Static versus dynamic respiratory mechanics for setting the ventilator


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The lower inflection point (LIP) of the inspiratory limb of a static pressure-volume (PV) loop is assumed to indicate the pressure at which most lung units are recruited. The LIP is determined by a static manoeuvre with a PV-history that is different from the PV-history of the actual ventilation. In nine surfactant-deficient piglets, information to allow setting PEEP and VT was obtained, both from the PV-curve and also during ongoing ventilation from the dynamic compliance relationship. According to LIP, PEEP was set at 20 (95% confidence interval 17–22) cm H2O. Volume-dependent dynamic compliance suggested a PEEP reduction (to 15 (13–18) cm H2O). Pulmonary gas exchange remained satisfactory and this change resulted in reduced mechanical stress on the respiratory system, indirectly indicated by volume-dependent compliance being consistently great during the entire inspiration.

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Traditionally, three distinct features of the static pressure-volume (PV) loop of the respiratory system1 are used to assess the mechanical stress imposed by artificial ventilation to the lung. The lower inflection point (LIP) of the inspiratory limb of the PV-loop is thought to indicate the pressure at which the majority of lung units are recruited.2 The upper inflection point (UIP) indicates the pressure at which overdistension starts. The linear steep segment of the PV-curve between LIP and UIP is assumed to indicate the zone between end-expiratory collapse and overdistension although there is evidence that re-inflation of collapsed lung units continues above LIP and throughout the linear part of the PV-loop and perhaps even above UIP. Hence, it is hoped that lung injury from both shear stress and overdistension is avoided when tidal ventilation occurs on the linear segment of the PV-curve between LIP and UIP. This concept is intuitively appealing and it may improve ventilatory support in patients.3 Recent studies have challenged these concepts, however,4–10 as the mechanical properties of the respiratory system may depend on the pressure-volume history of the current tidal ventilation.11 The assumption that information obtained from static manoeuvres like the PV-loop can be applied to tidal ventilation may be incorrect, given the pronounced differences in PV-history. Rather than studying the respiratory system under artificial conditions, we have assessed dynamic mechanics (slice-compliance)12 during uninterrupted ventilation, and, hence, without affecting the actual PV-history of the lung. We analysed compliance within the tidal breath, taking into account the endotracheal-tube related flow-dependent resistance.

We studied surfactant-deficient piglets, and obtained information for setting PEEP and VT both from the static PV-curve and from the slice-compliance technique. We compared settings of PEEP and VT derived from static mechanics with those derived from the slice-compliance curve, in terms of the mechanical stress imposed to the
respiratory system (end-inspiratory plateau pressure ($P_{\text{plat}}$) and the shape of the volume-dependent compliance curve), and gas exchange (arterial $P_{O_2}$).

**Materials and methods**

The investigations were performed at the experimental laboratories of the Department of Anaesthesiology and Intensive Care Medicine at the University Hospital of Uppsala, Sweden, and were conducted in conformity with the Helsinki convention for the use and care of animals. The Local Ethics Committee for Animal Experimentation reviewed and approved the study. We studied nine healthy male and female piglets of Swedish landrace breed (25 (SD 2) kg).

**Anaesthesia and fluid management**

**Lavage**

Lavage was performed as previously described$^{13,14}$ with 11 broncho-alveolar lavages (1.2–1.5 litres normal saline, corresponding to 50–60 ml kg$^{-1}$) which we have found causes a $P_{O_2}/F_{O_2}$ of <20 kPa. Between each lavage, the animals were ventilated for 5 min with pressure-controlled ventilation, $F_{O_2}$ 1.0, PEEP 15 cm H$_2$O and $V_T$ 15 ml kg$^{-1}$. The effects of lavage on gas exchange, respiratory mechanics, and extravascular lung water (double-indicator dilution$^{15,16}$) were compared between volume-controlled ventilation at ZEEP during healthy conditions and the surfactant-deficient conditions immediately after lavage. After lavage the animals were allowed to stabilize for 20 min.

**Study design**

After lavage, all animals underwent volume-controlled ventilation with the ventilator set according to both static (STAT) and dynamic (DYN) measurements, each setting being applied for 40 min (see Fig. 1). To compensate for time-related effects and to use the individual animals as their own controls, the animals were allocated randomly to settings by either method first. The effects of STAT and the DYN settings were also compared with the healthy conditions before lavage, with PEEP set to 4 cm H$_2$O (PEEP 4).

