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Delayed derecruitment after removal of PEEP in patients with acute lung injury

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Background: A step decrease in positive end-expiratory airway pressure (PEEP) is not followed by an instantaneous loss of the PEEP-induced increase in end-expiratory lung volume (EELV). Rather, the reduction of EELV is delayed, while adverse PEEP effects on hemodynamics are immediately attenuated upon the drop in airway pressure. Step PEEP increments were applied to the lungs of patients with acute lung injury. It was investigated retrospectively whether enlargement of end-expiratory lung volume and changes in lung mechanics persist 45 min after removal of the PEEP increment.
Methods: In 14 patients with acute lung injury (LIS score 2.7) EELV and volume-dependent dynamic compliance of the respiratory system ($C_{dyn,rs}$) were determined 45 min after removal of an additional PEEP increment (0.64 kPa added to baseline PEEP of 1.0 kPa).
Results: Nine patients kept an EELV gain of 13% (SD 7) and showed improved $C_{dyn,rs}$. In 5 patients, EELV was reduced (by 9% (SD 6)) and $C_{dyn,rs}$ unchanged after removal of the PEEP increment compared to baseline.
Conclusion: A subgroup of patients with acute lung injury, the characteristics of which remain to be defined, benefit from prolonged recruitment effects up to 45 min after removal of a PEEP increment, while sequelae of continuously increased airway pressures are minimised.

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Key words: Alveolar recruitment; dynamic compliance, lung physiology, clinical; positive end-expiratory pressure.

EARLY studies of Bernstein (1), Mead (2), and Anthonisen (3) showed that there is a progressive loss of compliance and alveolar volume during breathing in the resting tidal range which can be reversed by application of periodic deep inflations (2), or the application of PEEP (3). These observations are supported by more recent observations from which it can be concluded that the lung owns a mechanical hysteresis, i.e. that the lung is reluctant to accept deformation under stress but, once deformed, it is again reluctant to assume its original shape. Deformational stress forces induced by PEEP might follow different time courses. Firstly, a PEEP-induced increase in lung volume will occur within one breath by expansion of already open alveoli and splinting of alveoli throughout the entire respiratory cycle. Secondly, PEEP might further increase the lung volume by overcoming forces that require a longer time than that available during one tidal breath. The question is whether the delayed increase in lung volume after a step increase in PEEP (4) corresponds to a delayed loss of lung volume and persistency of other mechanical PEEP effects after removal of PEEP, an effect which, if existing, might be used therapeutically: while, upon removal of PEEP, its recruitment effects are maintained and fade away gradually, the adverse PEEP effects on hemodynamics are immediately attenuated upon the drop in airway pressure. As the time constants for alveolar reclosure following the application of PEEP are long compared to the respiratory cycle (5), it might suffice to apply PEEP increments for short periods only, thereby minimizing its adverse effects. Although it is not exactly known how long such effects last and whether they can be observed in ARDS patients (6), previous studies (5, 7) support the idea, and contemporary concepts like airway pressure release ventilation are based on the assumption that this mechanical hysteresis can be used therapeutically.

PEEP increments were applied stepwise to the lungs of patients with acute lung injury as part of the routine procedure to determine "best" PEEP. It was investigated retrospectively whether 45 min after removal of a PEEP increment any enlargement of end-expiratory lung volume and changes in lung mechanics persisted.

Patients and methods

Fourteen patients (11 males; mean age 62, range 33–79 years; lung injury score according to Murray (8) 2.7, range 2.5–3; PaO_2/FiO_2 15, range 10–24 kPa) were investigated 7 (range 2–14) days after start of mechanical ventilation (see Table 1). The protocol was approved by the hospital's ethics committee and informed consent was obtained from the patients' next of kin as required by the institutional review board. The lungs of the patients were ventilated with the EV-A ventilator (Dräger Werke, Lübeck, FRG) in the volume-controlled mode (tidal volume 912 mL (SD 184); end-inspiratory pause 52 ms (SD 47) ; ventilatory rate 15 min^{-1} (SD 2); FiO_2 0.6). Under adequate analgesia and sedation, the patients were paralysed (pancuronium bromide 0.1 $mg \cdot kg^{-1}$) 30 min prior to the start of the investigation, followed by additional aliquots of 0.05 $mg \cdot kg^{-1}$ every 60 min. All measurements were taken with the patient in the supine position and under steady-state conditions.

