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New aspects of pulmonary mechanics: "slowly" distensible compartments of the respiratory system, identified by a PEEP step maneuver

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Abstract *Objective:* The aims of the present study were 1) to evaluate a method for identification of "slowly" distensible compartments of the respiratory system (rs), which are characterized by long mechanical time constants (RC) and 2) to identify "slowly" distensible rs-compartments in mechanically ventilated patients.
Design: Prospective study on a physical lung model.
Setting: Intensive Care Unit, University Hospital, Tübingen
Patients and participants: 19 patients with severe lung injury (acute respiratory distress syndrome, ARDS) and on 10 patients with mild lung injury.
Measurements and results: Positive end-expiratory pressure (PEEP)-increasing and -decreasing steps of about 5 cmH_2O were applied and the breath-by-breath differences of inspiratory and expiratory volumes (ΔV) were measured. The sequence of ΔVs were analyzed in terms of volume change in the "fast" compartment (V_{fast}), the "slow" compartment (V_{slow}), total change in lung volume (ΔVL) and mechanical time constant of the slow compartment (RC_{slow}). Thirty-eight measurements in a lung model revealed a good correlation between the preset $V_{slow}/\Delta VL$ and $V_{slow}/\Delta VL$ measured: $r^2 = 0.91$. The $V_{slow}/\Delta VL$ measured amounted to 0.94 ± 0.15 of $V_{slow}/\Delta VL$ in the lung model. RC_{slow} measured was 0.92 ± 0.43 of the RC_{slow} reference. Starting from a PEEP level of 11 cmH_2O PEEP-increasing and PEEP-decreasing steps were applied to the mechanically ventilated patients. Three out of ten patients with mild lung injury (30%) and 7/19 patients with ARDS (36.8%) revealed "slowly" distensible rs-compartments in a PEEP-increasing step, whereas 15/19 ARDS patients and 1/10 patients with mild lung injury showed "slowly" distensible rs-compartments in a PEEP-decreasing step (78.9% vs 10%, $P < 0.002$, chi-square test).
Conclusions: The gas distribution properties of the respiratory system can be easily studied by a PEEP-step maneuver. The relative contribution of the "slow" units to the total increase of lung volume following a PEEP step could be adequately assessed. "Slowly" distensible rs-compartments could be detected in patients with severe and mild lung injury, however significantly more ARDS patients revealed "slow" rs-compartments in PEEP-decreasing steps. The influence of "slowly" distensible rs-compartments on pulmonary gas exchange is unknown and has yet to be studied.

Key words Acute respiratory distress syndrome (ARDS) · Respiration, artificial · Respiratory system, mechanics, time constants · Lung compliance · Airway resistance · Lung volume measurement

Introduction

Hypoxemia, a decrease in respiratory system compliance and alveolar consolidation on chest radiograph are the clinical hallmarks of acute respiratory distress syndrome (ARDS) [1, 2]. Though chest radiographic findings imply that the lung injury is spread homogeneously, computed tomographic examinations of the thorax show a rather inhomogeneous distribution of pulmonary consolidations in ARDS. Furthermore, the morphologic inhomogeneity is accompanied by an inhomogeneity of the mechanical properties of the respiratory system. Thus, within the ARDS lung fairly "normal" lung spaces with a normal "specific compliance" coexist with badly, or not, ventilated lung spaces [3]. Further clinical investigations indicating an inhomogeneous mechanical behavior of the respiratory system were made by Wolff et al. [4] and Katz et al. [5]. In 1981 Katz et al. [5] described the time course of the pulmonary volume change after positive end-expiratory pressure (PEEP) increase in patients with acute respiratory insufficiency. They noticed that after the PEEP was increased the volume uptake of the lung continued for 10–20 breaths. Thus, there must have been lung compartments in these patients which were not adequately ventilated within one breath. These compartments must be characterized by long mechanical time constants (RC_{slow}). They may be hypoventilated, and may therefore contribute to ventilation/perfusion mismatch or venous admixture.

Unfortunately, until now no method has been available to identify lung compartments with different mechanical time constants in mechanically ventilated patients. Therefore, the aim of the present study was, first, to evaluate a technique for the identification of respiratory system (rs-)compartments with long mechanical time constants and, second, to look for the presence of "slowly" distensible rs-compartments in patients with severe and mild lung injury.