**Ventilator and acquisition of pressure and flow data**

The animals’ lungs were ventilated through an endotracheal tube (#8, Mallinckrodt, Athlone, Ireland), connected by a 60 cm rigid tubing system to a Servo 300 ventilator (Siemens-Elema, Solna, Sweden). Airway pressure and flow were continuously measured with a pressure-flow transducer (BICORE CP100, Bicore Monitoring Systems, Irvine, CA, USA) placed between the tracheal tube and the ventilator circuit. The signals were sampled at 50 Hz and fed to a computer to be processed for the analysis of dynamic mechanics. Flow curves were continuously displayed and checked for ongoing flow at end-expiration as well as for any sign of respiratory muscle activity.

**Static measurements for ventilator adjustment**

Static mechanics were used to determine the LIP and the UIP for setting PEEP (at the level of LIP) and $V_T$ (below UIP).

The lower inflection point of the static PV curve of the respiratory system was determined by a modified multi-oclusion technique$^{17}$ as follows: a recruitment manoeuvre (see below) was performed to standardize the PV-history of the lung. Ventilation was started at zero PEEP, frequency of 16 min$^{-1}$, I:E 1:1 and with constant inspiratory flow. Seven breaths with a $V_T$ of 50 ml each were applied. At the end of the last breath, an end-inspiratory hold of 5 s was performed and the end-inspiratory airway pressure ($P_{\text{plat}}$) noted. For the next step, $V_T$ was increased to 100 ml at otherwise identical settings. The procedure was repeated with $V_T$ increased in steps of 50 ml up to 600 ml (corresponding to 24 ml kg$^{-1}$). The resulting values of plateau pressures after a 5 s end-inspiratory hold were used to construct the inflation limb of a static PV-loop (PV-curve) from which LIP and UIP were determined by tracing a straight line on the linear part as the best fit by eye.

**Dynamic measurements for ventilation adjustment**

Dynamic measurements were made to adjust the DYN settings and also to estimate indirectly the mechanical stress on the respiratory system after 40 min of ventilation at DYN and at STAT settings.

To detect non-linearities in dynamic respiratory system compliance within the tidal volume range, the slice method was used$^{12,18}$ which measures volume-dependent dynamic compliance and resistance breath by breath. The method continuously calculates tracheal pressure ($P_{\text{trach}}$)$^{19}$ by subtracting the flow-dependent resistive pressure drop caused by the resistance of the endotracheal tube (ETT) from the pressure measured at the airway opening. The resulting $P_{\text{trach}}-V_T$ loop is divided into consecutive volume slices and mean compliance (intrinsic PEEP considered) and mean resistance (ETT resistance excluded) is calculated for each slice by repeated application of the linear

![Fig 1 Schematic drawing of the study protocol. For further details please refer to the text.](image-url)
Fig 2 The slice-method (illustrated in one representative animal with surfactant deficiency). (a) Pressure as measured at the airway opening is plotted against volume (PAW/V-loop). Upward arrow denotes inspiration, downward arrow expiration. (b) The tracheal pressure $P_{trach}$ (inner loop, dashed area) is calculated point by point according to reference 19. The pressure difference between the outer $P_{AW/V}$-loop and the inner $P_{trach/V}$-loop mainly represents the flow-dependent resistive pressure drop across the endotracheal tube (ETT). The pressure-flow relationship of the ETT used had been determined in the laboratory beforehand. The $P_{trach/V}$-loop is subdivided into eight slices (indicated by horizontal lines) and respiratory mechanics are analysed separately for each slice. The upper and lower 5% of the tidal volume ($V_T$) (i.e. slices 1 and 8, respectively) are excluded from analysis because of interference due to the ventilator’s valve and the large volume acceleration. The remaining 90% of $V_T$ are divided into 6 slices, each comprising 15% of $V_T$. One volume-dependent dynamic compliance and resistance of the respiratory system ($C_{res,dyn}$ and $R_{res,dyn}$) are calculated per slice. (c) Quality check: $P_{trach}$ is recalculated point by point for each slice, using the calculated values for $C_{res,dyn}$ and $R_{res,dyn}$ and the measured volume and flow. This recalculated $P_{trach/V}$-loop is superimposed on the measured $P_{trach/V}$-loop, and the pressure difference between both loops reflects the accuracy of the calculated mechanical parameters. The measured and recalculated loops in c are barely distinguishable. (d) Plot of $C_{res,dyn}$ over the slices of the tidal volume. The shape of this particular plot indicates overdistension after about one third of the tidal volume has been delivered (i.e. beginning with the third slice), reduction of $V_T$ should be considered. (Values are mean of 20 consecutive breaths; SD omitted for the sake of readability.)