The computer-aided measuring system for the pulmonary function indices used has been previously described in detail (9, 10) . Flow and airway pressures were measured at the outer end of the endotracheal tube. Gas flow was measured with a heated Fleisch No. 2 pneumotachograph (Metabo, Epalinges, Switzerland) connected to a differential pressure transducer FC 040 (Furness Controls, Bexhill, UK). Airway pressure was measured with a pressure transducer SZ75120 (Sensym, Milpitas, CA, USA). The sensors were connected to the measuring site through three silicone tubes (180 cm long, 4 mm ID). To correct the flow for changes in gas viscosity, dry gas fractions were measured using a quadrupole mass spectrometer MGA-200 (Centronic, Croydon, UK). End-expiratory lung volume (EELV) was determined as described previously (for details see (9)). Briefly, a multiple-breath wash-in/wash-out method was used. The raw data were analyzed until the N_2-concentration fell to below 1%, taking at least 10 min for wash-in and wash-out, respectively. The coefficient of variation for double measurements with this method in patients is 3.1%, and the absolute accuracy, as tested in a physical model, is excellent with an overestimation of the volume of the physical model of 0.62% by this method (9).

Determination of volume-dependent compliance

To detect small changes in dynamic respiratory system compliance within the tidal volume, the recently developed slice method was used (10). A more detailed description of the method is given in the appendix.

Protocol

PEEP increments were applied stepwise as part of the routine procedure to determine "best" PEEP. Measurements were taken in the reference setting with PEEP 1.0 kPa (SD 3), (range 5–15). A PEEP increment of 0.64 kPa (SD 0.5), (range 0.58–0.71) was then added to the baseline PEEP; all other parameters of the initial reference ventilatory setting were fixed. After 41 min (SD 17), range 15–72) on the increased PEEP level measurements were taken. Reference setting with the initial PEEP level was resumed subsequently, and measurements were repeated after 45 min.

Data presentation and statistics

Ventilatory volumes were converted to BTPS conditions. Data are presented as mean (1 standard deviation, SD). Where appropriate, range and 95% confidence intervals are indicated as well. Differences were evaluated with a one-way analysis of variance for repeated measures. If significant differences were detected, these differences were evaluated using Scheffe's F-test. Linear regression analysis was performed when appropriate. Statistical significance is indicated as $P \leq 0.05$ (=*) and $P \leq 0.01$ (=**).

Results

The results are summarized in Tables 1 and 2 and in Figs. 1 and 2.

Overall, the mean end-expiratory lung volume (EELV) was 1838 mL (SD 674) with a reference PEEP of 1.0 kPa (SD 0.3), while it was 2616 mL (SD 797) ($P \leq 0.01$) with 1.6 kPa (SD 0.3) PEEP, and 45 min after PEEP had been reset to the reference level, it was 1922 mL (SD 690).

Two types of response could be distinguished: In 9 patients (arbitrarily defined as EELV "responders") EELV 45 min after removal of the additional PEEP increment was 13% (SD 7) higher compared to baseline (minimal gain 2%, maximal 26%) ($P \leq 0.01$). Five "non-responders" had lost 9% (SD 6) of their baseline EELV 45 min after removal of PEEP increment (minimal loss 3, maximal loss 19%) (see Table 1 and Fig. 1).

In all patients, the volume-dependent dynamic compliance of the respiratory system was unchanged after removal of the PEEP increment compared to reference (Fig. 2 top, panel). While the shape of the $C_{dyn,rs}$-curve remained essentially unchanged after PEEP-removal in non-responders (a representative patient is shown in Fig. 2, bottom panel), the responders

Table 1

Patient descriptive data, lung volumes and partial pressures of oxygen before and 45 min after a period of increased positive end-expiratory pressure. Patients are designated as "responders" (sustained gain in end-expiratory lung volume after removal of the PEEP increment) or "non-responders" (loss in end-expiratory lung volume after removal of the PEEP increment).