Material and methods

The presence or absence of lung units with long mechanical time constants can be investigated by the analysis of a PEEP-step maneuver [5] (for details, see Appendix). For this purpose, the cumulative difference between inspiratory and expiratory volume ($\Sigma\Delta V$) immediately following a PEEP step was analyzed. Figure 1 shows a typical breath-by-breath plot of $\Sigma\Delta V$ against time. Lung units that fill and empty within one breath are considered "fast" compartments. The assumption is made that the volume increase or decrease of these compartments caused by a PEEP step is finished within the first breath after application of the PEEP step. The volume change of these "fast" compartments is called V_{fast} (see Fig. 1). On the other hand, the value of $\Sigma\Delta V$ in steady state after the PEEP step yields the volume by which the total lung volume (VL) has changed (ΔVL). If ΔVL is larger than V_{fast}, slowly ventilated lung units must be assumed. These are called "slow" compartments. They can be characterized by two parameters: V_{slow} and RC_{slow}. The former is the volume by which slowly ventilated lung units are inflated or deflated by a positive or negative PEEP step, respectively. RC_{slow} is the mechanical time constant at which the volume changes take place (see Fig. 1).

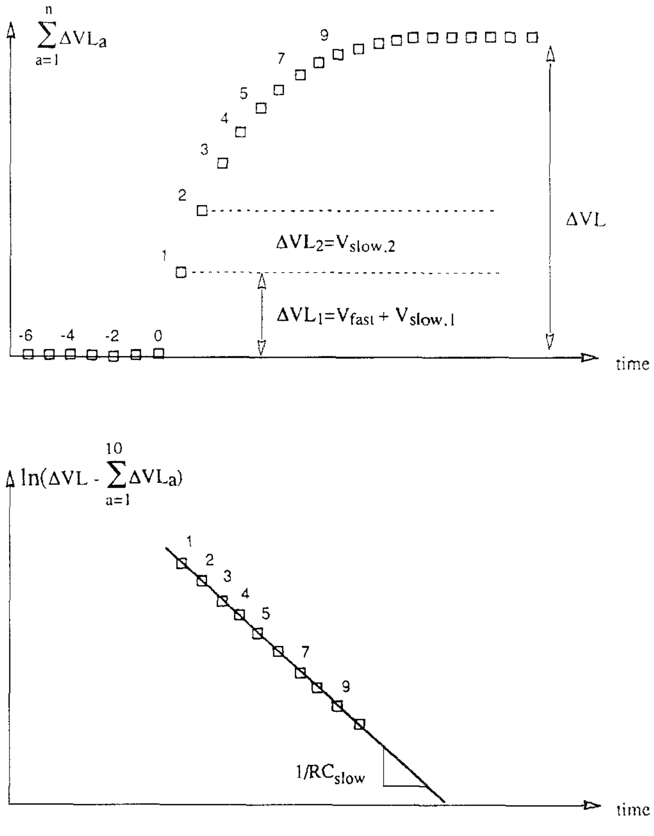

Fig. 1 Top: Running sum of drift-corrected inspiratory minus expiratory volume differences ($\Sigma\Delta V$) after a PEEP-increasing step is plotted breath-by-breath against time. Breaths are numbered, 0 being the last breath before PEEP step. Volume difference of first breath after PEEP step is $V_{fast} + V_{slow,1}$. Total pulmonary volume increase after PEEP step is ΔVL. The difference between ΔVL and V_{fast} is V_{slow}. Details see Appendix. Bottom: Logarithm of ΔVL minus $\Sigma\Delta V$ is plotted breath-by-breath against time. Figure shows the first ten breaths after PEEP step used to calculate the time constant of the "slow" compartment (RC_{slow}) by linear regression technique. Slope of regression line equals $1/RC_{slow}$ (for details see text)

Evaluation of the method in a physical lung model

A two-compartment water-manometer lung model was used for evaluation of the method [6]. A schematic representation of the lung model is given in Fig. 2. The lung model was built of plexiglas and consisted of a lung chamber with a pneumatic resistor attached to it, which connects the lung model to the ventilator. The lung chamber communicates with a second chamber which is divided by a sliding wall, thus creating three chambers. The model is partly filled with water which freely communicates between chambers 1 and 2, but whose flow is restricted to enter chamber 3 by a high resistance R_2. R_2 is created by the sliding wall and creates the resistance R_{slow} of the slow compartment. As the model was built of plexiglas, volume changes of the fast and slow compartments could be easily determined from changes of the water levels in the lung chamber and in chamber 3. The model is characterized by the compliance of a fast and a slow compartment (C_{fast} and C_{slow}) and by the corresponding mechanical time constants RC_{fast} and RC_{slow}, respectively. For evaluation of the PEEP-step method the reference value of the mechanical time constant of the slow compartment (RC_{slow} reference) was measured using a stop-watch and observing the water level of the slow compartment (chamber 3) drop from one equilibrium position to another. The 90% response time was measured and converted to RC_{slow} (division by 2.3). For each parameter setting, this measurement served as the method of reference. The RC_{slow} reference varied between 6 and 48 s.

