeated measures correlation (*rmcorr*) for correlation.
Results: Repeated measures ANOVA showed a significant difference ($p < 0.0001$) between values of Crs, MVe and Rinsp. *Rmcorr* showed a strong negative correlation between increasing degrees and Crs and Mve (r-0.87 [95% CI -0.79 to −0.92, $p < 0.0001$ and r-0.77 [95% CI -0.64 to −0.85, $p < 0.0001$]) and a moderate negative correlation for Rinsp (r-0.67; 95% CI -0.79 to −0.50; $p < 0.0001$).
Conclusions: Increasing degree of HEE reduces compliance in moderate-to-severe COVID-19 ARDS. Reducing HEE may optimize ventilation and mitigate ventilator induced lung injury.

1. Introduction

The pathophysiology and optimal management of acute respiratory distress syndrome (ARDS) has stymied the medical fraternity for a long time. The underlying mechanism appears to be a dysregulated immune response leading to alveolar edema, producing impaired gas exchange, consolidation and atelectasis [1]. This pathological process is heterogenous, usually involving the dorsal regions more than the ventral. Only a small part of the lung remains functional and aerated, called the 'baby lung' [2]. In recent times, the Severe Acute Respiratory Syndrome Coronavirus-2 (SARS-CoV-2) has led to a massive surge in cases of ARDS. The mortality in COVID-19 (Coronavirus disease, 2019) ARDS is approximately 39% (95% confidence interval [CI]: 23–56%) worldwide [3]. As this virus continues its rampage, efforts to understand the pathophysiology, optimize management and reduce complications continue.

A frequently encountered problem after intubation is an inability to match the patients' minute ventilation demand with artificial ventilation, which gives rise to respiratory acidosis, hypoxia and hemodynamic instability. The cause is the tremendous amount of dead-space ventilation and increased shunt fraction associated with ARDS. This causes ventilation perfusion ($V_A/\dot{Q}$) mismatch and, ineffective gas exchange [4] and requires increased minute ventilation for compensation. The goal during mechanical ventilation in ARDS is to oxygenate while preventing further lung injury, and recruit collapsed lung units [5] by application of appropriate levels of positive end expiratory pressure (PEEP). Artificial ventilation of these severely affected lungs is challenging

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as they often have very low compliance requiring high airway pressures during positive pressure ventilation. This can give rise to ventilator induced lung injury (VILI), such as barotrauma, volutrauma, atelectrauma and biotrauma which can cause alveolar rupture, pneumothorax, pneumomediastinum and hemodynamic instability, etc. [6] Hence, there is a pursuit for techniques to avoid VILI while attempting to meet a patient's ventilatory demand.

The influence of posture on respiratory dynamics is considerable since factors like the intrapleural pressure gradient, perfusion distribution and mechanical effects on the volume and shape of the diaphragm and lungs, are affected by gravity [7]. While much benefit has been observed from 16 h of prone ventilation with 20–30° reverse Trendelenberg tilt, ventilation during the period of supine positioning remains challenging. Poor respiratory compliance and high airway pressures limit ventilation which can lead to the delivery of inadequate minute ventilation. This can even progress to respiratory acidosis which may be fatal.

For patients in the intensive care unit (ICU), in supine position, an elevation of head-end of bed ≥30° is recommended to prevent aspiration of enteral feeds (and ventilator associated pneumonia [8]), and due to favorable respiratory mechanics in this position [9]. This occurs due to a descent of the diaphragm which leads to an increase in the functional residual capacity (FRC), respiratory system compliance (Crs) and, hence, oxygenation. However, during the management of COVID-19 patients with moderate-to-severe ARDS, we observed that elevating the head-end in the supine position leads to progressive reduction of respiratory system compliance and producing higher airway pressures and limiting ventilation. The opposite effect is noticed on lowering the head-end. This implied a potential rescue maneuver when poor compliance-limited ventilation produces critical respiratory acidosis. We, hence put forward the research hypothesis that the degree of head-end elevation and compliance are inversely related in patients with moderate-to-severe COVID-19 ARDS.

2. Methods, aims and outcomes

This pilot study was a single-centre, observational study conducted over a period of one month from to June 15 to July 15, 2021, in a dedicated COVID-19 ICU, in a tertiary care centre. After approval from the Institutional Ethics Committee (NK/7057/Study/145), the study was registered in Clinical Trials Registry – India (CTRI/2021/06/034,182). As all patient data was de-identified and the intervention involved a routine maneuver for a short duration, written consent was waivered by the ethics committee.