	Male/ female	Clinical course	Outcome	Age (years)	Ventilated before study (days)	EELV/ FRC_{exp} (%)	PaO_2/FiO_2 (kPa)	LIS	PaO_2 1 (kPa)	PaO_2 2 (kPa)	$EELV_1$ (ml/kg)	$EELV_2$ (ml/kg)
Responders												
1	m	Gall bladder perforation, peritonitis	discharged	65	4	31	25	2.5	15	19	10	11
2	m	Chondrosarcoma, chest wall resection, bronchopneumonia, MOF	died	64	7	58	21	2.8	12	20	24	28
3	m	Colon carcinoma, hemicolectomy, peritonitis, bronchopneumonia, MOF	died	79	2	51	41	2.5	24	20	23	25
4	f	Bleeding ventricular ulcer, bronchopneumonia, MOF	discharged	56	10	62	16	3	10	12	23	26
5	m	Rectum carcinoma, abdomino-sacral resection, relaparatomy for volvulus, aspiration	died	75	10	65	18	2.8	11	13	36	40
6	m	Coronary artery bypass, acute cholecystitis, cholecystectomy, bronchopneumonia, MOF	died	73	7	38	30	3	18	20	20	24
7	m	Recurrent bleeding ventricular ulcer, 3 laparotomies, hemorrhagic shock, MOF	died	59	12	57	33	3	20	30	16	20
8	m	Hemorrhagic-necrotizing pancreatitis, MOF	discharged	51	18	68	18	2.5	11	16	33	36
9	f	Multiple perforation of colon, peritonitis, MOF	died	66	13	79	34	3	21	16	39	42
Non-responders												
10	f	Carcinoma of sigma, resection and relaparatomy for insufficiency of anastomosis, peritonitis, MOF	died	64	3	41	26	2.5	16	11	14	13
11	m	Multiple trauma, brain injury, laparotomy , trepanation, hemorrhagic shock	discharged	60	3	59	24	2.5	14	13	33	30
12	m	Pleural empyema, decortication, MOF	discharged	50	2	68	26	2.5	16	19	31	29
13	m	Bleeding ventricular ulcer, bronchopneumonia, MOF	died	79	3	92	21	2.8	12	12	48	47
14	m	Multiple trauma, hemorrhagic shock	died	33	8	34	19	3	11	10	12	10
Mean {min/max}	m:11 f:3		died:9 dischg.:5	62 {33/79}	7 {2/14}	57 {31/92}	25 {16/41}	2.7 {2.5/3.0}	15 {10/24}	16 {10/30}	26 {10/48}	27 {10/48}

EELV/FRC exp: End-expiratory lung volume in % of expected FRC (25) (sitting position), determined by nitrogen washout. LIS: Lung injury score according to Murray and co-workers (8). MOF: Multiple organ failure. EELV1: End-expiratory lung volume with reference ventilation (PEEP 1.0 kPa). EELV2: End-expiratory lung volume with reference PEEP 45 min after removal of PEEP increment. PaO_2 1: PaO_2 with reference ventilation (PEEP 1.0 kPa). PaO_2 2: PaO_2 with reference PEEP 45 min after removal of PEEP increment.

Table 2 a

Cardiorespiratory parameters in all patients with reference ventilation (PEEP 1.0 kPa); with a PEEP increment added (+ 0.6 kPa PEEP) and 45 min after removal of the PEEP increment (=with reference PEEP) . Values are mean and 95% confidence intervals.

	Reference	Reference plus PEEP increment	Reference after removal of PEEP increment
All patients (n=14)			
Peak inspiratory	4.0	4.9	3.7
airway pressure [kPa]	3.7–4.4	4.2–5.7**	3.2–4.2††
Mean airway	1.9	2.6	1.9
pressure [kPa]	1.6–2.1	2.2–2.9**	1.6–2.1††
End-expiratory	1838	2616	1922
lung volume [ml]	1449–2228	1969–3071**	1523–2320††
$PaCO_2$	5.5	5.5	5.4
[kPa]	5.0–5.8	5.0–6.0	4.8–5.9
PaO_2	15	21	16
[kPa]	12–17	15–24**	13–19
SvO_2	73	71	72
[%]	68–78	62–81	66–78
Qva/Qt	25	12	23
[%]	18–29	7–31**	14–28††
AoP	81	77	78
[mmHg]	71–90	65–91	70–85
CVP	10	12	12
[mmHg]	8–12	10–15	9–14
PAOP	14	18	15
[mmHg]	12–15	17–19**	12–17††
PAPmean	30	32	29
[mmHg]	27–32	28–35	26–32

Table 2 b

Changes in some respiratory parameters in responders and non-responders during the study. The patients who showed a sustained gain in end-expiratory lung volume after removal of the PEEP increment are designated "responders". Those who suffered a loss in end-expiratory lung volume after removal of the PEEP increment are designated "non-responders".

	Reference	Reference plus PEEP increment	Reference after removal of PEEP increment
Responders (n=9)			
End-expiratory	1772	2460	1978
lung volume [ml]	1299–2246	1984–3155**	1484–2472††**
paO_2	16	24	19
[kPa]	12–20	18–27**	14–22
SvO_2	70	68	69
[%]	62–77	61–74	62–75
Qva/Qt	22	12	17
[%]	12–32	7–16**	10–24
Non-responders (n=5)			
End-expiratory	1958	2173	1820
lung volume [ml]	927–2988	1092–3254	780–2862
PaO_2	14	18	13
[mmHg]	11–16	9–27**	9–17
SvO_2	78	79	77
[%]	70–86	68–90	65–89
Qva/Qt	26	19	28
[%]	16–36	4–33 *	12–44