Thirty-eight diagnostic PEEP steps of 5 cmH_2O were applied for 28 combinations of C_{fast} and C_{slow}, and RC_{fast} and RC_{slow}, respectively. The lung model was ventilated by pressure-controlled breaths (Veolar, Hamilton Bonaduz, Switzerland) at an inspiratory pressure level set to achieve a minimum tidal volume of 350 ml if C_{fast} was low, and a maximum of 1000 ml if C_{fast} was large. The respiratory rate was 20 breaths/min.

Inspiratory and expiratory flow was measured by a pneumotachograph (Screenmate box, Jäger GmbH, Würzburg, FRG) and the inspiratory and expiratory tidal volumes (Vi, Ve) as well as inspiratory and expiratory times (Ti, Te) were calculated [6]. The effects of gas viscosity, temperature and water vapor saturation were taken into account [6]. For this purpose gas fractions of oxygen (FO_2) (Capnomac, Datex, Helsinki, Finnland) and carbon dioxide (FCO_2) (Novametrix 1260, Novametrix, Wallingford, CT, USA) were measured. The nitrogen concentration (FN_2) was expected to be $FN_2 = 1 - FO_2 - FCO_2$. The pneumotachograph was calibrated with a defined volume of room air. Linearity of the Jäger pneumotachograph is comparable to the Fleisch penumotachograph (± 3.5% in a flow range of ± 31/s) [7]. The accuracy of volume calculations is 5%. Simultaneously, airway pressure was measured (HP 78905A, Hewlett Packard, Böblingen, FRG) and the data transmitted to a computer (Tandon PCA/12 Moorpark, CA, USA; DT2801, Data Translation, Marlboro, MA, USA). The frequency of data acquisition was 60 Hz. Mean airway pressure (Paw_{mean}) and end-expiratory airway pressure (Paw_{EE}) were calculated by the computer.

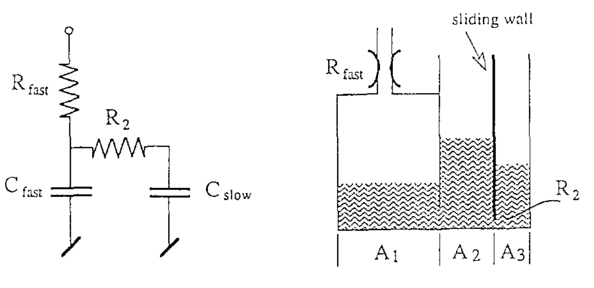

Fig. 2 Electrical and schematic representation of the two compartment lung models used in this study. Compliances of the two compartments are given as C_{fast} and C_{slow}, resistances as R_{fast} and R2. As the two compartments are connected in series, R_{slow} is given as ($1/R_{slow} = 1/R_{fast} + 1/R2$). C_{fast} is given as $C_{fast} = A1 * A2/(A1 + A2)$; Compliance of the lung model as $C_{fast} + C_{slow} = A1 * (A2 + A3)/(A1 + A2 + A3)$

As the pressure (Paw(t)), flow (V′(t)) and volume (V(t)) were measured multiple times during a respiratory cycle, the resistance (Rtot), compliance (Ctot) and the dynamic intrinsic PEEP (PEEPi) of the respiratory system could be calculated by the least square fit from [6]:

$$\mathrm{Paw}(t) = V'(t) * \mathrm{Rtot} + V(t)/\mathrm{Ctot} + \mathrm{PEEPi} \qquad \text{(Eq1)}$$

Fifteen breaths were recorded preceding a PEEP step and 100 breaths were recorded following the PEEP step.