2.1. Aims and outcomes

The aim of the study was to assess the respiratory mechanics with different degrees of head end elevation (HEE) of bed in severe COVID-19 ARDS patients on mechanical ventilation using pressure control ventilation (PCV).

1. The primary outcome was to find out the correlation coefficient between HEE and static respiratory system compliance (Crs).
2. The secondary outcomes were to analyze the association between HEE and expired minute ventilation (MVe), airway resistance (Rinsp), and oxygen saturation.

2.2. Patient population

Twenty consecutive patients over 18 years of age, diagnosed with COVID-19 by reverse transcriptase polymerase chain reaction (RT-PCR), having moderate-to-severe ARDS (by Berlin criteria) [10], and on invasive mechanical ventilation in the intensive care unit (ICU), were recruited. Patients with hemodynamic instability (mean arterial pressure [MAP] < 75 mmHg or requirement of more than one vasopressor), with clinical or laboratory evidence of secondary bacterial lower respiratory tract infection, pre-existing lung pathology, cardiac cause of hypoxia, connective tissue disorders, high intra-abdominal pressure and those with structural deformities of the spine and rib cage were excluded from the study.

2.3. Intervention

In this observational study, HEE was performed on all patients starting from the supine position, and values from the same patient in different degrees of HEE were compared. Each patient was continuously monitored with a pulse oximeter, electrocardiography, invasive intra-arterial blood pressure and a skin temperature probe. Sedation and muscle relaxation was maintained with a titrated infusion of intravenous fentanyl at 1–2 μg/kg/hr and atracurium at 10–15 μg/kg/min. The HAMILTON C3® ventilator (Hamilton Medical® AG, Switzerland) was used for ventilation and parameter measurement. All patients were ventilated by pressure control mode of ventilation, the parameters of which were targeted to a partial pressure of arterial oxygen (PaO_2) of ≥60 mmHg and an allowable partial pressure of arterial carbon dioxide ($PaCO_2$) not resulting in respiratory acidosis (pH ≤ 7.2), as determined by arterial blood gases measured 15 min prior to the intervention. Optimum PEEP was individualized in each patient as per measurement of the upper inflection point on the expiratory limb of the pressure volume loop obtained from the P/V Tool® Pro of the HAMILTON® C3 ventilator for PEEP responsive patients. The ventilator settings and FiO_2 were not altered during the experiment.

Prior to starting the maneuver, adequate inflation of the cuff of the endotracheal tube was ensured to eliminate any leak and minimize the risk of pulmonary aspiration of gastric contents. A recruitment maneuver using the P/V Tool® Pro (PEEP of 40 cmH_2O for 10 s) was then executed in the supine position to ensure homogeneity of ventilation. After a 15-min pause, the head-end of the patient's bed was elevated sequentially from 0° to 30°, and measurements noted at each position, as elaborated subsequently. For accuracy, a goniometer was used for adjusting the degree of tilt. The measurements noted were static respiratory system compliance (Crs), expired tidal volume (Vte), minute ventilation (MVe) and airway resistance (Rinsp), with monitoring of SpO_2, MAP, systolic and diastolic blood pressure and heart rate.

The baseline measurements were taken at 0° in supine position. The subsequent positions were head end elevation of bed to +10° supine, +20° supine and +30°. Each position was maintained for 2 min, and measurements taken subsequently. The total time of 2 min was allowed for homogenization of the gravitational gradient of perfusion distribution and intra-pleural pressure along with hemodynamics. A Trendelenburg position was not assessed due to the risk of regurgitation of gastric contents if such a position were to be maintained for a prolonged period. The intervention was to be aborted in the event of any desaturation >4% or hemodynamic compromise (reduction of MAP >20% of the baseline value).

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2.4. Statistical analysis

An exploratory pilot study was done in the absence of any prior data in this regard.

Normality of the data was checked with Shapiro Wilks test, and the parameters were described as mean ± standard deviation (SD) if found normal. The null hypothesis was that increase in degree of HEE would not lead to a significant decrease in Crs.

Repeated measures ANOVA was used to test if Crs, Mve and Rinsp varied with change in head-end elevation. Mauchly's test was used to verify the assumption of sphericity, and Greenhouse-Geisser correction was employed if its violation was found. A post-hoc pairwise *t*-test with Bonferroni correction was also done for each variable.

