Increasing positive end-expiratory pressure (re-) improves intraoperative respiratory mechanics and lung ventilation after prone positioning

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Abstract

Background: Turning a patient prone, changes the respiratory mechanics and potentially the level of positive end-expiratory pressure (PEEP) that is necessary to prevent alveolar collapse. In this prospective clinical study we examined the impact of PEEP on the intratidal respiratory mechanics and regional lung aeration in the prone position. We hypothesized that a higher PEEP is required to maintain compliance and regional ventilation in the prone position.

Methods: After ethical approval, 45 patients with healthy lungs undergoing lumbar spine surgery were examined in the supine position at PEEP 6 cm H2O and in the prone position at PEEP (6, 9 and 12 cm H2O). Dynamic compliance (Crs) and intratidal compliance-volume curves were determined and regional ventilation was measured using electrical impedance tomography. The compliance-volume curves were classified to indicate intratidal derecruitment, overdistension, or neither.

Results: Crs did not differ between postures and PEEP levels (P>0.28). At a PEEP of 6 cm H2O a compliance-volume profile indicating neither derecruitment nor overdistension was observed in 38 supine, but only in 20 prone positioned patients (P<0.001). The latter increased to 33 and 37 (both P<0.001) when increasing PEEP to 9 and 12 cm H2O, respectively. Increasing PEEP from 6 to 9 cm H2O in the prone position increased peripheral ventilation significantly.

Conclusions: Respiratory system mechanics change substantially between supine and prone posture, which is not demonstrated in routine measurements. The intratidal compliance analysis suggests that in most patients a PEEP above commonly used settings is necessary to avoid alveolar collapse in the prone position.

Clinical trial registration: DRKS 00005692.

Key words: circulatory and respiratory physiological phenomena; lung-compliance; lung; positive-pressure respiration; posture; prone position; respiration, artificial; respiration; respiratory mechanics

Mechanical ventilation during anaesthesia promotes alveolar collapse, even in patients with healthy lungs.1 PEEP is applied in order to prevent alveolar collapse, avoiding the stress and strain at alveolar units that is caused by cyclic derecruitment and recruitment, a phenomenon known to result in atelectrauma.2 However, the optimal level of PEEP is still not known in healthy...
Editor’s key points

- There are few data on optimum PEEP during anaesthesia in the prone position.
- In this study, prone positioning had no effect on dynamic respiratory compliance but gas distribution was greater in non-dependent regions.
- PEEP of 6 cm H₂O was adequate for almost all patients when supine, but a PEEP of 9 cm H₂O or greater was required to minimize cyclical alveolar collapse in the prone position.
- Higher than usual PEEP settings may be required when patients are positioned prone.

Patients. Recently, ventilation with optimal PEEP and recruitment manoeuvres (i.e. peroperative lung protective ventilation), has been associated with fewer postoperative pulmonary complications and lower mortality. While published studies focus on patients in the supine position, little is known about the effects on the lung during ventilation in the prone position, and surgery in the prone position is increasing as the global incidence of spine disorders increases. Positioning of anaesthetized, lung healthy patients in the supine position and in the prone position is increasing as the global incidence of spine disorders increases. Positioning of anaesthetized, lung healthy patients from supine to prone increases functional residual capacity (FRC) and arterial oxygenation (paO₂). Additionally, it also effects regional ventilation and thus ventilation homogeneity as the gravitational forces act conversely, compared with supine.

Based on the modified physiological conditions, patients turned in the prone position might require adjustment of PEEP to avoid intratidal derecruitment.

This study investigates the mechanics of the respiratory system of lungs in healthy patients in the supine position and in three different PEEP levels in the prone position. In addition to respiratory system compliance, the course of the intratidal compliance-volume curves were analysed and classified. An improved respiratory mechanical situation was defined as the presence of a horizontal compliance-volume profile, as this indicates neither tidal derecruitment nor end-tidal overdistension. In order to measure regional lung ventilation we used electrical impedance tomography (EIT), which is a radiation free, real-time imaging technique for displaying the regional ventilation within a cross-sectional plane in the lungs.