Using a spread sheet program (Microsoft EXCEL) the differences between inspiratory and expiratory volumes (ΔV) were calculated breath-by-breath, and a drift compensation was performed manually (see Appendix). The cumulative sum of ΔV (ΣΔV) was then analyzed (for calculations see Appendix) and yielded V_{fast}, V_{slow} and ΔVL. The determination of RC_{slow} involved the analysis of the first ten breaths immediately following the PEEP step. For this purpose, the logarithm of ΔVL − ΣΔV of each breath was plotted against time as shown in Fig. 1 and analyzed using linear regression. The slope of the regression line corresponds to $1/RC_{slow}$.

The results of the analysis were compared to the reference values as set on the lung model. Since reference values for V_{slow}, V_{fast}, and ΔVL are not directly available, they had to be derived from the parameters of the lung model. The conversion was made using Paw_{EE} and Paw_{mean} differences. Differences before and after the PEEP steps were calculated and used in the following equations:

$$V_{fast}\ (\text{reference}) = dPaw_{EE} * C_{fast} \qquad \text{(Eq2)}$$

$$V_{slow}\ (\text{reference}) = dPaw_{mean} * C_{slow} \qquad \text{(Eq3)}$$

$$\Delta VL\ (\text{reference}) = V_{fast}\ (\text{reference}) + V_{slow}\ (\text{reference}) \qquad \text{(Eq4)}$$

The bias and precision were calculated as a mean difference between measured and reference value and its standard deviation, respectively. Comparisons were made using linear regression analysis.

Application of the method in patients

The presence or absence of "slowly" distensible rs-compartments was evaluated in 19 patients with severe lung injury (ARDS group, lung injury score > 2.5 [2]) and in 10 patients with mild lung injury (control group, lung injury score < 1). The investigation was approved by the Local Ethics Committee of the Medical Faculty of the University of Tuebingen and was performed after written consent of the patients (control group) or their next of kin (ARDS group).

The control group consisted of 10 patients after coronary bypass surgery. Patients suffering from chronic obstructive pulmonary disease, with a left ventricular end-diastolic pressure above 15 mmHg and with instable angina pectoris, and those after cardiac decompensation were excluded from this study. The investigation was performed after the surgical treatment at the Intensive Care Unit, as soon as hemodynamic conditions were stable and the rectal temperature of the patients was higher than 37 °C. The ARDS group consisted of 19 patients.

All patients were sedated (midazolam 0.1–0.2 mg/kg per h, fentanyl 1–2 μg/kg per h) and paralyzed (Vecuronium 0.2–0.25 mg/kg per h). Patients of both groups were mechanically ventilated in a pressure – controlled mode (Veolar, Hamilton Bonaduz, Switzerland). The respiratory rate was 20/min and the ratio between inspiratory and expiratory time was 1:1. The pressure difference between peak inspiratory and end-expiratory pressure was set individually. The aim was an arterial partial pressure of carbon dioxide ($paCO_2$) between 30 and 40 mmHg in the control group, whereas ARDS patients were allowed to be hypercapnic ($paCO_2 < 80$ mmHg). Dynamic PEEP was measured and adjusted to 11 cmH_2O by altering the extrinsic PEEP at the ventilator. Starting from a PEEP level of 11 cmH_2O a PEEP-increasing and a PEEP-decreasing step of about 5 cmH_2O was applied in each patient. After the first PEEP step the dynamic PEEPi was readjusted to 11 cmH_2O. Fifteen minutes later the second PEEP step was applied.

In 10 patients a PEEP increasing step was applied at first, in 9 patients a PEEP-decreasing step was applied at first. PEEP steps and analysis of the volume change of the respiratory system were performed as described above. According to Eqs 2 und 3 the compliances of the "fast" and "slow" compartments were calculated. The compliance of the total respiratory system determined during a PEEP step was calculated as $C_{PEEP} = C_{fast} + C_{slow}$. Thus the relative amount of the slowly distensible compartment could be given as C_{slow}/C_{PEEP}. A significant "slowly" distensible compartment of the respiratory system was accepted, if C_{slow}/C_{PEEP} was greater than 0.2. The frequency of "slowly" distensible compartments of the respiratory system in both patient groups was compared using the chi-square test for statistically significant differences (if $p < 0.05$).