(Footnote to Tables 2 a and 2 b)
$PaCO_2$=arterial partial pressure of CO_2. PaO_2=arterial partial pressure of O_2. Qva/Qt=venous admixture, shunt fraction. SvO_2=mixed venous oxygen saturation. AoP=aortic pressure. CVP=central venous pressure. PAOP=pulmonary arterial occlusion pressure. PAPmean=pulmonary arterial mean pressure.
=significant difference when compared to reference (: $P \leq 0.05$; **: $P \leq 0.01$)
†=significant difference when compared to PEEP increment (††: $P \leq 0.01$).

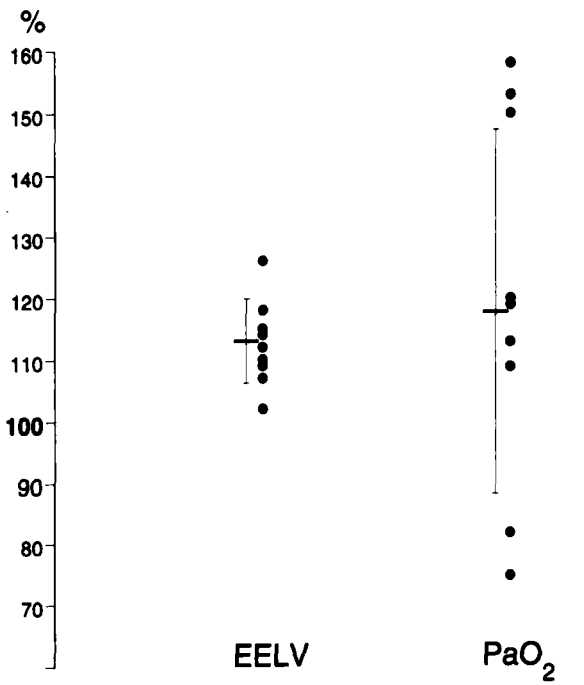

Fig. 1. Individual percent changes in end-expiratory lung volume (EELV) [left] and PaO_2 [right] during reference setting 45 min after removal of the PEEP increment in the responder group. Baseline reference setting=100%. Heavy bars: Mean value (±1 SD).

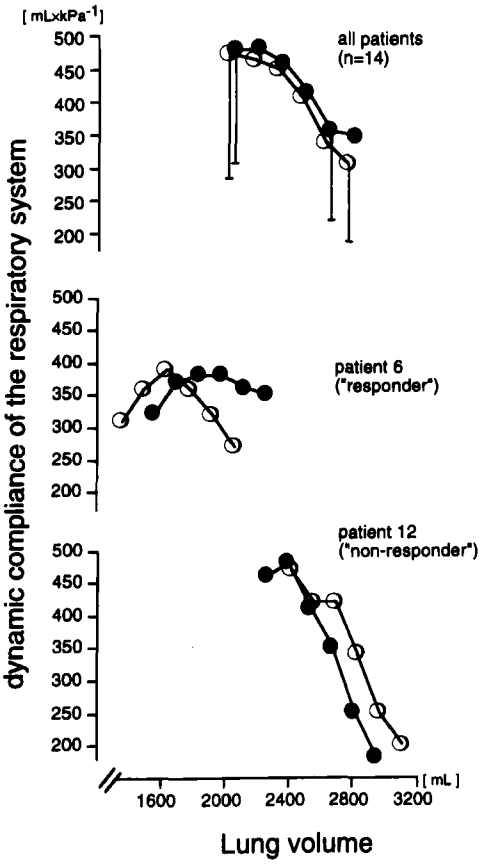

Fig. 2. Dynamic respiratory system compliance ($C_{dyn,rs}$) as a function of the pulmonary gas volume (VL) in: (top panel): all patients, mean tidal volume 912 mL, mean PEEP 1.0 kPa; (middle panel): Patient 6 ("responder"), tidal volume 940 mL; PEEP 1.1 kPa; (bottom panel): Patient 12 ("non-responder"), tidal volume 925 mL, PEEP 1.1 kPa. ○=compliance curve obtained with respective baseline PEEP level. ●=compliance curve obtained with baseline PEEP 45 min after removal of the additional PEEP increment. Values are mean + 1 SD (top panel), in the middle and bottom panel each point of the curve corresponds to the dynamic compliance of 1 volume slice averaged over 15 consecutive breaths (for the sake of clarity standard deviations are omitted).

had a higher percentage of the tidal volume delivered within the higher range of compliance, as shown by the more horizontal course of their compliance curve (Fig. 2, middle panel, representative patient). The absolute level of compliance at the onset of tidal volume delivery (slice 2) had decreased in 4 out of 5 non-responders (by 2% (SD 13), while it had increased in 7 out of 9 responders (by 6% (SD10) after PEEP removal, although these changes did not reach statistical significance.