The advantage of considering the derivative (compliance) curve rather than the original (PV) curve is that compliance, as a differential value, is very sensitive to changes in the shape of the PV-curve. A horizontal course of the dynamic slice-compliance within a single tidal volume suggests that a constant volume change per pressure change be obtained. If an ascending shape was present, PEEP was increased to see whether this resulted in a greater initial compliance level and a longer horizontal course of the compliance over the $V_T$. If a descending shape was found, an inappropriately high PEEP and/or $V_T$ was assumed and adjustments were made (see below) to obtain a horizontal slice-compliance curve at a high absolute compliance level.

Before each study mode the animals’ lungs were thoroughly suctioned. To make sure that any potential partial tube obstruction due to secretions or kinking had not influenced the results, the expiratory flow curves were measured.
Fig 3 Representative plot (animal #8) of slice-compliance over tidal volume to illustrate the procedure for setting PEEP and tidal volume. (A) Slice compliance ($C_{s\text{dyn}}$) starting from low level and the descending shape of the plot indicate overdistension at the onset of inspiration. (b) A reduction of PEEP and $V_T$ result in an increase in the level of $C_{s\text{dyn}}$, overdistension is still prominent. (c) A further reduction of both PEEP and $V_T$ results in decreased $C_{s\text{dyn}}$, recruitment during the early phase of the delivery of $V_T$ and overdistension continuing at end-inspiration. (d) An increase in PEEP results in a more horizontal shape of the compliance plot for the major part of the tidal volume, although there is still overdistension at end-inspiration. Grey area: Tidal volume. Values are mean (SD) for 20 consecutive breaths. Settings and resulting gas exchange: (a) PEEP 20 cm H$_2$O, $V_T$ 330 ml, $P_{A_{CO_2}}$ 17 kPa, $P_{A_{CO_2}}$ 5.8 kPa, stroke index (SI) 30 ml; (b) PEEP 15 cm H$_2$O, $V_T$ 300 ml, $P_{A_{CO_2}}$ 18 kPa, $P_{A_{CO_2}}$ 6.0 kPa, SI 45 ml; (c) PEEP 13 cm H$_2$O, $V_T$ 280 ml, $P_{A_{CO_2}}$ 15 kPa, $P_{A_{CO_2}}$ 6.2 kPa, SI 48 ml; (d) PEEP 15 cm H$_2$O, $V_T$ 250 ml, $P_{A_{CO_2}}$ 18 kPa, $P_{A_{CO_2}}$ 6.2 kPa, SI 46 ml. Please note: there is a 90-min interval between situation A and the final situation D during which the condition of the lung probably changes, affecting the shape of the plot in addition to changes in PEEP and $V_T$ settings.

Ventilatory settings

Ventilatory frequency was 25 min$^{-1}$, $F_{I_{O_2}}$ 0.3, inspiration-to-expiration ratio 1:1 and inspiratory flow constant during all study modes.

Both mechanics as well as $P_{A_{CO_2}}$ were taken into account for setting PEEP and $V_T$:

For the STAT settings, PEEP was set to the level of LIP, and $V_T$ initially at 10 ml kg$^{-1}$. During the subsequent 40 min, blood gases were checked every 10 min and $V_T$ was adjusted with respect to $P_{A_{CO_2}}$ while PEEP was adjusted with respect to the two point compliance of the respiratory system ($C_{rs, 2p}$). If $P_{A_{CO_2}}$ was above 6.5 kPa, $V_T$ was increased in steps of 1 ml kg$^{-1}$ until $P_{A_{CO_2}}$ 5.5–6.5 kPa. With $P_{A_{CO_2}}$ <5.5 kPa, $V_T$ was reduced in steps of 1 ml kg$^{-1}$. Airway pressures were also measured every 10 min and $C_{rs, 2p}$ was determined. If $C_{rs, 2p}$ decreased to 90% or less of its initial level where PEEP=LIP, reduction of PEEP in steps of 2 cm H$_2$O was considered.