We hypothesized that during mechanical ventilation in the prone position (a) the routinely applied PEEP level is too low to protect against intratidal derecruitment and that (b) a moderate increase in PEEP would improve compliance and regional lung ventilation.

Methods

In this prospective cross-over clinical study we included adult patients undergoing elective minimally invasive surgery of the lumbar spine. All patients underwent spirometry (Vitalograph In2itive, Hamburg, Germany) in a sitting position the day before surgery. Patients were included if the fraction of forced expiratory value in 1 s (FEV₁) was higher than 0.8 of the predicted value and the fraction of the ratio of FEV₁ and forced vital capacity (FVC), FEV₁/FVC, was higher than 0.7. Criteria for exclusion were age <18 yr, pregnancy, obesity (BMI>35), acute or chronic pulmonary disease (requiring bronchodilator medication) and any contraindication to the use of EIT (i.e. implanted electrical device). The study was approved by the ethics committee of the University Medical Center Freiburg (EK 14/14) and pre-registered at the German Register for Clinical Trials (DRKS 00005692). Written informed consent was obtained from all patients before intervention.

Anaesthesia

To perform EIT measurements, an electrode belt with an array of 16 electrodes was placed around the thorax, at the fifth intercostal space. After establishing standard monitoring, anaesthesia was induced with sufentanil (0.5 µg kg⁻¹) and target-controlled infusion (TCI) of propofol (3–4 µg ml⁻¹; Schnider model). Rocuronium (0.4–0.6 mg kg⁻¹) was used for muscle relaxation. Neuromuscular monitoring was performed using mechanomyography (Stimpod NMS450, Xavant Technology Ltd, South Africa). Sufficient conditions for intubation were presumed at a train-of-four ratio less than 0.25. After face mask ventilation the patient was intubated with a high-volume, low-pressure cuffed tracheal tube (Mallinckrodt™, Dublin, Ireland). Intratracheal placement of the tracheal tube was confirmed by bilateral auscultation and end-expiratory CO₂ measurement. The tracheal tube’s cuff pressure was kept within a range of 20 to 25 cm H₂O. Anaesthesia was maintained as total i.v. anaesthesia by continuing TCI of propofol (2–3 µg ml⁻¹) and continuous infusion of remifentanil (0.1–0.2 µg kg⁻¹ min⁻¹). Hypotension (mean arterial pressure <60 mm Hg) was treated with continuous infusion of norepinephrine (0.02–0.1 µg kg⁻¹ min⁻¹).

Study protocol

During the measurements patients’ lungs were ventilated in the volume controlled mode (Zeus, Draeger, Luebeck, Germany) with a tidal volume (VT) of 6–8 ml kg⁻¹. Normal body weight was calculated using Broca’s index (normal weight=height [cm] – 100). The end-inspiratory plateau-pause was 20% and the fraction of inspired
oxygen was 0.6. The ventilation frequency was adjusted to achieve end-expiratory partial CO₂ pressure between 4.6 and 5.9 kPa.

Figure 1 illustrates the time course of interventions of the study protocol. PEEP was 6 cm H₂O in the supine position. After prone positioning PEEP was set to 6, 9 and 12 cm H₂O following a randomized order, previously determined for each patient. Before each PEEP-interval, lung recruitment manoeuvres were performed to set the lungs to a defined baseline status. Therefore, the working pressure of the ventilator was limited to 40 cm H₂O and PEEP was gradually increased to a maximum of 15 cm H₂O at constant tidal volume, and held for 10 breaths. To allow for equilibration of the respiratory system, each PEEP level was maintained for at least 15 min, in both the supine and prone position. In the last five min of the respective PEEP interval, airway pressure (Paw), end-inspiratory plateau pressure (Pplat) and flow rates were measured by means of a main stream sensor system (CO₂/Flow Sensor, M2781A, Philips, Germany). Simultaneously, EIT images were recorded at 20 frames per s (PulmoVista® 500, software version 1.10, Dräger, Lübeck, Germany). All measurements were performed in immediate sequence after intubation (i.e. independent of the duration of surgery).