PaO_2 was not influenced by the preceding PEEP-history in the non-responder group. In the responder group it was 16 kPa (SD 5) at baseline and 19 kPa (SD 5) (difference not significant) in the reference setting after removal of PEEP increment (see Fig. 1). In all patients, the pulmonary artery occlusion pressure increased from 14 to 18 mmHg with the additional PEEP increment, and returned to 15 mmHg after its removal. Mixed venous saturation was slightly, albeit insignificantly, reduced during the application of the PEEP increment. Venous admixture (Qva/Qt) tended to be higher in the non-responders, decreased with PEEP increment and returned to reference level after removal of PEEP increment.

Regression analysis of the baseline parameters (see Table 1), level of PEEP increment, and its application time did not reveal any consistent relationship to the gain or loss in EELV.

Discussion

The main results of this retrospective study are: In 9 out of 14 patients with acute lung injury a PEEP increment of 0.6 kPa resulted in a sustained gain of end-expiratory lung volume (+13%) that could be measured 45 min after PEEP had been reduced to its previous baseline level again (see Fig. 1). The course of the volume-dependent dynamic compliance of the respiratory system ($C_{dyn,rs}$) had also changed, resulting now in a delivery of the major part of the tidal volume within the higher range of $C_{dyn,rs}$. In 5 pa-

tients, EELV had decreased and $C_{dyn,rs}$ remained unchanged after PEEP removal.

Critique of methods

The data for the present study were collected during the search for best PEEP. The time schedule for this procedure was extended for the purpose of this study which was performed in a period of time during which large tidal volumes were used at our institution. Meanwhile, we have adopted a pressure-targeted small-volume approach to ventilation. For clinical reasons it was impossible to strictly standardize both the height and the application time of the PEEP increments. The scanty set of hemodynamic data leaves more space for speculation than we would like. The choice of PEEP and tidal volume would be different today, making application of these results to contemporary ventilatory strategies questionable. For therapeutic purposes it would, moreover, be helpful to have details about the temporal pattern of the decline of the PEEP-effect on EELV. However, as the measurement of FRC, as used in this study, takes at least 20 min and, depending on the lung status, sometimes considerably more, we could not measure at shorter intervals, which restricts conclusions to the 45 min interval after PEEP removal, which we choose as a compromise. We also realize that the *post-hoc* allocation of patients to a "responder" and a "non-responder" group according to their gain in EELV is arbitrary and improper from a statistical point of view. We could not detect a single parameter or a combination of parameters which predicted the response to PEEP increment (see also Table 1). More specifically, the following parameters did not predict whether a sustained gain in EELV would be obtained: duration of ventilation or severity of lung injury, the size of baseline EELV, baseline compliance, the level to which PEEP had been raised, and the application time of the PEEP increment. Thus, it was only the response to the PEEP challenge itself which distinguished between responders and non-responders. Owing to these obvious drawbacks, we regard our results as preliminary and to be tested in a prospective study.

End-expiratory lung volume

Sustained enlargement of end-expiratory lung volume after removal of PEEP increment has been observed by other workers (4, 14, 15), although, to our knowledge, not for this prolonged period of time. While the benefits of intermittent recruitment manoeuvres on respiratory mechanics have been convincingly shown in small animals and infants (16–18), the situation is less clear in large animals and adult patients. Given a coefficient of variation for EELV measurements in a patient of 3.1% (9) we consider an increase of 13% 45 min after removal of PEEP (see Fig. 1) as seen in the responders as biologically significant. Valta and co-workers (14) in patients after open heart surgery by the end of a first run of PEEP increments/decrements (0.2 kPa, 1 to 2 min each, up to PEEP of 1.0 kPa followed by stepwise reduction of PEEP to baseline) found an increase in end-expiratory lung volume of 109 mL (SD 44) and an additional increase of 32 ml (SD 30) by the end of a second run. They assumed that this increase in end-expiratory lung volume reflected persistent recruitment of collapsed alveoli after removal of PEEP, which was also confirmed by a significant increase in compliance after inflation-deflation runs. In ARDS patients, however, with a similar protocol (PEEP up to 1.4 kPa) Valta and co-workers (19) did not find this effect in terms of increased end-expiratory lung volume at zero PEEP. The difference from the results of the present study might be explained by the comparatively short time during which the inflation-deflation runs were performed in Valta and co-workers' study. It might be enough to apply PEEP increments during 15 to 30 min to recruit atelectatic regions in the otherwise healthy lungs of cardiac surgery patients. Longer periods of higher PEEP may be needed to find a similar effect in ARDS patients. The same argument applies to the results of Katz and co-workers (4). The increases and decreases of lung volume that follow a 10 min application and removal of 1.0 kPa PEEP in their acute lung failure patients were found to have a time course of less than 1 min. After this time no further mechanical PEEP effects were seen.