Repeated measures correlation was used to assess correlation between degree of head end elevation and the respiratory parameters *viz.* Crs, Mve and Rinsp. R 4.0.2 (R Foundation for Statistical Computing, Vienna, Austria) was used for statistical analysis.

3. Results

3.1. Demographics

Data from 23 consecutive patients were collected. Three patients were excluded as tracheal aspirate culture revealed bacterial colonization at the time the study was conducted. Finally, data from twenty patients were analyzed. Sixty percent were males, with mean (±SD) age of 59 ± 13.2 years. The median (IQR) days of illness (after onset of symptoms) on which the measurements were taken was 14 (10,15.25) days. All patients uniformly received steroid in the form of injection Dexamethasone 6 mg once daily and injection Remdesivir for 5 days and anticoagulation with prophylactic dose of injection Enoxaparin subcutaneously. The median (IQR) days after intubation on which the intervention was done and measurements taken was 2 (1,2) days. The average $PaO_2:FiO_2$ (mean [±SD]) was 94.2 ± 27.9. The average PEEP (mean [±SD]) set was 8.7 ± 1.9 cmH_2O (Table 1).

3.2. Primary outcome

The Crs at 0° supine, 10°, 20° and 30° head-end elevated position was 21.69 ± 6.45, 20.68 ± 6.12, 19.2 ± 6.02 and 17.31 ± 5.61 ml/cmH_2O, respectively (Table 2). Repeated measures ANOVA with Greenhouse-Geisser correction for violated sphericity showed Crs to be significantly different at all head angle increments ($F(1.19,22.64) = 65.475$, $p < 0.001$, generalized eta squared = 0.072). Pairwise post-hoc tests with Bonferroni correction demonstrated significant differences between all levels (Table 3). Crs showed a strong negative correlation with HEE (correlation coefficient −0.87; 95% CI -0.92 to −0.79; $p < 0.0001$) in all patients.

Table 2
Values of respiratory system compliance (Crs), tidal volume (Vte) minute ventilation (Mve) and respiratory resistance (Rinsp) presented (mean ± SD).

	0°	10°	20°	30°
Crs (ml/cmH$_2$O)	21.69 ± 6.45	20.68 ± 12	19.2 ± 6.02	17.31 ± 5.61
Vte (L)	4.29 ± 0.89	4.11 ± 0.84	3.89 ± 0.86	3.64 ± 0.82
Mve (L/min)	12.9 ± 2.25	12.57 ± 2.21	11.98 ± 2.07	11.2 ± 2.04
Rinsp (cmH$_2$O/L/s)	13.45 ± 5.33	13.3 ± 5.23	12.95 ± 5.44	12.05 ± 5.51

3.3. Secondary outcomes

The SpO_2 value remained same during the experiment in all the subjects. Similarly Mve ($F(1.13,21.43) = 30.145$, $p < 0.001$, generalized eta squared = 0.086, Greenhouse-Geisser correction for violated sphericity applied) and Rinsp ($F(3,57) = 20.31$, $p < 0.001$, generalized eta squared = 0.011) also significantly differed with the angle. Pairwise post-hoc tests with Bonferroni correction demonstrated significant differences between all levels of Mve, but there was no difference between Rinsp at 0, 10 and 20° (Table 3). The variations in Crs, Mve and Rinsp all showed significant repeated measures correlation with the degree of head-end elevation. Mve (correlation coefficient −0.77; 95% CI -0.86 to −0.64; $p < 0.001$) and Rinsp (correlation coefficient −0.67; 95% CI -0.79 to −0.50; $p < 0.0001$) showed a moderate negative correlation with wider confidence intervals. Fig. 1 shows the rmcorr analysis for correlation of observed values of Crs, Mve and Rinsp at various increments of head-end elevation.

No complications occurred during the intervention, and the experiment did not require to be aborted or repeated in any subject.

4. Discussion

Maintaining normoxia and normocarbia in ARDS is difficult due to an increased shunt fraction (often >40%) and increased dead space ventilation (may exceed 70% [11]).

