ORIGINAL

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Different ventilatory approaches to keep the lung open

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Abstract *Objectives:* To study the
ability of different ventilatory ap-
proaches to keep the lung open.
Design: Different ventilatory pat-
terns were applied in surfactant de-
ficient lungs with PEEP set to
achieve pre-lavage PaO_2.
Setting: Experimental laboratory of
a University Department of
Anaesthesiology and Intensive Care.
Animals: 15 anaesthetised piglets.
Interventions: One volume-con-
trolled mode ($L\text{-}IPPV_{201:1.5}$) and
two pressure-controlled modes at 20
breaths per minute (bpm) and $I:E$
ratios of 2:1 and 1.5:1 ($L\text{-}
PRVC_{202:1}$ and $L\text{-}PRVC_{201.5:1}$), and
two pressure-controlled modes at
60 bpm and $I:E$ of 1:1 and 1:1.5
($L\text{-}PRVC_{601:1}$ and $L\text{-}PRVC_{601:1.5}$)
were investigated. The pressure-con-
trolled modes were applied using
"Pressure-Regulated Volume-Con-
trolled Ventilation" (PRVC).
Measurements and results: Gas ex-
change, airway pressures,
hemodynamics, FRC and in-
trathoracic fluid volumes were mea-
sured. Gas exchange was the same
for all modes. FRC was 30% high-
er with all post-lavage settings. By
reducing inspiratory time MPAW
decreased from 25 cmH_2O by
3 cmH_2O with $L\text{-}PRVC_{201.5:1}$ and
$L\text{-}PRVC_{601:1.5}$. End-inspiratory air-
way pressure was 29 cmH_2O with L-
$PRVC_{201.5:1}$ and 40 cmH_2O with L-
$IPPV_{201:1.5}$, while the other modes
displayed intermediate values. End-
inspiratory lung volume was
65 ml/kg with $L\text{-}IPPV_{201:1.5}$, but it
was reduced to 50 and 49 ml/kg
with $L\text{-}PRVC_{601:1}$ and L-
$PRVC_{601:1.5}$. Compliance was 16
and 18 ml/cmH_2O with L-
$PRVC_{202:1}$ and $L\text{-}PRVC_{201.5:1}$, while
it was lower with $L\text{-}IPPV_{201:1.5}$, L-
$PRVC_{601:1}$ and $L\text{-}PRVC_{601:1.5}$. Oxy-
gen delivery was maintained at pre-
lavage level with $L\text{-}PRVC_{201.5:1}$
(657 ml/min·m²), the other modes
displayed reduced oxygen delivery
compared with pre-lavage.
Conclusion: Neither the rapid fre-
quency modes nor the low frequen-
cy volume-controlled mode kept the
surfactant deficient lungs open.
Pressure-controlled inverse ratio
ventilation (20 bpm) kept the lungs
open at reduced end-inspiratory air-
way pressures and hence reduced
risk of barotrauma. Reducing $I:E$
ratio in this latter modality from
2:1 to 1.5:1 further improved oxy-
gen delivery.

Key words Intrinsic PEEP ·
Respiratory failure · Pressure-con-
trolled ventilation · Inverse ratio
ventilation · Functional residual ca-
pacity · Alveolar distension

Introduction

Recent studies [1, 2] provide evidence for the benefit of reducing alveolar pressures and avoiding alveolar over-distension [3–5] in mechanically ventilated patients.

Continuing and extending our studies in the piglet lavage model [6, 7], which is characterised by reduced gas exchange, reduced compliance, pulmonary hypertension and interstitial oedema, we investigated the short-term effects of continuous positive-pressure ventilation settings, which are especially designed to reduce airway pressures and to produce a mean airway pressure (MPAW) sufficient to maintain the lung open [8–13] during the entire ventilatory cycle. We compared one volume-controlled mode to 4 pressure-controlled modes. In the pressure-controlled modes, we compared a low frequency setting (20 bpm) to a rapid frequency setting (60 bpm). In the low frequency pressure-controlled mode an inverse inspiration-expiration ratio (I : E 2 : 1, or 1.5 : 1) was used. In the rapid frequency pressure-controlled modes we also investigated an additional setting with reduced I : E ratio in order to see whether this would improve hemodynamic performance without influence on gas exchange. $PaCO_2$ was kept constant. Mean airway pressure was kept at 25 cm H_2O and it was allowed to fall in the modes with reduced inspiratory time.

Material and methods

Two papers describing the methods in detail have been published previously [6, 7]. To ensure full post-lavage alveolar recruitment, pressure-controlled ventilation was applied with the minute volume set at the pre-lavage level, and with PEEP set to produce a peak inspiratory pressure (PIP) of 55 cm H_2O for 5–10 min. After this opening procedure the mode under study was started with the PEEP valve of the ventilator set to a level resulting in a MPAW of 25 cm H_2O, and the ventilatory volume was adjusted to produce $PaCO_2$ 5±0.2 kPa. Total PEEP was defined as the sum of the PEEP set with the PEEP valve of the ventilator and the intrinsic PEEP measured by the end-expiratory hold procedure.

Animals

Healthy piglets ($n = 15$) of Swedish country breed (mean weight 24.1 kg±1.6 SD) were used. The investigations were performed at the Experimental Laboratories of the Department of Anesthesiology and Intensive Care, the Department of Diagnostic Radiology and the Department of Anatomy at the University Hospital in Uppsala. The local ethics committee for animal experimentation reviewed and approved the protocol.