Results

Measurements on lung models

The results are summarized in Table 1. The volume change of the "fast" compartment after the PEEP step, V_{fast}, was measured with a mean error of 41 ml which corresponds to a relative error of 37% of the expected value. The precision of the V_{fast} measurement was ± 33 ml or ± 37%. The determination of V_{slow} turned out to be more accurate. The mean error was − 24 ml or 0% of V_{slow} expected in the lung models. The precision, determined as the standard deviation of V_{slow} measurements, was ± 101 ml or ± 33%. ΔVL could be measured with accuracy and precision comparable to V_{slow}. The mean error was 17 ml or 5%. The precision was ± 109 ml or ± 23%.

The relative contribution of the "slow" compartments to the overall effect of the PEEP step was calculated as $V_{slow}/\Delta VL$ and could be measured with a mean error of − 0.06 or − 6%. The precision was ± 0.1 or ± 15%. The results are plotted in Fig. 3. The mean error of RC_{slow} measurement in the lung models was 0.9 s or 8%, precision being ± 5 s or ± 43% (see Fig. 4).

Table 1 Bias and precision of measurement. Results from 38 PEEP steps in the physical lung model (V_{fast} volume change of the fast compartment, V_{slow} volume change of the slow compartment, ΔVL total volume change in the lung model after PEEP step, RC_{slow} time constant of the slow compartment). Values are given as mean relative error (measured value − reference value)/(reference value, and its standard deviation)

Parameter	Mean relative error	± STD
V_{fast}	0.37	± 0.37
V_{slow}	0.00	± 0.33
ΔVL	0.05	± 0.23
$V_{slow}/\Delta VL$	− 0.06	± 0.15
RC_{slow}	0.08	± 0.43

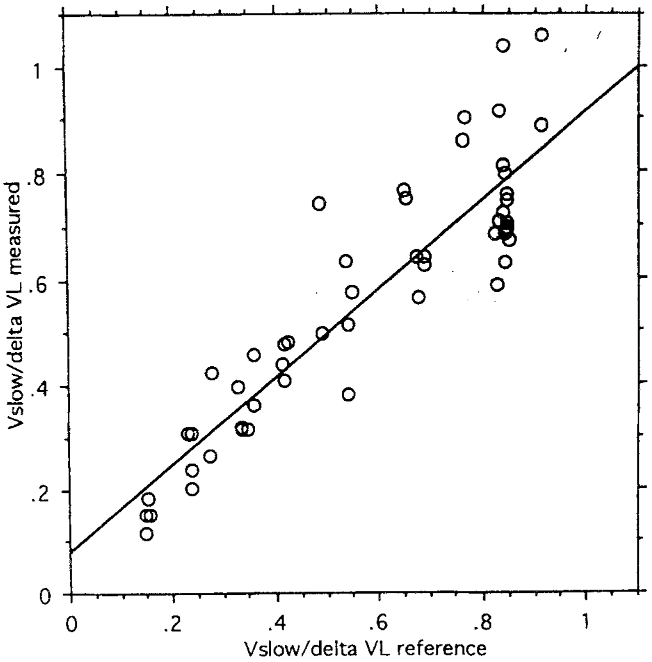

Fig. 3 The measured relative ventilation of the "slow" compartment (V_{slow}/dVL measured) is plotted against its reference value (V_{slow}/dVL-ref). Line is regression line

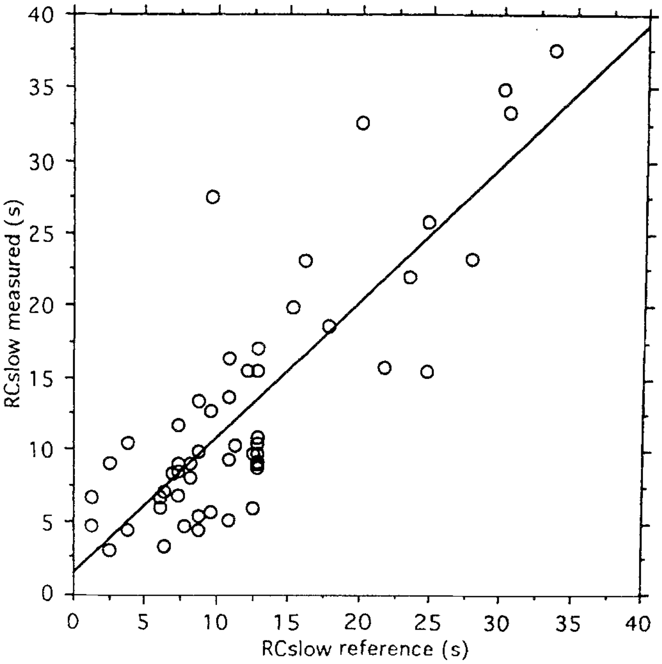

Fig. 4 The measured time constant of the slow compartment (RC_{slow} measured) is plotted against the reference value (RC_{slow} ref). Line is regression line