This physiology mandates high minute ventilation. While prone ventilation improves respiratory mechanics and V_A/Q matching, meeting the ventilatory demand during periods of supine ventilation is challenging. An inability to match the patient's minute ventilation demand may lead to fatal respiratory acidosis. Hence, we investigated the phenomenon of decreasing respiratory compliance with reverse Trendelenberg position, to be able to utilize it as a rescue measure in severe hypercapnea, by matching ventilatory requirements in supine position.

We performed this pilot observational study on adult COVID-19

Table 1
Population parameters.

Age (years)	59 ± 13.2
Sex	12 males (60%) 8 females (40%)
Weight (in kgs)	66.4 ± 21.1
Height (in cm)	170.2 ± 8.2
Body mass index (kg/m^2)	23.2 ± 3.2
Day of Illness at measurement (in days)	14 (10,15.25)
Duration of mechanical ventilation at measurement (in days)	2 (1,2)
PaO$_2$:FiO$_2$ ratio (PaO$_2$ in mmHg)	94.2 ± 27.9
Moderate ARDS (PaO$_2$:FiO$_2$ > 100 ≤ 200)	6 (30%)
Severe ARDS (PaO$_2$:FiO$_2$ ≤ 100)	14 (70%)
FiO$_2$ (mean, ± SD)	0.75, ±0.14
Vasopressor use	8 (40%)
Antibiotic use	18 (90%)
APACHE II score (median, IQR)	8 (6,9)

Continuous parametric variables are presented as mean ± SD (standard deviation), non-parametric variables as median (interquartile range [IQR]) and nominal variables are presented as absolute number and percentage.
Abbreviations: APACHE II: Acute Physiology and Chronic Health Evaluation II, ARDS: acute respiratory distress syndrome; FiO_2: fraction of inspired oxygen, $PaO_2:FiO_2$: ratio of partial pressure of arterial oxygen to fractional oxygen concentration.

Table 3
Pairwise post hoc t tests with between the different levels of head-end elevation (HEE) for Crs (static respiratory system compliance in ml/cm H_2O); Mve (minute ventilation in L/min) and Rinsp (inspiratory resistance in cm H_2O/L/s). P values with Bonferroni correction are reported.

Crs			
HEE	0°	10°	20°
10°	<0.001	–	–
20°	<0.001	<0.001	–
30°	<0.001	<0.001	<0.001
Mve			
HEE	**0°**	**10°**	**20°**
10°	<0.001	–	–
20°	<0.001	0.002	–
30°	<0.001	<0.001	<0.001
Rinsp			
HEE	**0°**	**10°**	**20°**
10°	1.000	–	–
20°	0.126	0.659	–
30°	<0.001	<0.001	<0.001