In the prone position, the pelvis and the chest were supported by pads with the arms directed over the head; the knees were semi-flexed and the head lay in a headrest. Thus, free movement of the abdomen was ensured. After positioning, the unchanged location of the EIT belt was confirmed by visual inspection of its position with respect to anatomical landmarks.

Respiratory data analysis

After the experiments the data were processed with Matlab (R 2014a, Natick, USA). Volume data were calculated by numerical integration of the flow rate. The dynamic compliance of the respiratory system (Cdyn) was calculated at each posture and PEEP level. Volume-dependent intratidal compliance curves were calculated and categorized using the gliding-Slice method as described previously. In brief, the tidal pressure-volume-curve was subdivided into 31 equidistant volume portions (slices; Fig. 2A). For each slice, the volume specific compliance was determined via multiple linear regression analysis of data lying within the volume range surrounding the slice by 1/6 of the tidal volume (Fig. 2B). The resulting intratidal compliance-volume curves were assigned to one of six compliance profiles (Fig. 2C). An increasing compliance profile is assumed to indicate intratidal derecruitment. A decreasing compliance profile is assumed to indicate intratidal overdistension. A horizontal compliance profile is assumed to indicate ventilation with neither derecruitment nor overdistension. Combinations of increasing, horizontal and decreasing profile sections indicate either transitions between two neighbouring profiles (increasing to horizontal profile and horizontal to overdistension profile) or the inclusion of all profiles.

EIT data analysis

End-expiratory and tidal EIT images were generated from measurements in the supine position and from the different PEEP levels in the prone position. An average tidal EIT-image from all patients was generated at each respective condition. Impedance tidal variation (ITV) was calculated as the difference between the end-inspiratory and the end-expiratory relative impedance. The anterior to posterior centre of ventilation was determined from the EIT-image, as its balance point in the ventrodorsal axis.

To calculate regional gas distribution, tidal EIT-images were subdivided into two regions of interest (ROI: ventral (V) and dorsal (D); each 32×16 pixels) and the global ITV was subdivided into eight iso-volume parts. The fraction of regional gas distribution during inspiration was then calculated as the quotient of ITV within the respective ROI and the respective volume part of the global ITV.

Regional compliance and the fraction of cumulated alveolar collapse were calculated from measurements in the prone position. Therefore, ITV was divided by the respective driving pressure (Pplat – PEEP) on a pixel by pixel basis. Based on the regional compliance images at PEEP 12 cm H₂O, a ‘ventilated lung area’ was defined within the images by identifying pixels that changed impedance by ≥5% of the maximum ITV. Alveolar collapse was calculated as the percentage of change in pixel compliance in relation to its ‘best compliance’ from all PEEP levels and then averaged for all pixels within the ‘ventilated lung area’.

Regional end-expiratory ventilation for each respective posture and PEEP level was calculated as the fraction of end-expiratory lung impedance within four ROIs (ventral (V), mid-ventral (MV), mid-dorsal (MD) and dorsal (D); each 32×8 pixels).
Statistics

Mean respiratory system compliance (Crs) was used as a surrogate parameter to calculate the number of patients required for statistical analysis before the study. Assuming a mean Crs of 50 ml·cm H2O⁻¹ and a standard deviation (SD) of 8 ml·cm H2O⁻¹, 41 patients were required to achieve a study power of 80%. To compensate for a dropout rate which we assumed to be above the ordinary (as a result of potential interferences in the EIT measurements) 50 patients were enrolled. Ventilation and haemodynamic data are presented as mean (SD) if not indicated otherwise. To compare frequencies of compliance profiles χ² tests were applied on a contingency table with multiple columns and rows, followed by Fisher’s exact test as post hoc test. Differences in the dynamic compliance and other ventilation and haemodynamic values were compared using two-way ANOVA, followed by Tukey’s multiple comparison test as post hoc test, if applicable. For EIT analyses, means of ITV were compared between ROIs using two-way ANOVA, followed by Tukey’s multiple comparison test as post hoc test, if applicable.