Table 2 Relevant patient data of the ARDS and control group. Age, lung injury score (according to MURRAY [2]) (*Crs* compliance of the respiratory system, *FiO₂* inspiratory oxygen fraction, *Vi* tidal volume, *Pawmax* maximal airway pressure, *Paw mean* mean airway pressure, *PEEPi* intrinsic end-expiratory pressure)

	ARDS	Control
Age (years)	46.7 ± 11.6	58.5 ± 9.4
Lung injury score	3.13 ± 0.46	0.67 ± 0.33
Crs (ml/cmH_2O)	31.9 ± 9.2	55.7 ± 11.6
FiO_2	0.65 ± 0.14	0.36 ± 0.05
Vi (ml)	532 ± 107	460 ± 69
Paw max (cmH_2O)	30.0 ± 5.2	20.7 ± 1.4
Paw mean (cmH_2O)	20.2 ± 2.6	15.7 ± 0.8
PEEPi (cmH_2O)	11.1 ± 0.6	11.1 ± 0.4

Measurements on patients

The relevant data characterizing both patient groups may be taken from Table 2. Three out of ten patients with mild lung injury (30%) and 7/19 patients with ARDS (36.8%) revealed "slowly" distensible rs-compartments ($C_{slow}/C_{PEEP} > 0.2$) in a PEEP-increasing step, whereas 15/19 ARDS patients and 1/10 patients with mild lung injury showed "slowly" distensible rs-compartments in a PEEP-decreasing step (78.9% vs 10%, $p < 0.002$, chi-square test). The mean time constants of the "slowly" distensible rs-compartments were 9.4 ± 7.3 s in the ARDS group and 10.4 ± 4.8 s in the control group after PEEP-increasing steps, and 11.3 ± 11.2 s in the ARDS group and 7.5 ± 4.0 s in the control group after PEEP-decreasing steps.

Discussion

The presence or absence of "slowly" distensible lung units may be easily determined from the time-dependent volume change of the respiratory system after a diagnostic PEEP step. Obviously, this approach neglects the complexities of the mechanics of the tracheobronchial tree, non-linearities of respiratory system mechanics, hysteresis and visco-elastic effects. Instead, it lumps all of these into the parameters of two distinct compartments, a "slow" compartment and a "fast" compartment.

Evaluation of the method in a physical lung model shows that it was rather difficult to measure V_{fast} and V_{slow} with acceptable precision, whereas the change of total lung volume after a PEEP step could be better estimated. V_{slow} was measured with a precision of ± 33%. This means that, for a single measurement, one has to expect an error of up to 60% in 95% of the cases. This seems too inaccurate for clinical application. The relative fraction of the total volume change after a PEEP step which yields the volume increase of the "slow" compartment ($V_{slow}/\Delta VL$), however, is calculated with an acceptable accuracy and precision, of − 6% and ± 15%, respectively. It seems surprising that the precision of the quotient V_{slow}/VL is so much better than the precision of its single parameters V_{slow} and ΔVL. The reason is that V_{slow} and VL determined from a single measurement are related parameters. If V_{slow} is large, ΔVL will be large. If V_{slow} is greatly overestimated, ΔVL will be greatly overestimated. Thus, the quotient of $V_{slow}/\Delta VL$ can be measured with better precision than V_{slow} and ΔVL alone (see Table 1). RC_{slow} is measured with an acceptable accuracy of 8%, the precision, however, is poor and amounts to only ± 43%. Nevertheless, it seems possible to estimate the magnitude of RC_{slow}.

Determining the model parameters of a two-compartment lung from the time-dependent volume change after a PEEP step, the accuracy and precision of the measurements are dependent of the accuracy of the volume measurement. Therefore, the limiting factor of the PEEP step method is the limited accuracy of currently available pneumotachographs.

Applying the PEEP step method in mechanically ventilated patients, changes of PEEPi, when due to both a shortening of expiratory time and flow limitation, must be taken into account, as PEEPi may affect the Paw_{mean} which is a major determinant of C_{slow} (Eq 3) and may alter the intrapulmonary distribution of ventilation. Therefore, dynamic PEEPi was calculated breath-by-breath and was readjusted between two consecutive PEEP step procedures.