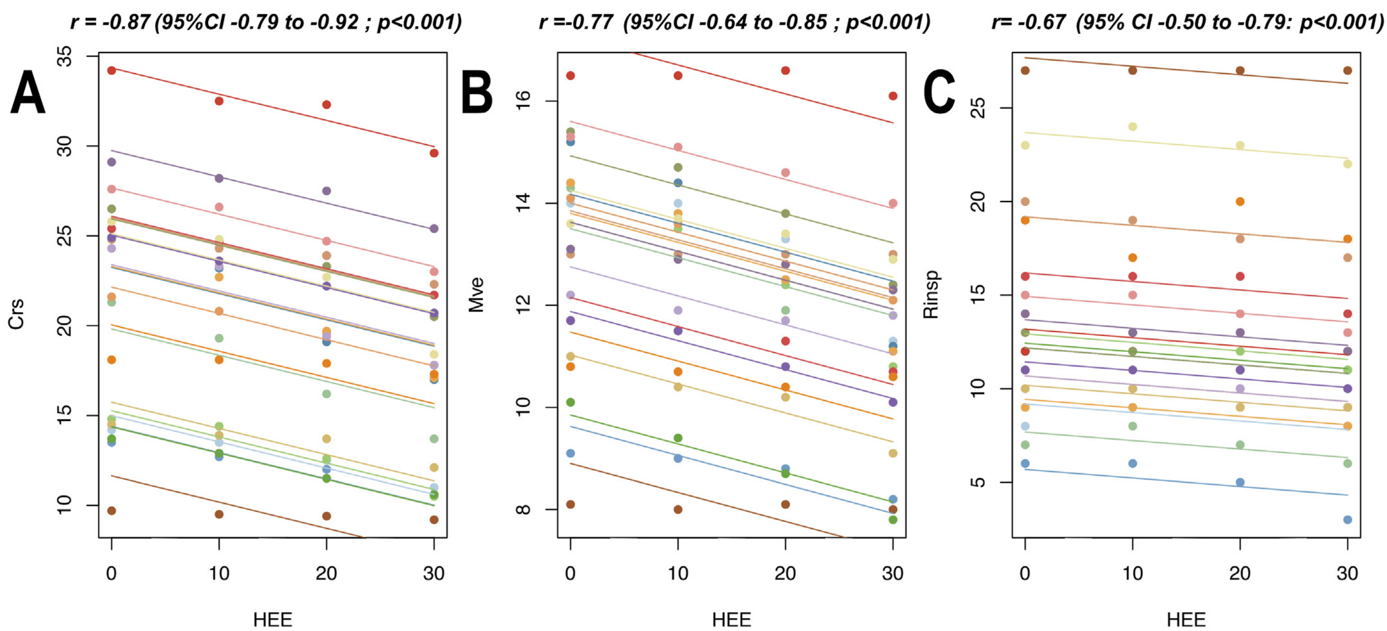

Fig. 1. Showing correlation of degree of Head End Elevation (HEE) with static compliance in ml/cm H_2O (Crs), Minute ventilation in L/min (Mve) and Inspiratory resistance in cm H_2O/L/s (Rinsp). Each patient data is presented in a different color, dots represent each individual data points for each subject and the lines are regression lines fitted for each patient. There is a strong negative correlation of the Crs, Mve and Rinsp with increasing degrees of HEE (Repeated measure correlation coefficient [rmcorr] 'r' for Crs, Mve and Rinsp are −0.88725, −0.7714 and −0.6727 respectively). (For interpretation of the references to color in this figure legend, the reader is referred to the Web version of this article.)

patients with moderate-to-severe ARDS, undergoing invasive mechanical ventilation, using a routine intervention. The results suggest a strong negative linear correlation between the degree of HEE and the Crs in COVID-19 ARDS. Accordingly, as the measurements are mathematically tied, a fall in the Crs is associated with a decrease in TV and MVe.

While much data supports the increase of compliance in the upright and head-up positions due to an increase in the FRC (Fig. 2) [12], a decrease in compliance with head of bed elevation has indeed been previously described in ARDS, although this finding is not uniformly present in all patients. Richard et al. performed a similar study on 16 mechanically ventilated ARDS patients and found two types of responses to verticalization – an increase in oxygenation ('responders') and a decrease in or no change in oxygenation ('non-responders') [13]. They found that respiratory compliance decreased upon verticalization in 'responders' (40 ± 15 vs. 31 ± 9 ml/cmH_2O, supine and vertical, respectively) and increased in 'non-responders'. They also found a gradual increase in end expiratory lung volume in 'responders'. Therefore, they posited that this phenomenon may be due to progressive alveolar recruitment, which gradually reduces compliance as the alveoli expand. On the contrary, Dellamonica et al., in their study on 40 ARDS patients, reported that the 'non-responders' group showed a decrease in compliance with verticalization [8]. They attributed it to an increase in intra-abdominal pressure in the seated position which decreases compliance, but did not address why only a subset of their patients demonstrated this finding. The primary drawback in both these studies [8,13] is that the etiology of the ARDS was not mentioned, and mild cases of ARDS were also included. The PaO_2:FiO_2 ratios and respiratory compliance in these studies were higher, indicating comparatively less diseased lungs. In our study, we encountered a decrease in compliance with HEE, uniformly in

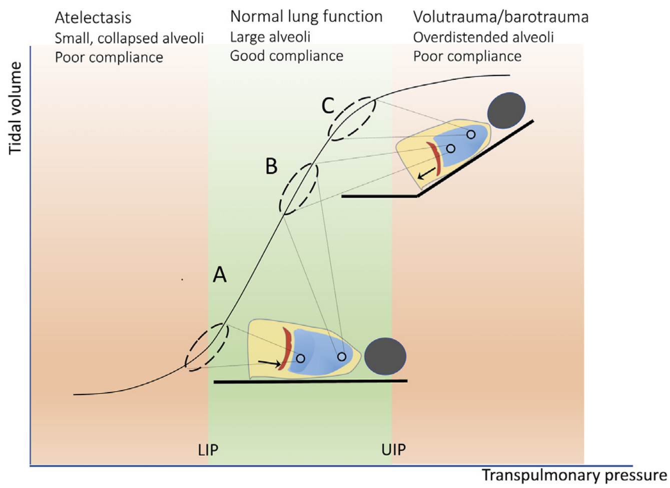

Fig. 2. Normal Lung physiology in an awake individual: The basal and dorsal segments of the lung are collapsed in supine position. With the change in position from supine to head end elevated position, the functional residual capacity and the compliance of the lower lung zone reach the zone B (vertical part of compliance curve). The upper parts of the lung (which form smaller fraction of lung) which are already open move on the compliance curve (zone C). The overall compliance of the respiratory system is improved.

all patients with moderate-to-severe COVID-19 ARDS.