Results

Patients

63 patients were prospectively screened for this study (Supplementary data, Fig. S1); 13 patients were excluded because of cancelled surgery (n=1), body positioning during surgery deviating from standard (n=2) or insufficient preoperative spirometry (n=10). Another five patients were excluded after intervention because of violation of the study protocol (n=1) and poor data quality from EIT or respiratory measurements because of artifacts (n=4). Data from the remaining 45 patients were analysed. Indications for surgery were lumbar disc hernia (n=43), implant removal after dorsal lumbar stabilization (n=1) and screw loosening after dorsal lumbar stabilization (n=1). Patient characteristics are given in Table 1. Frequencies of random PEEP sequences in the prone position were homogenously distributed (sequence 6/9/12: n=8; sequence 6/12/9: n=7; sequence 9/6/12: n=8; sequence 9/12/6: n=7; sequence 12/6/9: n=7; sequence 12/9/6: n=8).

Ventilation and haemodynamic variables

Intraoperative ventilation and haemodynamic variables are given in Table 2. Body weight adjusted tidal volume (Vt/kg) was at the upper end of the target range [8.1 (0.9) ml kg⁻¹ normal body weight]. Both, Vt and Vt/kg were higher in the supine than in the prone position, but did not vary significantly at the different applied PEEP levels in the prone position. In the prone position Ppl and Pplat increased with the applied PEEP level, accordingly. The Crs was 60 (14) ml cm H2O⁻¹ and differed neither between supine and prone position nor between the PEEP levels applied in the prone position (all P>0.44). Heart rate was significantly lower in the prone compared with supine position (all P<0.001). Mean arterial blood pressure differed neither between postures nor applied levels of PEEP.

Compliance profiles

The compliance profiles differed between all postures and PEEP levels (P<0.001). In the supine position a horizontal compliance profile was found in 38, an increasing turning into horizontal profile in five and a merely increasing profile in two patients (Fig. 3). In contrast, a horizontal compliance profile was found in only 20 patients at an identical PEEP level in the prone position (P<0.0001). This number increased significantly when increasing PEEP from 6 to 9 cm H2O (33 patients; P=0.0097), but insignificantly when increasing PEEP from 9 to 12 cm H2O (37 patients; P=0.31) in the prone position. At a PEEP of 9 cm H2O the horizontal compliance profile was achieved in 12 patients who had shown an increasing turning into horizontal profile and in four patients who had shown an increasing profile at PEEP 6 cm H2O. At a PEEP of 12 cm H2O the horizontal compliance profile was achieved in 2 patients who had shown an increasing turning into horizontal profile and in three patients who had shown an increasing profile at PEEP 9 cm H2O. Decreasing compliance profiles were never observed.

EIT measurements

In the supine position tidal volume was mainly distributed to the ventral ROI (Fig. 4). After prone positioning at unchanged PEEP level, tidal volume distribution decreased in the ventral ROI but increased in the dorsal ROI simultaneously (all P<0.001). Thereby, the centre of tidal ventilation shifted towards dorsal in the ventrodorsal axis (median supine: pixel No. 15 (CI 15–16) vs prone: pixel No. 18 (CI 17–18); range 1–32 pixel; P<0.001, Supplementary data, Fig. S2). Increasing PEEP in the prone position decreased tidal ventilation in the dorsal ROI and increased it in the ventral ROI. The respective changes in ventilation were significant when PEEP increased from 6 to 9 cm H2O but not when PEEP increased from 9 to 12 cm H2O. Comparison of tidal ventilation on a pixel by pixel basis, revealed a more pronounced increase in ventilation in the ventral lung regions, when increasing PEEP from 6 to 9 cm H2O compared with 9 to 12 cm H2O.

In the prone position, regional compliance images appeared similar to tidal ventilation images at the respective PEEP level (Supplementary data, Fig. S3). The percentage of cumulated alveolar collapse was lower at PEEP 9 cm H2O (10 (6) %; P=0.004) and PEEP 12 cm H2O (11 (9) %; P=0.043) compared with PEEP 6 cm H2O (15 (8) %), but did not differ between PEEP 9 and 12 cm H2O (P=0.37).