Experimental procedure

A Siemens Servo Ventilator 300 (Siemens-Elema AB, Solna, Sweden) was used. A paediatric humidifier and heated circuit with a compressible volume of 55 ml and an internal static compliance of 0.7 ml/cm H_2O was employed (Fisher and Paykel, New Zealand; for details of the method, see [6, 7]).

Following anaesthesia and preparation each animal was placed in prone position. An inspired oxygen fraction of 1.0 was used. Baseline values were obtained after stabilisation. Lavage was performed as described in [6, 7, 14]. Thereafter the different modes were applied to each animal. The sequence of patterns had been determined in advance for each animal in a Latin square type of design to ensure the maximal number of possible pattern combinations in 15 animals. Each mode was continued for at least half an hour and all measurements were performed under conditions of ventilatory and hemodynamic steady state. Between the ventilatory modes under study IPPV without PEEP was interposed, in order to reproduce alveolar collapse.

Anaesthesia and fluid management

Premedication

Pentobarbital 15 mg/kg+0.5 mg atropine intraperitoneally 15 min pre-induction.

Induction

500 mg ketamine (Ketalar®, Parke-Davis) and 0.5 mg atropine i.v., followed by Ketalar infusion at 20 mg/kg·h plus 20 mg i.v. morphine.

Relaxant

Pancuronium bromide 0.26 mg/kg·h. The animals were tracheotomized and ventilated through an 8 mm diameter double lumen (1 : 10 lumen ratio) HiLo jet endotracheal tube (Mallinckrodt Inc., Glens Falls, NY). A thermostatically controlled heating pad was used to keep the animal's body temperature normal.

Fluid replacement was titrated according to measurements of the intrathoracic blood volume (ITBV), aiming at a normovolemic level of 22 ml/kg ITBV. An i.v. infusion of 0.45% NaCl with 2.5% glucose (Rehydrex, Pharmacia Infusion AB, Uppsala, Sweden) was maintained (up to 40 ml/kg·h). If required, a 100 ml bolus of dextran-70 (Macrodex 70, Pharmacia Infusion AB) was given to achieve the normovolemic ITBV.

Monitoring

Intravascular catheters were surgically placed for the measurement of central venous, pulmonary artery (via the external jugular vein) and aortic pressures (via the carotid artery). A thermo-dye COLD Computer (Pulsion Medizintechnik KG, München, Germany) was used. The fiberoptic catheter was introduced via the femoral artery and advanced to the descending aorta (for a detailed description of the method, see [15, 16]). Exact position of catheters was confirmed by pressure tracing. All pressures were displayed on a bedside monitor (Siemens Sirecust) and recorded with reference to atmospheric pressure at mid thorax level and at end-expiration. Continuous monitoring of ECG was performed (Siemens Sirecust). Intermittent analysis of arterial and mixed venous blood gases at 37 °C was included (ABL 300, Radiometer A/S, Copenhagen, Denmark). Ventilatory volumes were obtained using the readings from the Servo Ventilator 300. The compressible volume of the tubing system and

the humidifier (55 ml) was subtracted and the values converted to BTPS. Carbon dioxide production was recorded by a metabolic monitor (Datex Deltatrac, Datex Instrumentation Corp., Helsinki, Finland).

In five animals a static pressure/volume (PV-) loop of the lungs could be obtained using a prototype of a graphical program (Siemens-Elema, Solna, Sweden). This program uses the signals from the pressure and flow transducers of the Servo Ventilator 300 to present the PV-loops. From this PV-loop the inflection point could be estimated [17, 18].

Airway pressures

The airway pressures were obtained from the Servo Ventilator 300 digital displays. The static chest-lung compliance was calculated according to the formula: Tidal volume/(end-inspiratory pressure − end-expiratory pressure). When the end-inspiratory and end-expiratory pressures were measured the hold functions of the Servo Ventilator 300 were used.

Functional residual capacity (FRC)

For the measurement of FRC the SF_6 tracer gas method, described by Larsson et al. was used (for details of the method, see [19]).

Lavage

The lavage was performed as described elsewhere [6, 7]. Surfactant was removed by 10−11 instillations of 37 °C normal 0.9% saline, each of 1−1.5 l volume. We used volume-controlled IPPV with 8 cmH_2O PEEP in the intervals between the lavage procedures.

Computed tomography (CT)

Computer tomography (CT) scans of the chest of 4 piglets were performed using a Somatom HiQ (Siemens AG, Erlangen, Germany) with a 512×512 matrix, 133 kV, 225 mA, exposure time 2.0 s and 4 mm collimation. The table position was kept constant throughout the CT scans in each individual animal. Each observation consisted first of a scan during inspiratory breath-holding, and shortly followed by a scan during expiratory breath-holding (see illustrated sequence in Fig. 3; Servo Ventilator 300: "Pause hold−Exp"). With the object of scanning an area with as much lung parenchyma as possible, all scans were at the level of the lower portion of the thorax. Detailed results on radiological observations using CT during PRVC in severe respiratory distress will be presented elsewhere.

Ventilator modes

Three pressure flow volume patterns were studied as illustrated in Fig. 1 and the characteristics of the different patterns are summarised in Table 1.