In moderate-to-severe COVID-19 ARDS, in the upright position, with descent of the diaphragm, the basal, consolidated segments exert a downwards tractional force on the remaining functional lung segments, thus distending them and reducing their compliance. This takes the lung higher up on the compliance curve, to the plateau beyond the upper inflection point (Fig. 3). In the supine position, the cephalad ascent of the diaphragm [14] relieves this pull on the rest of the lung, thereby increasing the compliance. This explanation agrees with a study by Kummer et al. in which application of pressure over the upper abdomen was shown to improve respiratory system compliance [15]. This contrasts with the normal lung physiology, where a more upright posture leads to improvement in the Crs and $V_A/\dot{Q}$ matching (Fig. 2).

We also found that resistance decreases linearly with HEE. This is expected because the increase in lung volume in upright position stretches the airways, resulting in an increased diameter which decreases airway resistance [8,13].

Further research exploring the respiratory mechanics along with volume studies with position change will further our knowledge in understanding the respiratory mechanics in severe ARDS and COVID ARDS.

This study has certain limitations. Firstly, since this study was a feasibility study, the data is presented from a small sample size. Second, the findings of the study are not supported with blood gas analysis, which would have strengthened the study. Third, we did not confirm the change in lung compliance by reversing the sequence of head end elevation from 30° to zero°. Fourth, like previously conducted studies randomization was not done for the sequence of position changes. Fifth, transpulmonary pressures could not be measured as we did not use an esophageal balloon.

The duration of this intervention is limited by its propensity for gastric acid micro-aspiration, hence can only be used as a rescue-maneuver in life-threatening hypercapnea. It, therefore, also warrants strict monitoring of ETT cuff pressure, subglottic suction and administration of antacids and prokinetics and low volume feeds. In an extended study the above measurements could provide more accuracy.

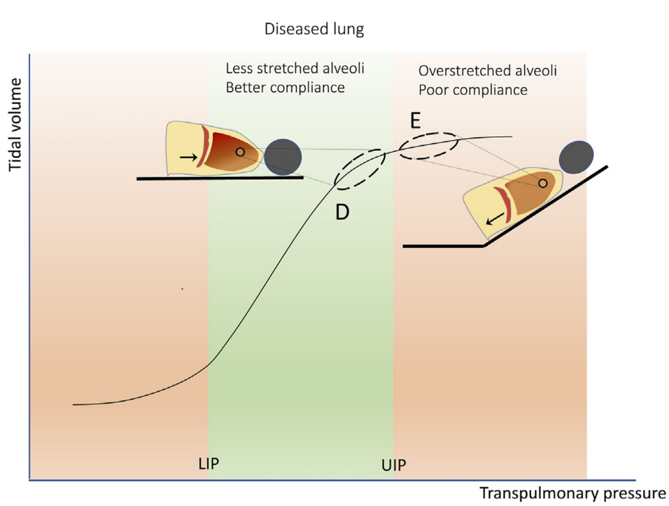

Fig. 3. COVID-19 ARDS lung. The functional alveolar units spared from the COVID-19 ARDS are placed higher up on the compliance curve (zone D) due to positive pressure ventilation, the partial damage due to the disease itself and the tractional forces from the adjacent consolidated lung units. Upon elevation of the head end, the already distended alveoli get overstretched and the compliance is reduced further (zone E).

5. Conclusions

The respiratory system compliance, minute ventilation and respiratory resistance all decreased with increasing degrees of head-end elevation. This may be used as a rescue measure in optimizing mechanical ventilation in moderate-to-severe COVID-19 ARDS patients with poor respiratory system compliance, in whom hypoventilation due to limitation by high airway pressures causes critical respiratory acidosis with subsequent hemodynamic compromise.

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Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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