Volume-dependent dynamic compliance of the respiratory system

Data on PEEP-induced changes in compliance of ARDS patients are controversial (20–22) and few data exist on medium-term compliance changes after removal of PEEP. Increased compliance after removal of a stepwise raised PEEP was seen by Gay and co-workers (15). PEEP steps increased static compliance of the total respiratory system in 7 out of 20 patients, the increase being proportional to the baseline compliance. That compliance is a function of the preceding pressure-volume history has already been shown by Mead and Collier (2) in healthy dogs. They found that the progressive decrease in lung compliance to 60% of control levels in 2 h was immediately and nearly completely reversed following resumption of periodic

inflations every 10 min. Most of the change took place within the first inflation, but the mechanical hysteresis further delayed the downward trend of compliance in the intervening periods. In a recent study, Cereda and co-workers (6) in patients with acute lung injury observed that a PEEP of at least 1.5 kPa was necessary to prevent progressive loss of C_{rs} during a 30 min period. In general, patients who suffer from late stages of acute lung injury (our patients had been ventilated for an average of 7 days prior to the study) are not assumed to show an increase in compliance on recruitment manoeuvres as structural re-modelling of the lung parenchyma usually has taken place by this time. In the present study, there was a tendency for an increase in $C_{rs,dyn}$ (slice 2, i.e. at low volume) in responders, while the non-responders tended to show a decreased compliance in the same slice. This corresponded to the gain of EELV in the responder, and a loss of EELV in the non-responder group, respectively. More important is the fact that, upon PEEP removal, the shape of the compliance curve consistently had changed to a more horizontal course in the responders (see Fig. 2, middle panel), while in the non-responders it declined rapidly from the onset of inspiration on (see Fig. 1, bottom panel). We interpret this as a lasting mechanical recruitment effect of PEEP: After recruitment in the responder group, more of the tidal volume could be delivered in the horizontal segment of the compliance-over-lung volume curve. It was only at end-inspiration that tidal volume tended to overdistend the lung, as judged from declining compliance in slice 7 and 8 (see Fig. 2, middle panel). The mechanical effects of inspiratory volume within a single breath cannot be studied with the more conventional methods to determine C_{rs}. (Using the difference between end-inspiratory plateau pressure and end-expiratory pressure to determine compliance, for example, assumes compliance to be linear within the tidal breath, which much too often is not the case). The non-responder in Fig. 2 had an even higher compliance at onset of inspiration compared to the responder, despite the fact that the major part of the tidal volume was applied at increasing, potentially harmful, overdistension, as indicated by the rapid decline of compliance during the delivery of tidal volume. We feel it a definite advantage of the slice-compliance method that the non-linear mechanical behaviour of the respiratory system can be studied manoeuvre-free at the actual PEEP and tidal volume. Looking at the shape of the compliance-curve for all patients (Fig. 2, top panel), we assume that at the prevailing PEEP levels and size of tidal volume some degree of overdistension was a common result of our ventilatory strategy. This is indicated by the very short horizontal segment of the compliance-volume curve, rapidly falling to about 50% of the initial $C_{dyn,rs}$ at end-inspiration. This, among other reasons, has prompted us to reduce the tidal volume during mechanical ventilation.

Could these findings have clinical implications? The PEEP increment increased peak inspiratory pressure disproportionally, which, together with the course of volume-dependent dynamic compliance indicated overdistension. Cardiovascular performance was slightly depressed. This excluded constant application of the high PEEP level in our patients. However, in order to avoid tidal closure and re-opening (23), the small-volume approach might need a complementary high PEEP level. Reduction of adverse PEEP effects, therefore, remains a therapeutic challenge which, among other methods, could be accomplished by taking benefit from the prolonged recruitment effects of intermittent PEEP increments observed in our responder group. This requires detailed studies of the PEEP levels and application periods necessary for effective recruitment as well as the decline of this effect.

We conclude that in a subgroup of patients with acute lung injury, the characteristics of which remain to be defined, a step PEEP increment induces an increase in end-expiratory lung volume along with improved dynamic compliance of the respiratory system. This effect lasts up to 45 min after the removal of the PEEP increment.