For the DYN settings, PEEP was initially set at 12 cm H$_2$O and $V_T$ at 10 ml kg$^{-1}$, which we have found gives adequate gas exchange in most animals. During the subsequent 40 min, blood gases were checked and dynamic mechanics were analysed every 10 min, and PEEP and $V_T$ were adjusted for an approximately horizontal shape of the slice-compliance curve. If an ascending shape of the slice-compliance appeared, PEEP was increased in steps of 2 cm H$_2$O. If a descending shape appeared, PEEP was reduced in steps of 2 cm H$_2$O. $V_T$ was adjusted to keep the $P_{A_{CO_2}}$ within 5.5–6.5 kPa and increased or decreased in steps of 1 ml kg$^{-1}$. (A representative example of the approach is given in Fig. 3.)

Respiratory mechanics determined at PEEP and $V_T$ after ventilator settings made using static/dynamic measurements

The end-inspiratory plateau pressure ($P_{plat}$) for both the STAT and the DYN settings was determined by performing an end-inspiratory hold for 5 s using the inspiratory hold function of the ventilator. The hold was performed with the $V_T$ and the PEEP level applied that had been set according to static or dynamic mechanics.

Two point compliance of the respiratory system ($C_{rs, 2p}$) was calculated according to the formula: Tidal volume/ (end-inspiratory pressure – end-expiratory pressure). To measure the end-expiratory pressure, the expiratory hold function of the ventilator was used for 5 s. $C_{rs, 2p}$ was determined with the $V_T$ and the PEEP level applied that had been set according to static or dynamic mechanics, respectively. Intrinsic PEEP was considered when expiratory flow had not decreased to zero at end-expiration.

Re-expansion

The lungs were re-expanded immediately after lavage, as well as before STAT and DYN by a 5-min period of pressure-controlled ventilation with a frequency of 20 min$^{-1}$, I:E 1:1, $F_{I_{O_2}}$ 0.3, PEEP 25 and a peak inspiratory airway pressure of 50 cm H$_2$O. The re-expansion effect immediately after lavage was assessed in terms of $C_{rs, 2p}$ setting the ventilator for 2 min to the pre-lavage PEEP 4 settings.
Monitoring

Intravascular catheters were surgically placed to measure central venous, pulmonary artery (via the external jugular vein), and aortic pressures (via the carotid artery). The position of the catheters was confirmed by pressure tracing. Cardiac output was determined from arterial thermodilution curves\textsuperscript{21} (Pulsion Medical Systems, Munich, Germany). Unlike measurements of right heart flow with thermodilution in the pulmonary artery, arterial thermodilution is influenced minimally by ventilation-induced intrathoracic pressure changes. The anaesthetised-paralysed animals were studied in the physiological prone position. At the end of the experiment, the animals were killed with potassium chloride.

Anesthesia and fluid management

Anaesthesia was induced with an injection of tiletamine 3 mg kg\textsuperscript{-1}; zolazepam 3 mg kg\textsuperscript{-1}; xylazine 2.2 mg kg\textsuperscript{-1}; atropine 0.04 mg kg\textsuperscript{-1} intramuscularly and deepened with ketamine 100 mg, and morphine 1 mg kg\textsuperscript{-1} i.v. Anaesthesia was maintained with infusions of ketamine (20 mg kg\textsuperscript{-1} h\textsuperscript{-1}) and morphine (0.5 mg kg\textsuperscript{-1} h\textsuperscript{-1}), and muscle relaxation obtained by continuous infusion of pancuronium bromide (0.25 mg kg\textsuperscript{-1} h\textsuperscript{-1}). The animals were given a solution of 4.5 g litre\textsuperscript{-1} NaCl with 25 g litre\textsuperscript{-1} glucose (Rehydrex, Pharmacia Infusion AB, Uppsala, Sweden) at 10 ml kg\textsuperscript{-1} h\textsuperscript{-1} and a bolus of dextran-70 10 ml kg\textsuperscript{-1} (Macrodex 70, Pharmacia Infusion AB) to ensure normovolaemia.

Data presentation and statistics

Data are presented as mean (SD) or mean (95% confidence interval). Differences were evaluated with a non-parametric analysis of variance (Friedman test). Significant differences were evaluated using the paired sign test with correction for multiple comparisons,\textsuperscript{12} and significance was accepted with $P \leq 0.05$. Where appropriate, the exact $P$ value is also indicated.