The pre-lavage PEEP level of 8 cmH_2O was selected as in morphological studies we had seen that a PEEP of 5 cmH_2O was not sufficient to prevent major structural changes when applied with IPPV to healthy lungs. The post-lavage PEEP level was set to yield a MPAW of 25 cmH_2O as in previous experiments [7] we had seen that with this MPAW the PaO_2 was back to pre-lavage which in our previous studies was considered to be an open lung condition.

Pressure-regulated volume-controlled ventilation (PRVC)

The pressure-controlled modes were applied using a new modality with volume-control, called "Pressure-Regulated Volume-Controlled Ventilation" (PRVC), which has been developed by the R&D Department of Siemens-Elema Life Support Systems Division (and, among others, in collaboration with one of the authors, UHS). PRVC is inherent in the Servo Ventilator 300 − during PRVC the inspiratory pressure is regulated to a value based on the pressure/volume relation (i.e. dynamic compliance) for the previous breath, i.e. in order to provide breath-by-breath regulated levels of pressure-controlled ventilation to maintain the pre-set target tidal and minute volumes.

Fig. 1 Pressure (cm H_2O) and flow (l/min) recordings from the Servo Ventilator 300 and simultaneously calculated volume (ml) in a piglet after lavage and under normoventilation with three modes of ventilation: *L-IPPV, L-PRVC$_{202:1}$* and *L-PRVC$_{601:1}$*. Note the constant flow inspiration with the volume-controlled mode (*IPPV*), and the decelerating inspiratory flow with the PRVC-modes (PRVC 20 and PRVC 60)
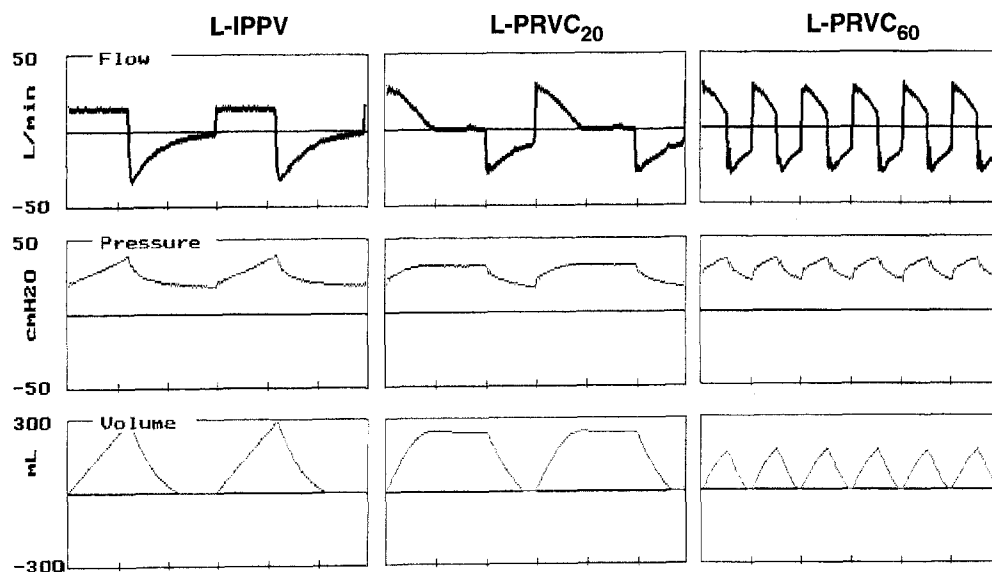
Table 1 Characteristics of different ventilatory patterns used

Modes	Inspiratory flow pattern	Working principle	I : E	Set PEEP	Set MPAW	Ventilatory rate	FIO$_2$
IPPV	Constant	Volume-controlled	1 : 1.5	8		20	1.0
L-IPPV$_{201:1.5}$	Constant	Volume-controlled	1 : 1.5		25	20	1.0
L-PRVC$_{202:1}$	Decelerating	Pressure-controlled	2 : 1		25	20	1.0
L-PRVC$_{201.5:1}$	Decelerating	Pressure-controlled	1.5 : 1			20	1.0
L-PRVC$_{601:1}$	Decelerating	Pressure-controlled	1 : 1		25	20	1.0
L-PRVC$_{601:1.5}$	Decelerating	Pressure-controlled	1 : 1.5			20	1.0

Lung morphology

In some piglets the morphology of the lungs were studied at the end of the experiment. These studies utilising light microscopy, transmission and scanning electron microscopy are presented elsewhere. In order to illustrate the topographical morphology of open and collapsed alveoli, two scanning electron micrographs are included.

Calculations and statistics

Calculations were made according to standard formulae, some of which have been described in detail in previous articles [6, 7]. Values are given as mean and standard deviation (SD). Differences between the different ventilatory settings were evaluated with a one-way analysis of variance (ANOVA) for repeated measures for all paired comparisons within each variable. If significant differences were detected, these differences were evaluated using Fisher's PLSD-test. Statistical significance is given as $p \leq 0.05$.