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Appendix

Determination of volume-dependent compliance (slice method)

The slice method is a new computer-based multipoint method for simultaneously determining volume-dependent dynamic compliance and resistance (10). The method is based on continuously determined tracheal pressure (Ptrach) thus preventing the lung mechanics analysis being affected by the resistance of the endotracheal tube (ETT) (11). The basic principle of the slice method is that the tidal volume is subdivided into consecutive volume slices of equal size. With repeated application of the linear RC-model (12), 1 mean compliance (intrinsic PEEP considered) and 1

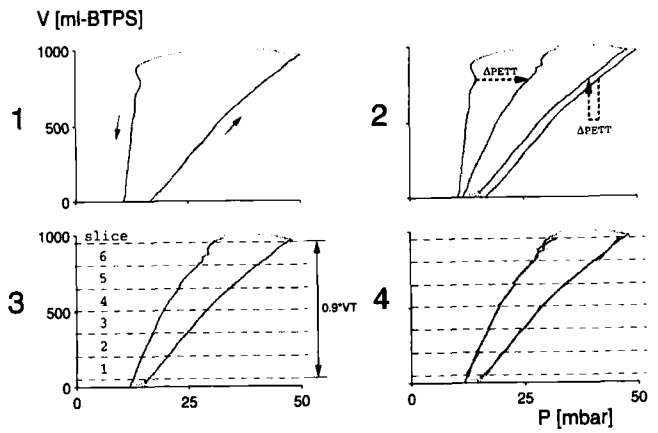

Fig. 3. The four steps of the slice-method illustrated by the V/P-loop of one ARDS patient.
STEP 1: Generation of volume equidistant data sets. Fig. 3: 1 shows the V/Paw-loop of 1 mechanical breath with volume equidistant sample points (volume step: ΔV=10 mL). Upward-pointing arrow signifies inspiration, downward-pointing arrow signifies expiration.
STEP 2: Point-by-point calculation of tracheal pressure. Fig. 3: 2 shows the V/Paw-loop with the corresponding V/Ptrach-loop inside it. Dashed arrows indicate the pressure drop across the ETT.
STEP 3: Subdivision into slices and analysis of lung mechanics. In Fig. 3: 3 the limits of the 6 slices are indicated as horizontal broken lines. The lung mechanics analysis is performed separately for each slice. The 6 slices comprise 90% of the total tidal volume. The upper and lower 5% of the tidal volume are excluded from analysis.
Step 4: Quality check. Fig. 3: 4 shows the V/Ptrach-loop recalculated point-by-point for each slice and graphically superimposed on the measured V/Ptrach-loop. The difference in pressure between the loops gives a quantitative measure of the accuracy of the calculated parameters of lung mechanics. Note that the measured and the recalculated V/Ptrach-loops are practically identical. (Reprinted from Technology and Health Care, vol. 2 no. 3 , Guttmann J et al. Determination of volume-dependent respiratory system mechanics in mechanically ventilated patients using the new SLICE method, 175–191, 1994, with kind permission of Elsevier Science-NL, Sara Burgerhartstraat 25, 1055 KV Amsterdam, The Netherlands)

mean resistance (ETT resistance excluded) value per slice is calculated. Combining the compliance and resistance values of all the slices gives the course of compliance and resistance within the tidal volume, i.e., the volume-dependent compliance and resistance within one breath. The relative error of the method is smaller than ±5% (10, 24). The method needs no particular ventilatory pattern and allows continuous monitoring of non-linear respiratory mechanics on a breath-by-breath basis at the bedside.

The V/P-loops of one patient under volume-controlled ventilation are presented to illustrate the four steps of our method (Fig. 3).

STEP 1: Generation of volume equidistant data sets (Fig. 3: 1): In order to prevent either inspiratory or expiratory data samples from predominating, an equal number of each is used (I–E balance). The flow and airway pressure data sampled at a constant rate of 60 Hz are thus transformed into volume-equidistant data by linear interpolation. A volume step of ΔV=10 mL was selected to ensure that each step should contain at least two measured data points.

STEP 2: Point-by-point calculation of tracheal pressure (Fig. 3: 2): Tracheal pressure, Ptrach, is continuously calculated as the difference of continuously measured airway pressure, Paw, minus flow-dependent pressure drop, $\Delta P_{ETT}(\dot{V}(t))$, across the ETT:

$$P_{trach}(t)=P_{aw}(t)-\Delta P_{ETT}(\dot{V}(t)) \quad [1]$$

The pressure-flow relationship of the ETT was measured in the laboratory. The measured relationship is described by a simple non-linear mathematical model. According to this model, the flow-dependent pressure drop across the ETT is described by equation [2] for inspiration and by equation [3] for expiration:

$$\Delta P_{ETT}=K_{1i}\times\dot{V}^{K2i} \quad [2]$$

$$\Delta P_{ETT}=K_{1i}\times\dot{V}^{K2e} \quad [3]$$

The four coefficients of equations [2] and [3] were determined by approximating the mathematical model to the measured data (non-linear least-squares fit method).