End-expiratory percentages of regional ventilation were relatively uniformly distributed to mid-ventral and mid-dorsal ROIs.

Table 1 Patients characteristics (n=45). Data are given as mean (sn) or absolute number of patients. VC, vital capacity; FVC, forced vital capacity; FEV1, forced expired volume in one s; *percent of predicted value (referred to sex, age and height)

<table>
<thead>
<tr>
<th>Sex (female/male)</th>
<th>19/26</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (yr)</td>
<td>57 ± (27-82)</td>
</tr>
<tr>
<td>Height (cm)</td>
<td>172 (10)</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>84 (15)</td>
</tr>
<tr>
<td>BMI (Kg/m²)</td>
<td>28.2 (0.6)</td>
</tr>
<tr>
<td>ASA (I/II/III)</td>
<td>9/31/5</td>
</tr>
<tr>
<td>Smoking (yes/no)</td>
<td>7/38</td>
</tr>
<tr>
<td>Preoperative pulmonary function</td>
<td></td>
</tr>
<tr>
<td>VC (% predicted)*</td>
<td>98 (13)</td>
</tr>
<tr>
<td>FVC (% predicted)*</td>
<td>96 (12)</td>
</tr>
<tr>
<td>FEV1 (% predicted)*</td>
<td>99 (13)</td>
</tr>
<tr>
<td>FEV1/FVC (% predicted)*</td>
<td>104 (7)</td>
</tr>
</tbody>
</table>
in the supine position. Prone positioning shifted regional gas distribution towards dorsal (non-dependent) ROIs. In the prone position an increase of PEEP from 6 to 9 cm H₂O partially redistributed ventilation towards ventral (dependent) ROIs. This trend was reversed and less distinct with a further increase of PEEP (Fig. 5).
**Discussion**

The main findings of this study are: (i) dynamic compliance of the respiratory system does not change between the supine and prone position; (ii) prone positioning shifts tidal gas distribution towards dorsal lung regions; (iii) in the prone position a PEEP of 6 cm H₂O is not sufficient to avoid intratidal derecruitment of the lungs whereas an increase of PEEP by only 3 cm H₂O can effectively reduce end-expiratory alveolar collapse.

**Respiratory mechanics analyses**

The analysis of dynamic respiratory system mechanics, allows assessment of the lungs’ condition during mechanical ventilation. In this study, we calculated the intratidal course of the patient’s individual respiratory system compliance, based on routinely measured ventilator variables. The variation in compliance during tidal ventilation, can be considered as representing the section of the hypothetical compliance curve that includes vital capacity. Best PEEP is set if neither derecruitment nor overdistension takes place during tidal ventilation (i.e. when intratidal compliance shows a horizontal profile). In our study we found considerable differences between the intratidal compliance-volume profiles with respect to position and PEEP in lung healthy patients. The number of patients showing intratidal derecruitment at the respective PEEP level was considerably higher in the prone position than in the supine position, indicating that a higher PEEP would be required to prevent potential atelectrauma. Increasing PEEP from 6 to 9 cm H₂O led to a disproportional decrease in intratidal derecruitment. In 45% of the patients showing intratidal derecruitment at PEEP 6 cm H₂O, intratidal derecruitment was avoided when PEEP was increased by only 3 cm H₂O. However, 44% of the patients did not show intratidal derecruitment at PEEP 6 cm H₂O. In these patients unnecessarily high PEEP levels can be avoided and the well described side-effects, such as reduced cardiac output or increased venous bleeding at the surgical site can be reduced. We therefore expect a benefit from an individualized, more differentiated regulation of the PEEP (e.g. based on the intratidal analysis of respiratory system mechanics).