V_{slow}, V_{fast}, and RC_{slow} are determined by the mechanical properties of lung, chest wall, and diaphragm. Conventionally, the assessment of lung mechanics is carried out by the measurement of compliance. The super-syringe method [8–10], the interrupter technique [11–13], and the least square fit method [14] are among the methods used to measure compliance. However, all of those methods neglect the fact that, in a non-homogeneous lung, compliance and resistance are time-variant [15]. In other words, the compliance values vary with the time interval in which they are measured [16].

The PEEP step maneuver tries to assess the effect of time on compliance measurements. Obviously, the model used in this study is characterized by linear compliance and more or less flow-independent resistance. It may be argued that this does not represent the real physiologic and/or pathophysiologic conditions, where compliance is volume-dependent and resistance flow-dependent [16–18]. However, the physical model used represents one of the possible arrangements of resistance and compliance to create a PEEP step response as the one observed by Katz et al. [5]. In fact, it represents the simplest model that explains the time-dependent volume change after a PEEP step [5]. The introduction of non-linear compliance and/or flow-dependent resistance would add complexity which, in turn, would require sophistication in identifying the pertinent parameters. Spontaneous breathing would present additional challenges to the analysis of a diagnostic PEEP step. The present study was carried out with models simulating completely paralyzed subjects and the results may therefore not be applicable to spontaneous breathing.

"Slowly" distensible compartments of the respiratory system must be assumed in mechanically ventilated patients, whether or not they are suffering from ARDS. This observation supports the statement of Chelucci and co-workers [19], that a single-compartment model cannot describe sufficiently passive expiration in intubated, paralyzed humans. Unfortunately there are only a few studies concerning "slowly" distensible compartments of the respiratory system. Dall'Ava-Santucci [20] studied the time constant of the total respiratory system from the pressure decay of an expiration lasting for 10 s. She calculated a mean time constant of 0.8 ± 0.2 s, however she did not differentiate a "fast" and a "slow" component of the airway pressure tracing. Chelucci [19] could demonstrate that a bi-exponential analysis of the airway pressure decay during passive expiration revealed a "fast" and a "slow" component, with corresponding mean time constants of 0.5 s and 3.27 s, respectively. In contrast, the mean mechanical time constant of the "slow" compartments in this study was about 3 times longer. This may be explained by the different methods, and essentially by the time in which RC_{slow} was measured.

The measurement of time constants of the respiratory compartments must be time-dependent. The volume change of a rs-compartment following a rapid, step-wise pressure change is described by an exponential curve and it takes three time constants until 95% of the maximal volume change has taken place [21]. "Slow" compartments with mechanical time constants of 30 s will need about 90 s to exhale 95% of the maximal expiratory volume during a passive expiration. So, these compartments will contribute only little to the pressure or volume change of a passive expiration lasting 10 s and may therefore not be detected during such a short observation period. Using the PEEP step, "slow" mechanical time constants were calculated from the volume change of the respiratory system within the first ten breaths, i.e. 30 s in this study. Within this observation period rs-compartments with "slow" mechanical time constants of about 10 s could be detected. There is good reason to believe that some rs-compartments may be characterized even by mechanical time constants of some hours [4]. The limited accuracy of the presently available pneumotachographs, however, makes it impossible to prolong the observation time of the PEEP step maneuver.

The results from PEEP-increasing and -decreasing steps do not differ markedly in control group patients. "Slow" compartments could be detected in 2/10 patients in PEEP-increasing and in 1/10 patients in PEEP-decreasing steps. Acute respiratory distress syndrome patients, however, behave rather differently. "Slow" compartments could be detected in only 7/19 patients in PEEP-increasing, however in 15/19 patients in PEEP-decreasing steps. Furthermore, significantly more ARDS than non-ARDS patients revealed "slow" compartments in PEEP-decreasing steps. Increasing PEEP may cause alveolar recruitment, i.e. an increase in the number of aerated lung units, or alveolar distension. Decreasing PEEP may cause alveolar derecruitment, i.e. alveolar collapse and a reduction of the number of aerated lung units, or only a decrease in the volume of aerated alveoli. Both effects may play a role during PEEP-increasing and PEEP-decreasing steps.