Results

Results are presented in Table 2, as well as in Figs. 1 and 2. Gas exchange (PaO$_2$ and PaCO$_2$) was the same for all modes whether applied pre-lavage or post-lavage. FRC was increased from 904 ± 131 ml pre-lavage to about 1200 ml in all post-lavage modes. Total PEEP was 19 cmH$_2$O with L-IPPV$_{201:1.5}$, 17 and 16 cmH$_2$O with L-PRVC$_{202:1}$ and L-PRVC$_{201.5:1}$ and 22 and 20 cmH$_2$O with L-PRVC$_{601:1}$ and L-PRVC$_{601:1.5}$. MPAW was 25 cmH$_2$O with L-IPPV$_{201:1.5}$, L-PRVC$_{202:1}$ and L-PRVC$_{601:1}$. It was reduced to 22 cmH$_2$O (L-PRVC$_{201.5:1}$) and 23 cmH$_2$O (L-PRVC$_{601:1.5}$) with reduced inspiratory times.

Tidal volumes were 12 ml/kg with L-IPPV$_{201:1.5}$, 10 ml/kg with the inverse ratio settings and 5 ml/kg with the rapid frequency settings. End-inspiratory lung volumes were 65 ml/kg with L-IPPV$_{201:1.5}$, 56 and 58 ml/kg with L-PRVC$_{202:1}$ and L-PRVC$_{201.5:1}$, respectively, and 50 ml/kg and 49 ml/kg with the rapid frequency settings.

End-inspiratory (occlusion) pressure was increased in all post-lavage modes compared with pre-lavage. It was

40 cmH$_2$O with L-IPPV$_{201:1.5}$, 32 and 29 cmH$_2$O with L-PRVC$_{202:1}$ and L-PRVC$_{201.5:1}$, and 35 and 31 cmH$_2$O with L-PRVC$_{601:1}$ and L-PRVC$_{601:1.5}$.

Serial deadspace was higher with L-IPPV$_{201:1.5}$ and both rapid frequency settings (115, 109 and 107 ml, respectively) compared with L-PRVC$_{202:1}$ and L-PRVC$_{201.5:1}$ (94 and 92 ml, respectively). Alveolar mixing efficiency displayed the same pattern: it was lower with L-IPPV$_{201:1.5}$ and both rapid frequency settings (76, 70 and 74%, respectively) compared with L-PRVC$_{202:1}$ and L-PRVC$_{201.5:1}$ (88 and 85%).

Oxygen delivery was reduced in all post-lavage settings compared to the pre-lavage level of 687 ml/min·m^2, except with L-PRVC$_{201.5:1}$. The latter settings displayed no statistically significant difference to pre-lavage, and also higher oxygen delivery than all other post-lavage modes.

Post-lavage intrathoracic blood volume was reduced in all settings by $3-4$ ml/kg (= 18%) compared to its pre-lavage level (23 ml/kg) – except with L-PRVC$_{201.5:1}$. Extravascular lung water increased from 7.2 ml/kg pre-lavage to about 19 ml/kg in all post-lavage settings.

Central venous pressure and pulmonary capillary wedge pressure (referenced to atmospheric pressure) were increased in all post-lavage settings.

Discussion

The open lung

One criterion for full alveolar recruitment in this model is whether PaO$_2$ has returned to pre-lavage level. In previous experiments we had seen [7] that at a mean airway pressure (MPAW) of 25 cmH$_2$O this criterion was fulfilled. This is also illustrated in the CT-scans in Fig. 3: The sequence represents 5 min time intervals from MPAW of 25 cmH$_2$O (open lung, left), to MPAW of 8 cmH$_2$O (extensive and widespread densities compatible with alveolar collapse, middle) and back again to the previous MPAW of 25 cmH$_2$O (re-opened lung with immediate restoration

Table 2 Results are given as mean ± SD. (* = significant at the 5% level; ANOVA: Fisher's PLSD test). The differences are given in numbers, i.e. "*1" means that the difference to the ventilatory pattern number 1 (IPPV) was found to be significant