Fig. 4 shows the approximation curve of an ETT of 8 mm ID which was used in the patient whose V/P-

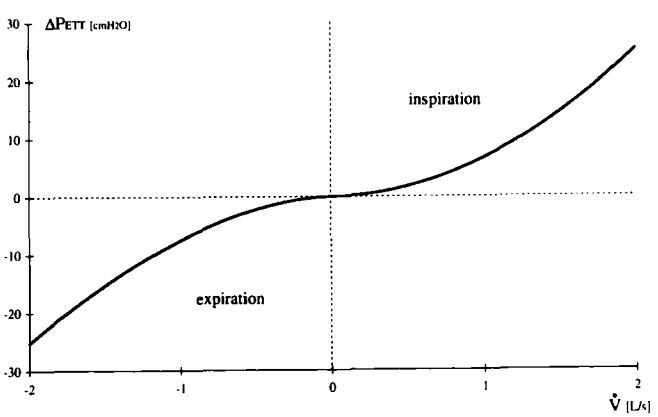

Fig. 4. Pressure difference ΔPETT across ETT versus flow through ETT (8 mm ID, original length). The diagram shows the approximation curve according to the non-linear approximation (equations [2] and [3]). Note that the curve shows a slight I/E asymmetry due to the additional pressure loss at the tip of the ETT where the cross-sectional area rapidly changes from ETT to trachea. In inspiration, the gas flow passes an abrupt sectional expansion, leading to a larger pressure loss, compared with expiration when the gas flow passes an abrupt sectional contraction.

loops are presented in Fig. 3. Using equation [2] or [3], respectively, equation [1] can be rewritten:

$$P_{trach}(t)=P_{aw}(t)-(K_1\times\dot{V}(t)^{K2}) \quad [4]$$

In inspiration, the coefficients K1 and K2 are replaced by K1i and K2i; in expiration, K1 and K2 are replaced by K1e and K2e, respectively. Fig. 3: 2 shows the V/Paw-loop with the corresponding V/Ptrach-loop inside it. The calculation of tracheal pressure is described in detail in (11).

STEP 3: Subdivision into slices and analysis of lung mechanics (Fig. 3: 3): The upper and lower 5% of the tidal volume are excluded from analysis because of interference due to the ventilator's valves and the large volume acceleration. 90% of the tidal volume is subdivided into 6 slices of equal size. Each slice consequently comprises 15% of the tidal volume. We found 6 volume slices to be a good compromise between two opposite tendencies: on the one hand, a large number of slices is desirable for a high resolution; on the other hand, cardiogenic oscillations limit the minimal useful size of a single slice.

The analysis of lung mechanics is performed separately for each slice i using the standard least-squares-fit technique. This is based on the simple linear RC-model of the respiratory system:

$$P_{trach}(t)=1/C_{dyn,rs}i\times V(t) + R_{dyn,rs}i\times\dot{V}(t)+iPEEP_{dyn}i \quad i=1...6 \quad [5]$$

Using the in- and expiratory data for P_{trach}, V and $\dot{V}$ pertaining to 1 slice i, 1 $C_{dyn,rs}i$ (dynamic compliance of the respiratory system), 1 $R_{dyn,rs}i$ (dynamic resistance of the respiratory system) and 1 $iPEEP_{dyn}i$ (dynamic intrinsic PEEP) is calculated per slice (i).

STEP 4: Quality check (Fig. 3: 4): To test the quality of the calculated results, the tracheal pressure is recalculated point-by-point for each slice according to equation 5, using the calculated values for $C_{dyn,rs}i$, $R_{dyn,rs}i$, $iPEEP_{dyn}i$, and the measured values for volume and flow. This gives the recalculated V/Ptrach-loop which is then superimposed on the measured V/Ptrach-loop and the recalculated loops differ only in pressure. This pressure difference between both loops gives a quantitative measure of the accuracy of the calculated $C_{dyn,rs}(i)$, $R_{dyn,rs}(i)$, and $iPEEP_{dyn}(i)$. The smaller the difference, the better the correspondence of the two V/P-loops and the higher the quality of the results. The measured and the recalculated V/Ptrach-loops of Fig. 3: 4 are so close together that they are barely distinguishable.

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