Results

Effects of lavage

With lavage, EVLW increased from 7 (95% confidence interval 6–8) to 19 (15–21) ml kg\textsuperscript{-1}. Mean pulmonary artery pressure increased from 19 (13–22) to 34 (26–38) mm Hg, calculated venous admixture ($Q_{v}/Q_{a}$) increased from 4 (3–4.5) to 47 (38–55)%; $C_{rs,2P}$ decreased from 35 (29–41) to 14 ml cm H\textsubscript{2}O\textsuperscript{-1}, and $PaO_{2}/FiO_{2}$ decreased from 72 (60–8–16) to 12 (6–18) kPa, all determined at zero PEEP ($P \leq 0.01$ for all differences). The lower inflection point was 20 (17–22) cm H\textsubscript{2}O (see Fig. 4 for the individual PV-curves). Upon re-expansion immediately after lavage, $C_{rs,2P}$ was 27 (20–36) ml cm H\textsubscript{2}O\textsuperscript{-1} ($P \leq 0.05$ to PEEP 4).

![Fig 4] Pressure volume (PV) curves with lavage-induced surfactant deficiency. The curves for the individual animals are given.

![Fig 5] Slice compliance curves for individual animals after 40 min ventilation at STAT settings (left) and after 40 min of DYN settings (right). Symbols indicate individual animals, values are mean for 20 breaths (SD omitted for the sake of readability).
Table 1 Variables indirectly indicating alveolar recruitment and mechanical stress during ventilation of healthy lungs and at PEEP 4 cm H$_2$O (PEEP4), and with surfactant deficiency after 40 min ventilation at static (STAT) or dynamic (DYN) settings. Values are mean (95% confidence interval). The symbols denote: $^\dagger$, difference to PEEP 4; $^{\ddagger}$, difference to STAT at the significance levels indicated. PIP, peak inspiratory airway pressure; MPAP, mean airway pressure; P$_{plat}$, end-inspiratory plateau pressure; C$_{rs,2P}$, two point compliance of the respiratory system; V$_T$, tidal volume; S$_{VCO_2}$, mixed venous saturation; CO, cardiac output; Q$_{a}$/Q$_{t}$, calculated venous admixture

<table>
<thead>
<tr>
<th>PEEP 4</th>
<th>STAT</th>
<th>DYN</th>
</tr>
</thead>
<tbody>
<tr>
<td>PIP (cm H$_2$O)</td>
<td>17 (16–18)</td>
<td>40 (34–47)·0.0001$^\dagger$</td>
</tr>
<tr>
<td>MPAP (cm H$_2$O)</td>
<td>9 (8–9)</td>
<td>25 (21–28)·0.0001$^\dagger$</td>
</tr>
<tr>
<td>P$_{plat}$ (cm H$_2$O)</td>
<td>13 (12–14)</td>
<td>35 (30–41)·0.0001$^\dagger$</td>
</tr>
<tr>
<td>PEEP (cm H$_2$O)</td>
<td>4 (4)</td>
<td>20 (17–22)·0.0001$^\dagger$</td>
</tr>
<tr>
<td>C$_{rs,2P}$ (ml cm H$_2$O$^{-1}$)</td>
<td>35 (29–41)</td>
<td>21 (17–24)·0.0001$^\dagger$</td>
</tr>
<tr>
<td>V$_T$ (ml)</td>
<td>251 (236–266)</td>
<td>310 (297–323)·0.0001$^\dagger$</td>
</tr>
<tr>
<td>P$_{AaCO_2}$ (kPa)</td>
<td>5.8 (5.3–6.3)</td>
<td>6.0 (5.6–6.3)</td>
</tr>
<tr>
<td>P$_{AaO_2}$ (kPa)</td>
<td>20 (19–22)</td>
<td>19 (17–20)·0.03$^\dagger$</td>
</tr>
<tr>
<td>S$_{VCO_2}$ (%)</td>
<td>65 (61–68)</td>
<td>53 (48–58)·0.006$^\dagger$</td>
</tr>
<tr>
<td>CO (ml kg$^{-1}$)</td>
<td>179 (152–207)</td>
<td>164 (132–196)</td>
</tr>
<tr>
<td>DO$_2$ (ml kg$^{-1}$)</td>
<td>17 (15–19)</td>
<td>14 (12–17)·0.07$^\dagger$</td>
</tr>
<tr>
<td>Q$<em>{a}$/Q$</em>{t}$ (%)</td>
<td>3.9 (2.6–5.1)</td>
<td>4.6 (3.7–5.5)</td>
</tr>
</tbody>
</table>