|	[1] IPPV	[2] L-IPPV	[3] L-PRVC	[4] L-PRVC	[5] L-PRVC	[6] L-PRVC
Respiratory rate [bpm]	20	20	20	20	60	60
Inspiratory flow pattern	Constant	Constant	Decelerating	Decelerating	Decelerating	Decelerating
Inspir. time [s]	1.2	1.2	2	1.8	0.5	0.4
I:E ratio	1:1.5	1:1.5	2:1	1.5:1	1:1	1:1.5
Mean airway pressure [cmH$_2$O]	12±1	25±0.5 *1	25±1 *1	22±1 *1, *2, *3	25±1 *1, *4	23±1 *1, *2, *5
Peak inspiratory pressure [cmH$_2$O]	25±5	46±5 *1	33±2 *1, *2	30±2 *1, *2	37±2 *1, *2, *3, *4	36±2 *1, *2, *4
End-inspiratory pressure [cmH$_2$O]	20±3	40±6 *1	32±2 *1, *2	29±2 *1, *2, *3	35±2 *1, *2, *3, *4	31±1 *1, *2, *4
Total PEEP [cmH$_2$O]	8±1	19±1 *1	17±1 *1, *2	16±2 *1, **2, **3	22±2 *1, *2, *3, *4	20±1 *1, *3, *5
Intrinsic PEEP [cmH$_2$O]	0	0	4±2 *1, *2	2±1 *1, *2, *3	6±2 *1, *2, *3, *4	4±2 *1, *3, *5
Minute ventilation [l/min]	4.7±0.7	5.7±0.8 *1	4.9±0.8 *2	4.9±0.8 *2	7.7±0.8 *1, *2, *3, *4	7.7±0.8 *1, *2, *3, *4
Tidal volume [ml/kg]	10±1	12±2 *1	10±2 *2	10±1 *2	5±0.5 *1, *2, *3, *4	5±0.5 *1, *2, *3, *4
Functional residual capacity [ml]	904±131	1254±166 *1	1166±188 *1	1203±266 *1	1231±157 *1	1226±157 *1
End-inspiratory lung volume [ml/kg]	46±4	65±10 *1	56±7 *1, *2	58±12 *2	50±10 *2, *3, *4	49±7 *2, *3, *4
Complicance [ml/cmH$_2$O]	20±4	12±2 *1	16±1 **1, **2	18±2 *1, **2	10±1 *1, *2, *3, *4	11±2 *1, *3, *4
Serial deadspace [ml]	88±8	115±10 *1	94±7 *1, *2	92±4 *2	109±10 *1, *2, *3, *4	108±6 *1, *2, *3, *4
Alveolar mixing efficiency [%]	89±14	76±24 *1	88±10	85±13	70±19 *1, *3, *4	74±17 *1, *3
PaO$_2$ [kPa]	78±5	73±6	74±8	75±7	77±5	73±9
PaCO$_2$ [kPa]	5±0.2	5±0.3	5±0.2	5±0.4	5±0.1	5±0.4
SaO$_2$ [%]	100	100	100	100	100	100
MAP [mmHg]	106±19	106±16	110±14	116±15	110±16	113±16
CVP [mmHg]	8±2	12±2 *1	12±2 *1	12±2 *1	12±2 *1	12±2 *1
PCWP [mmHg]	12±2	17±2 *1	16±3 *1	16±3 *1	17±2 *1	16±2 *1
PAP [mmHg]	24±5	36±6 *1	34±5 *1	35±4 *1	37±6 *1	37±6 *1
SvO$_2$ [%]	78±8	66±10 *1	66±7 *1	72±5	66±8 *1	69±7 *1
Qs/Qt [%]	8±1	10±1 *1	10±1 *1	9±1 *1	9±1 *1	10±1 *1
Stroke index [ml/m^2]	45±8	38±9 *1	39±9 *1	43±9 *2	36±7 *1, *4	38±8 *1
Cardiac index [l/min·m^2]	5.7±1.3	4.5±0.7 *1	4.6±0.9 *1	5.2±0.9 *2, *3	4.2±0.9 *1, *4	4.5±0.9 *1, 4
Right ventricular end-diastolic volume [ml/m^2]	102±25	100±31	92±41	91±29	94±31	90±37
O$_2$ delivery [ml/min·m^2]	687±161	558±106 *1	562±106 *1	657±131 *2, *3	524±110 **1, *4	566±104 *1, *4
Intrathoracic blood volume [ml/kg]	23±4	20±3 *1	20±3 *1	21±4 *2, *3	19±3 *1, *4	20±4 *1, *4
Extravascular lung water [ml/kg]	7±1	20±4 *1	20±4 *1	19±3 *1	19±3 *1	18±3 *1
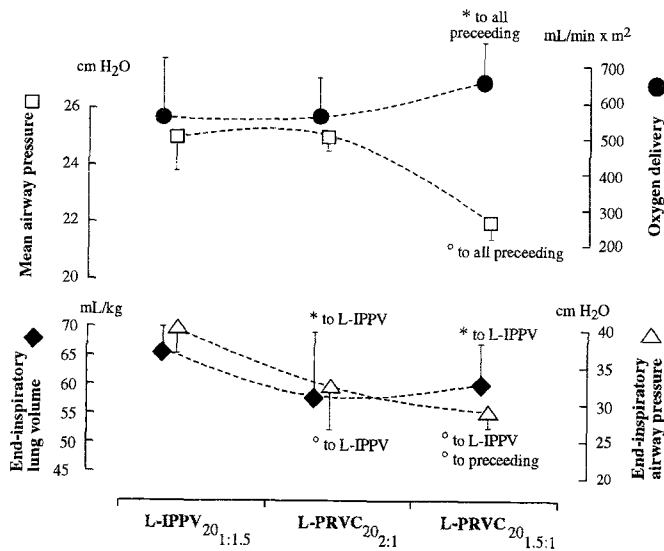
Fig. 2 *Top:* Oxygen delivery and mean airway pressure. *Bottom:* End-inspiratory lung volume and end-inspiratory airway pressure with one volume-controlled (L-$IPPV_{201:1.5}$), and with two pressure-controlled (L-$PVRC_{202:1}$ and L-$PRVC_{201.5:1}$) patterns. *Note:* Improved oxygen delivery was achieved with reduced mean airway pressure when inspiratory time was reduced in the pressure-controlled patterns. End-inspiratory lung volumes, as well as end-inspiratory airway pressures, were lower in both pressure-controlled patterns compared with the volume-controlled pattern ($n = 15$ piglets)

Our results also provide evidence that the open lung condition is not adequately described by the level of pulmonary gas exchange in terms of PaO_2. Post-lavage there was reduced compliance together with 30% increased FRC in all modes. L-$IPPV_{201:1.5}$ and the two rapid frequency settings indicated incomplete recruitment despite higher PEEP levels compared with the low frequency PRVC-settings. The incomplete recruitment in the former settings − compared with L-$PRVC_{202:1}$ and L-$PRVC_{201.5:1}$ − can also be derived from their higher serial deadspace [19], indicating increased volume of conducting airways with comparatively less recruitment of gas exchanging surface. In addition, lower alveolar mixing efficiency [19] in the same modes indicated an increased scatter of regional specific ventilation (regional ventilation/regional lung volume) between different lung compartments. As gas exchange was not impaired in these settings − despite assumed incomplete recruitment − the open lung condition had to fullfil additional criteria.