Interestingly, ‘one value’ CRS did not differ between supine and prone position. This is in accordance to earlier findings. Pelosi and colleagues found that the compliance of the lung and the chest wall did not change between supine and prone positioning. However, they also reported that the functional residual capacity (FRC) was increased in the prone compared with the supine position. It is well known that the intra-abdominal pressure and the weight of the mediastinum and the lung tissue,
impar the FRC in the paralysed supine patient. In contrast, in the prone position, the mediastinum faces downwards and the compression of the ventral lung tissue is reduced. As a consequence, the pleural pressure gradient in the ventrodorsal axis is reduced and the heterogeneity in density and elastic recoil pressure of the lungs are balanced.

High tidal volumes have been shown to be harmful, whereas PEEP seems to protect from postoperative pulmonary complications. Accordingly, driving pressure was identified as a major predictor for deteriorating lung injury. Driving pressure did not increase in our study when PEEP was increased. Accordingly, we did not observe compliance profiles indicating pulmonary overdistension. In a previous study, in patients in prone position, overdistension (assessed via computed tomography) was found to a relevant extent at a PEEP of 10 cm H₂O. As those patients received tidal volumes substantially higher than in our study, we attribute the absence of overdistension in our study to the lower tidal volumes we applied.

**EIT analyses**

In the supine position, tidal ventilation was predominantly distributed to the ventral lung regions. This is in accordance with the theory that, following gravitational forces, the insufflated gas is preferentially distributed to ventral, non-dependent lung regions. Turning the patient prone, shifted the centre of ventilation towards non-dependent (dorsal) regions, and led to a more central distribution of ventilation. Increasing PEEP in the prone position gradually redistributed ventilation towards peripheral dependent (ventral) regions, indicating the existence of recruitable lung tissue in these regions at the lower PEEP level. Accordingly, the analysis of the compliance profiles revealed less intratidal derecruitment when PEEP was nine, compared with 6 cm H₂O. Thus already a small increase in PEEP (3 cm H₂O) reduced alveolar collapse and improved ventilation homogeneity indicated by fewer poorly inflated lung regions. However, increasing PEEP from 9 to 12 cm H₂O was associated with a smaller and more centrally located increase in ventilation. Accordingly, the compliance profiles improved only in a small number of patients.

**Limitations of the study**

In a previous study in lung healthy volunteers in the prone position, the ventilation to perfusion matching decreased with increasing PEEP from zero to 10 cm H₂O. While pulmonary perfusion remained consistent with and without PEEP, the shift of ventilation from nondependent (dorsal) to dependent (ventral) lung regions was smaller when PEEP was applied. In these elaborate experiments volunteers lay with their chest and
abdomen on a plain table, unlike the type of prone positioning generally used during surgical intervention. In contrast, patients in our study were positioned prone while supporting the chest and the pelvis with pads, similar to the Jackson table. A support system which allows free movement of the abdomen and the lower chest wall, causes lower intra-abdominal and intra-thoracic pressure. Consequently, our findings apply only when free abdominal movement is ensured.

Our intention for the recruitment manoeuvres preceding each PEEP interval, was rather to set the lungs to a defined baseline before the respective measurement, than to fully recruit the lungs. Therefore, measurements of the recruitment manoeuvres were not part of our protocol and recruitment and peak pressures could not be determined. Based on the set tidal volume and compliance of the respiratory system, peak inspiratory pressures can be estimated to have reached approximately 30 cm H2O when a PEEP of 15 cm H2O was applied during the recruitment manoeuvres.

Conclusion
Under the restriction that recruitment preceding our measurements was not assessed, we found in summary that routinely measured lung compliance does not reflect the differences in respiratory system mechanics between supine and prone posture. In contrast, functional imaging and analysis of the intratidal compliance profile, revealed substantial differences in the condition of the lung between both postures. In most patients a PEEP level that is generally applied in the supine position, is insufficient to avoid cyclic derecruitment of the lungs in the prone position. A moderate increase in PEEP improves the situation in the lungs in most patients.

Authors’ contributions
Study design/planning: J.S., S.S.
Study conduct: J.S., K.D., U.G.
Data analysis: J.S., K.D., S.S.
Writing paper: J.S., K.D., U.G., S.W., S.S.
Revising paper: all authors

Supplementary material
Supplementary material is available at British Journal of Anaesthesia online.

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Declaration of interest
None declared.

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