Effects of settings according to dynamic mechanics versus static mechanics

According to the level of LIP, PEEP was set to 20 (17–22) cm H$_2$O during STAT settings, and 15 (13–18) cm H$_2$O ($P$≤0.01) during DYN settings (see Table 1 and Figs 5 and 6). As a result, P$_{plat}$ was 8 cm H$_2$O less during DYN (27 (22–32) compared with 35 (30–41) cm H$_2$O during STAT; see Fig. 6). C$_{rs,2P}$ was 28 (22–34) with DYN and 21 (17–24) ml cm H$_2$O$^{-1}$ with STAT, respectively ($P$≤0.01 for all differences). P$_{AaCO_2}$ did not differ between STAT and DYN. Arterial P$_{AaO_2}$ was 19 (17–20) with STAT and 16 (14–18) kPa with DYN ($P$=0.07 for the difference). During both settings P$_{AaO_2}$ was less than under healthy conditions at PEEP 4 (P$_{AaO_2}$: 20 (19–22) kPa, $P$≤0.05 for the differences compared with STAT and DYN).

For the individual animals, V$_T$ was 4.2 (5.5)% less with dynamic settings compared with static settings ($P$≤0.05).

An UIP immediately after lavage did not appear in all PV-curves. If present, it was 32 (28–36) cm H$_2$O (see Fig. 4 for the individual PV-curves). This corresponded to a rapidly descending shape of the slice-compliance curve. This shape was also quite often seen despite P$_{plat}$<UIP.

In all animals after 40 min of ventilation using STAT settings, the slice compliance curve showed a rapid decrease whereas it was nearly horizontal after 40 min of ventilation at DYN settings with only a slight tendency to decrease (see Fig. 5). Under no condition was intrinsic PEEP observed nor tube obstruction detected.

Cardiac index was greater with DYN (164 (132–196) during STAT, and 202 (169–235) ml min kg$^{-1}$ during DYN, $P$<0.01), (see Fig. 6) as was oxygen delivery (14 (12–17) compared with 17 (14–20) ml min kg$^{-1}$, $P$≤0.01).

Discussion

We found that PEEP was set at 20 cm H$_2$O, if LIP was used, while dynamic mechanics suggested that a PEEP of 15 cm H$_2$O was sufficient to keep the lung open. This reduction of PEEP decreased P$_{plat}$ and increased C$_{rs,2P}$. The dynamic compliance curve suggested that stress on the respiratory system was greater with STAT settings.

Critique of methods

The slice-compliance

There is increasing evidence that it is difficult, if not impossible, to infer the behaviour of lung units from the mechanical behaviour measured at the airway opening, i.e. from the PV-relations. Why then do we measure respiratory system mechanics? One obvious motive is to indirectly estimate and reduce the mechanical stress to the respiratory system with appropriate ventilator settings. The PV-relation reflects the sum of all mechanical events occurring within the respiratory system and being transferred to the airway opening. Events at specific structures or regions of the lung will not be evident from this sum signal. If the forces producing different mechanical events at different locations oppose each other, the resultant sum signal is difficult to analyse without far reaching assumptions about the relative contribution of those forces. Whether, for example, a particular volume is accommodated in the central airways, the terminal airways or the alveoli, and which of those structures are distended or overdistended by that volume cannot be derived from the PV-relation. However, some conclusions regarding the respiratory system as a whole can be drawn from the PV-relation. (1) A steep PV-relation (= high compliance) shows that insufflating the volume increment under study requires a relatively small pressure increment. No matter how the insufflated volume is distributed to the different lung structures, those lung structures that are filled will be subjected to a lower mechanical stress when compliance is great compared with a smaller compliance condition. (2) Since the PV-relation (and, consequently, the compliance)
the mechanical conditions of the respiratory system have probably improved (no matter what particular changes at what particular structures have brought about the improvement).