Another criterion of the open lung could then be the volume of the pulmonary vascular bed matching the alveolar gas volumes: Except with L-$PRVC_{201.5:1}$ hemodynamic performance was depressed in all settings compared to pre-lavage. The depressant effect was mainly, although not exclusively, related to the level of MPAW. With L-$PRVC_{201.5:1}$ a MPAW of 22 cmH_2O produced an oxygen delivery of 657 ml/min·m^2, while in L-$PRVC_{601:1.5}$ the same level of MPAW produced a significantly lower oxygen delivery (566 ml/min·m^2). We speculate that − beside its absolute level [20−27] − the par-

of normal aeration, right). Morphology (Fig. 4) demonstrated unaffected lung structure with MPAW of 25 cmH_2O (Fig. 4a), while partially collapsed alveoli can be seen with MPAW of 8 cmH_2O (Fig. 4b). In 5 animals we could determine the inflection point in the inspiratory limb of the static PV-loop of the respiratory system [17]. We found an inflection point at approximately 20 cmH_2O. We therefore assume MPAW of 25 cmH_2O to be well above the inflection point in these piglets, in some cases even high enough to produce alveolar overdistension and pronounced hemodynamic depression. This could have been avoided by an individual adaptation of the MPAW to the actual inflection point.

Fig. 3 Computed tomography (CT) scans of the chest during "Pause hold − Exp." of the Servo Ventilator 300 in one of the piglets. The time sequence between the different settings is 5 min. Mean airway pressure 25 cm H_2O, open lung (*left*): Note normal aeration of the lung parenchyma with dependent densities representing pleural effusion; fluid is also present in interlobar and segmental fissures. Mean airway pressure 8 cm H_2O (*center*): Note extensive and widespread densities compatible with reduced aeration ("alveolar collapse") and probably some alveolar edema. Mean airway pressure 25 cm H_2O, re-opened lung (*right*): Note the almost immediate restoration of aeration of the lung parenchyma
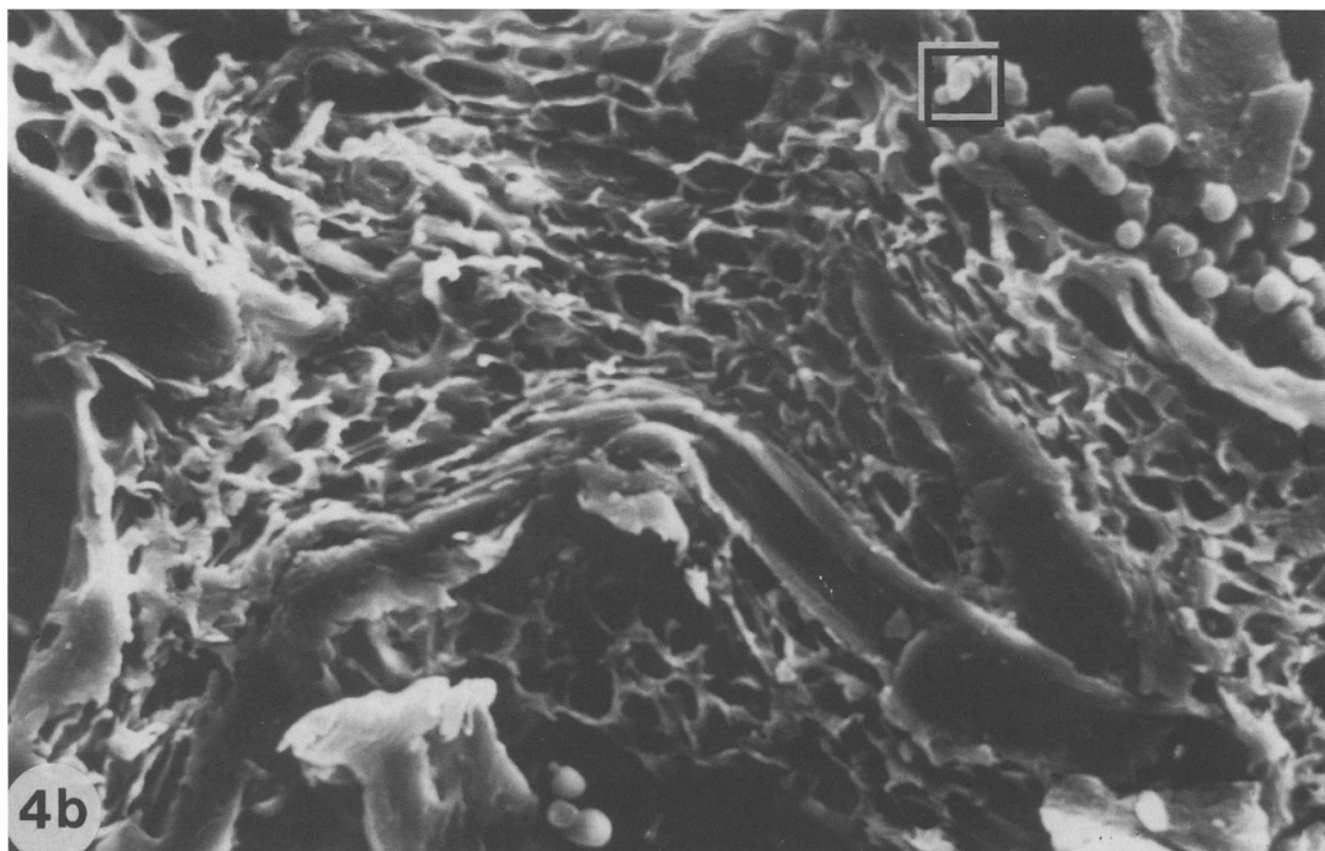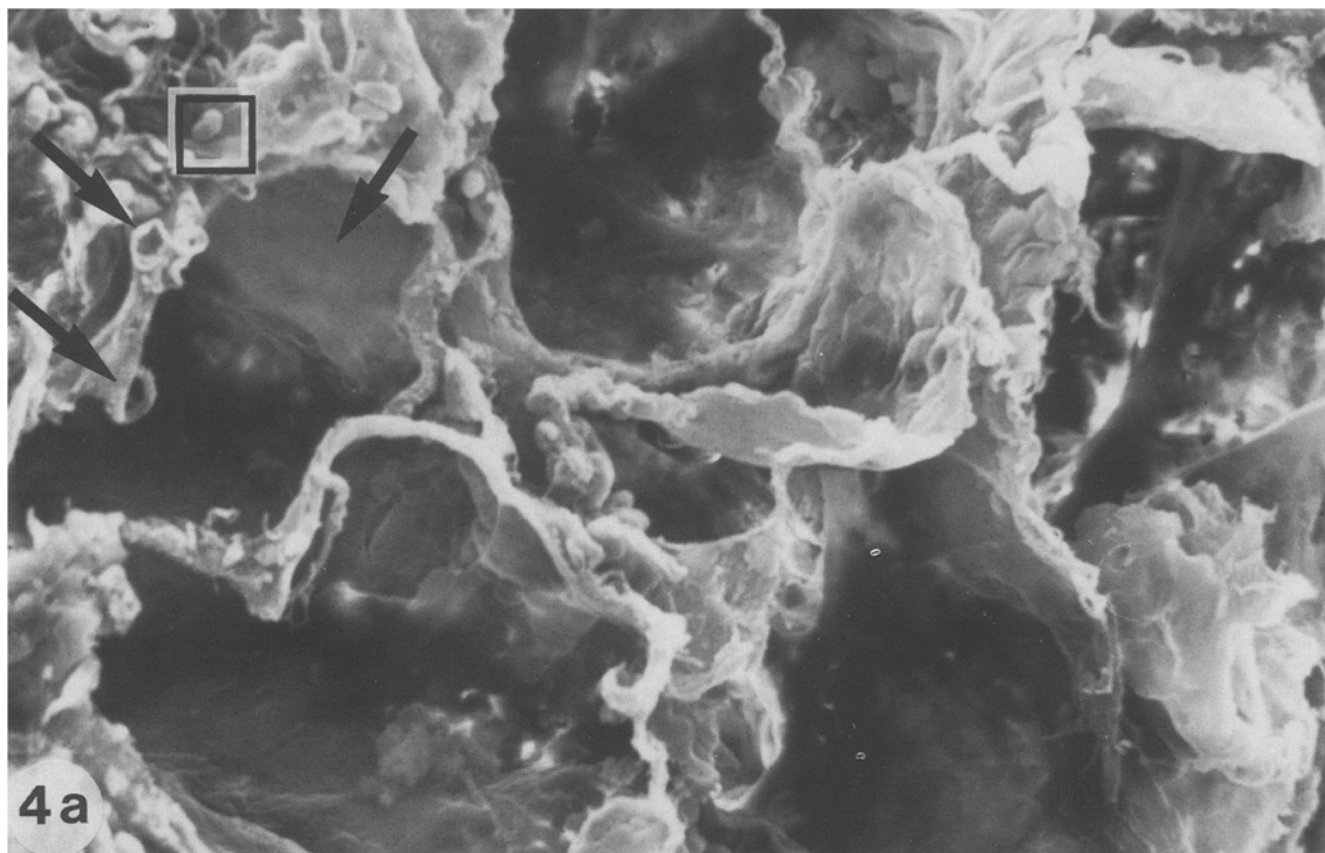
4a