The fact that during PEEP-decreasing steps significantly more "slowly" distensible compartments could be detected in ARDS patients than during PEEP-increasing steps may therefore be explained by the hypothesis that recruitment, or alveolar expansion after a PEEP-increase, takes more time (and may therefore not be identified by the PEEP step method) than derecruitment, which begins immediately after the onset of a PEEP-decreasing step. Then, different amounts of C_{slow}/C_{PEEP} in a PEEP-increasing step starting at a PEEP-level of n cmH_2O and a PEEP-decreasing step starting at $n + 5$ cmH_2O might indicate lung units which could be expanded or recruited by PEEP. To prove this hypothesis, further studies will be necessary. Other questions which should be studied concern the influence of "slowly distensible" rs-compartments on pulmonary gas exchange and whether these compartments may be better ventilated by PEEP, an increased inspiratory time or by special ventilatory modes.

Appendix: Assumptions and calculations

The following assumptions are made:

1. The mechanical properties of the passive respiratory system may be represented by a two-compartment lung model. A schematic representation of the lung model is given in Fig. 2.
2. If PEEP is increased during inspiration the end-expiratory volume of the "fast" compartment changes only within this respiratory cycle. During the following breaths there is no further increase of the end-expiratory volume of the "fast" compartment.
3. The time constant of the "slow" compartment (RC_{slow}) accounts for more than three inspiratory and expiratory times.

$$RC_{slow} > 3 * Ti \tag{Eq5}$$

and

$$RC_{slow} > 3 * Te \tag{Eq6}$$

4. Changes of end-expiratory volume in the "fast" compartment can be attributed to changes of end-expiratory airway pressure ($dPaw_{EE}$).
5. Changes of end-expiratory volume in the "slow" compartment can be attributed to changes of mean airway pressure ($dPaw_{mean}$)

6. The respiratory system behaves linearly and time constant.

With these assumptions the volume of the respiratory system (VL(t)) after a rapid change of expiratory pressure may be described as (see Fig. 1):

$$VL(t) = V_{\mathrm{fast}} + V_{\mathrm{slow}}(t) \qquad \text{(Eq7)}$$

$$VL(t) = V_{\mathrm{fast}} + V_{\mathrm{slow}} * (1 - e_{\mathrm{slow}}^{-t/RC}) \qquad \text{(Eq8)}$$

$$V_{\mathrm{slow}} = \Delta VL - V_{\mathrm{fast}} \qquad \text{(Eq9)}$$

$$VL(t) = V_{\mathrm{fast}} + (\Delta VL - V_{\mathrm{fast}}) * (1 - e_{\mathrm{slow}}^{-t/RC}) \qquad \text{(Eq10)}$$

The volume change of the first breath of the PEEP step ($\Delta VL1$) may therefore be calculated by means of the expiratory time of the first breath (Te_1; see assumption 10, with $t = Te_1$) as:

$$\Delta VL1 = V_{\mathrm{fast}} + \Delta VL * (1 - k) - V_{\mathrm{fast}} * (1 - k), \qquad \text{(Eq11)}$$

with

$$k = e^{-Te_1/RC_{\mathrm{slow}}} \qquad \text{(Eq12)}$$

So V_{fast} can be calculated as:

$$V_{\mathrm{fast}} = (\Delta VL1 - \Delta VL * (1 - k))/k \qquad \text{(Eq13)}$$

Drift compensation after a PEEP step:
The basic assumption for this method is that there are no time varying leaks. Steady state imbalance between inspiratory and expiratory volumes are assumed to be due to baseline drift of the flow sensors, constant leaks and/or asymmetry of the pneumotachograph. Also, any volume difference caused by a respiratory quotient greater or smaller than 1 is mathematically eliminated.

For the purpose of this description, the breaths are numbered as shown in Fig. 1. First, an offset factor F1 is calculated as the average ΔV of all 15 breaths before the PEEP step. Second, an offset constant F2 is calculated as the average ΔV of five breaths in the new steady state after the PEEP step. Steady state was identified by visual inspection of the ΔV versus time plot. The original series of ΔV was finally corrected as follows:

$$\Delta V(i)\ \text{corrected} = \Delta V(i) - F1 \quad i = -14....0 \qquad \text{(Eq14)}$$

$$\Delta V(k)\ \text{corrected} = \Delta V(k) - F2 \quad k = 1....100 \qquad \text{(Eq15)}$$

The corrected series of ΔV was then summed and subjected to further analysis (see Fig. 1).

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