The slice-compliance does not include a model of the visco-elastic properties of the respiratory system. Generally speaking, visco-elastic properties can only be determined by changing from dynamic conditions to static ones. Such conditions are obtained with an end-inspiratory occlusion manoeuvre where the energy stored in visco-elastic elements during actual inspiration is released and can be estimated by the slow pressure decrease to the plateau pressure (although not unequivocally, since different time constants can also affect this pressure change). Visco-elasticity has been expressed as a spring-and-dashpot model. Because the slice-compliance procedure does not model visco-elasticity, a small bias in favour of the STAT-settings may have been introduced since LIP is estimated during static conditions and, hence, without any visco-elastic pressure components.

Slice-compliance uses a linear RC-model successively applied to different volume slices, so that the linear RC-model is restricted to 1/8 of the volume range of the $V_T$. Using the linear RC-model repeatedly and separately for each of the consecutive slices preserves the robustness of the least-squares fit algorithm and analyses non-linearity, with the only assumption that this non-linearity can be divided into several consecutive, small and linear segments.

**Limitations of the study**

The determination of LIP by visual inspection (see Fig. 4) is inaccurate. Harris and colleagues have shown\(^7\)\(^\text{24}\) that inter-observer variability determining inflection points visually can be considerable with a maximum difference of 11 cm H$_2$O for the same patient. An objective method for determining LIP would have strengthened our study.

With respect to the adjustment of PEEP one might ask whether these adjustments were fully comparable between dynamic and static settings. The LIP was determined before the study settings. Since the PV-manoeuvre is itself a kind of recruitment,\(^7\)^10 determining LIP repeatedly was not considered. Adjustments of PEEP during STAT settings would have been necessary if $C_{rs.2P}$ (determined every 10 min) had changed. When $V_T$ was reduced to adjust for $P_{aCO_2}$, $C_{rs.2P}$ increased slightly ($\leq 5\%$; data not given). A decrease in $C_{rs.2P}$, however, was never observed during the 40-min period with static settings. Therefore we did not test the assumption that this would have indicated overdistention and required a PEEP reduction. We might have found that increasing $V_T$ (obtaining lower $C_{rs.2P}$) and decreasing PEEP in order to maintain $C_{rs.2P}$, as foreseen in the study protocol, might have produced end-expiratory collapse, and this would have revealed that, in retrospect, the protocol in this particular point was not based on a sound physiological rationale. Instead, PEEP, once set at the level of LIP, did not have to be changed during the STAT settings, nor was there
ever any need to increase $V_T$ to obtain normocapnia. The determination of LIP was not repeated since the PV-manoeuvre is stressful. A potential change in lung mechanics during the 40-min period of application could, therefore, have gone unnoticed.

The current study did not include oesophageal pressure data. In patients, LIP can be affected by chest wall mechanics.\textsuperscript{25,26} We cannot exclude the possibility that the high LIP was also influenced by chest wall mechanics.

Finally, the number of animals was too small to definitely exclude any difference in $P_AO_2$ between STAT and DYN, and we acknowledge that with more animals the tendency of $P_AO_2$ to decrease with DYN settings could be a relevant difference between both settings. (To detect a true difference in $P_AO_2$ of 2 kPa with 0.70 power and a SD of 3 kPa for $P_AO_2$, 28 animals would have been necessary.)

**Titrating PEEP during actual ventilation**

It was not possible that the (indirect) indicators of mechanical stress at end-inspiration ($C_{rs,2P}$ and $P_{plat}$) were less with the lower PEEP during DYN settings (see Fig. 6). Neither $C_{rs,2P}$ nor $P_{plat}$, however, reflect non-linearities of compliance during the course of inspiration. The assumptions for using LIP as a guide to optimal PEEP are (1) that inspiratory compliance during actual ventilation is as linear as is the compliance above LIP for the static circumstance, and (2) that this linear segment of the static PV-curve indicates complete alveolar recruitment. The latter assumption has been challenged.\textsuperscript{4,5,7-10} As regards the assumption of a linear compliance during the inspiratory phase of the actual ventilation, our data suggest that using the static PV-curve for setting PEEP (and $V_T$) results in pronounced non-linearities of the compliance, and the decreasing shape of the compliance curve indirectly suggests that inspiratory mechanical stress was higher with the STAT settings (see Fig. 5). In contrast, after 40 min of ventilation at DYN settings the slice compliance was greater and had a more horizontal shape (see Fig. 5). Adjustments of ventilator settings based on slice-compliance analysis are possible during uninterrupted ventilation, which is an advantage compared with the static approach which needs an artificial manoeuvre for constructing the PV-curve. Although clinical extrapolation is premature, these data challenge the uncritical use of the static PV-loop for making ventilator settings. Studies in which PEEP was set according to LIP and to a rather high level\textsuperscript{1} found reduced mortality, but whether this was due to an ‘open lung’ condition, i.e. to a reduction of mechanical stress during the entire ventilatory cycle, or to other PEEP effects, as yet unclear, has not been shown. The static conditions are so different from those of actual ventilation that it is hard to imagine how and why the former should apply to the latter. The difference between PEEP according to the LIP level and PEEP according to slice-compliance most likely reflects the different PV-history of the respiratory system during static compared to dynamic conditions.

**Assessment of full alveolar recruitment**

Our case is based on evidence for full alveolar recruitment, which can only be estimated indirectly. Different indicators for alveolar recruitment have been used.\textsuperscript{27-29} In the current study, in addition to $C_{rs,2P}$ upon re-expansion immediately after lavage, $P_AO_2$ was used despite evidence for a weak association of oxygenation and respiratory mechanics.\textsuperscript{30} With oxygenation and $C_{rs,2P}$ at (or near) its healthy level, full alveolar recruitment is likely. In our lavage-model, rigorous recruitment manoeuvres precede the ventilatory patterns under study and full alveolar recruitment is probably thereby achieved.

The $P_AO_2$ reduction of 3 kPa during dynamic settings compared with static settings was inconclusive ($P=0.07$ for the $P_AO_2$ difference STAT vs DYN, see Fig. 6 and Table 1). The small number of animals precludes definite conclusions. We assume, however, that functioning lung units were not de-recruited with the lower PEEP during DYN. First, lowering airway pressures during DYN increased cardiac output (see Fig. 6) which, as described by Dantzker and co-workers,\textsuperscript{31} might increase shunt and, hence, reduce $P_AO_2$. However, no major increase in venous admixture was observed (see Table 1). Also, we have found that in the porcine lavage model critically low $P_AO_2$ values rapidly develop once the airway pressure is below the threshold to keep the lung open. If the PEEP-reduction during DYN had induced local alveolar closure, we would have expected rapid progress to major collapse with life-threatening hypoxaemia. For this reason we considered a 40-min period sufficient for assessing short-term effects of different ventilator settings. The beneficial short-term circulatory effects of the DYN setting were not unexpected. Those effects have certainly a very limited impact on barotrauma / volutrauma, which is the clinically more relevant outcome variable but can only be studied in long-term experiments.

**Titrating $V_T$**

The study protocol also included adjustments of $V_T$ (see Fig. 3) according to mechanical and blood gas criteria, but we never had to increase $V_T$. (Strictly speaking, changes in volume at constant frequency and inspiratory time always imply changes in inspiratory flow, too, but the potential effect of each of these effects could not be evaluated separately.) The UIP derived from static mechanics indicated overdistension at higher pressure levels than dynamic mechanics did: during STAT settings, $P_{plat}$ (35 cm H$_2$O) was clearly above the UIP of about 32 cm H$_2$O, and this corresponded to a rapidly descending part of the slice-compliance plot. However, even when $P_{plat}$ was below UIP, we frequently found a descending slice-compliance curve,
indicating overdistension, which would not have been inferred from consideration of the UIP.

We conclude that in the atelectasis-prone porcine surfactant-deficient model, non-invasive analysis of volume-dependent dynamic compliance showed that, for keeping the lung open during ventilation, PEEP could be set 5 cm H2O lower than UIP. With pulmonary gas exchange maintained at an appropriate level, this gave a greater two-point compliance of the respiratory system (Ctm,2P), smaller end-inspiratory plateau pressure (Pplat), and greater slice-compliance with a more horizontal course, all indirectly suggesting less mechanical stress to the respiratory system.

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References
4 Hickling KG. The pressure-volume curve is greatly modified by recruitment. Am J Respir Crit Care Med 1998; 158: 194–202
15 Lewis FR, Elings VB, Hill SL, Christensen JM. The measurement of extravascular lung water by thermal-green dye indicator dilution. Ann NY Acad Sci 1982; 384: 393–410