4b
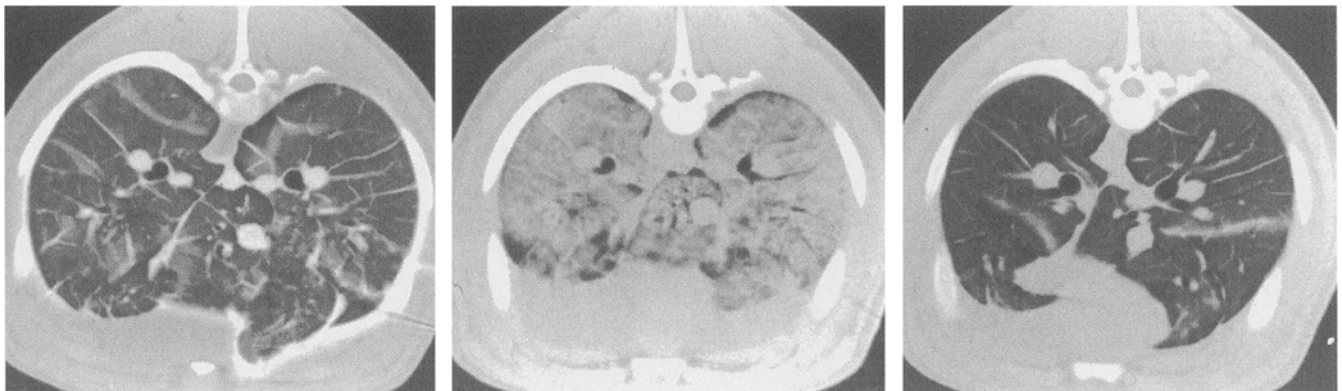
Fig. 4 a *Open alveoli:* A scanning electron micrograph of open alveoli approximately, 6 h after induced pulmonary insufficiency by broncho-alveolar lavage and ventilation with mean airway pressure 25 cm H_2O. During ventilation the animal was first trans-cardially perfused with saline, for exsanguination, and then, with a mixture of form- and glutaraldehyde, for fixation. Type I epithelial cells are seen with their typical smooth surface covering the interior wall of the alveoli (*single arrow*), which indicates intact morphology. In the left wall of the alveolus located in the left, upper portion of the micrograph, two small vessels are seen (*dual arrows*). Inside the *black/white box* (*left upper portion* of the micrograph) there is a red blood cell of the same size as shown in Fig. 4b. Magnification 550X.

b *Collapsed alveoli:* A scanning micrograph of partly collapsed alveoli approximately 6 h after induced pulmonary insufficiency by broncho-alveolar lavage and ventilation with mean airway pressure 8 cm H_2O. Inside the *black/white box* (*right upper portion* of the micrograph) there is a red blood cell of the same size as shown in Fig. 4a. Magnification 550X

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ticular way in which MPAW is achieved might modulate its influence on cardiac performance. This is illustrated in L-PRVC$_{201.5:1}$ in which the reduction of inspiratory time reduced MPAW but also produced a significantly increased oxygen delivery without any impairment in pulmonary gas exchange compared to the pre-lavage and all other post-lavage settings.

The decrease of cardiac index was mainly due to preload reduction. This can be deduced from the decreased intrathoracic blood volume (ITBV); [28] in all modes, except with the pressure-controlled low frequency mode with reduced inspiratory time. Despite reduced preload, the end-diastolic volume of the right ventricle remained on pre-lavage level in all modes, which indicates an increase in right ventricular afterload compensated by increased filling. We cannot therefore rule out the possibility that lung volumes above the level necessary to splint the lung open were responsible for the increased right ventricular afterload. Adding the criterion of vascular recruitment matched to alveolar recruitment, we have to consider that only L-PRVC$_{201.5:1}$ kept the surfactant deficient lungs open.

Airway pressures, lung volumes, and related risk of barotrauma

This issue has been addressed from various aspects and in many previous studies [29–31]. End-inspiratory (occlusion) airway pressure as well as end-inspiratory lung volume are assumed to reliably indicate peak alveolar pressure and alveolar volume [33]. Hence they are helpful in monitoring the risk of barotrauma and volutrauma [34] associated with the use of different ventilatory patterns.

For the same level of $PaCO_2$ end-inspiratory airway pressures and end-inspiratory lung volumes were highest with the volume-controlled pattern L-IPPV$_{201:1.5}$. This pattern imposed the highest risk of barotrauma. With the

rapid frequency modes end-inspiratory airway pressures and end-inspiratory lung volumes were considerably reduced. Reduced compliance and alveolar mixing efficiency, together with increased minute volume and dead space – as well as depressed cardiac performance – indicated that these patterns did not obtain open lung conditions. We therefore assume that, despite low end-inspiratory airway pressures and end-inspiratory lung volumes the risk for barotrauma was not reduced in the rapid frequency patterns.

Both, reduced end-inspiratory airway pressures and end-inspiratory lung volumes indicated reduced risk of barotrauma with pressure-controlled inverse ratio ventilation compared with the other post-lavage modalities. We cannot explain why end-inspiratory lung volume did not decrease with L-PRVC$_{201.5:1}$, while airway pressures where reduced compared with L-PRVC$_{202:1}$. It could be related to the problem that the inspiration hold time, and/or the expiration hold time, might have been to short to achieve true no-flow conditions in all animals. This would render incorrect pressure readings, at least in some instances.

Pressure-regulated volume-controlled (PRVC) mode

Marcy and Marini [32] – in a paper discussing the implementation of inverse ratio ventilation (IRV) – compare two general methods to administer IRV, i.e. pressure-controlled ventilation with a long inspiratory time, and volume-cycled ventilation with either an end-inspiratory pause, or with a slow, or decelerating, inspiratory flow. They point to the fact, that – with any pressure-limited mode of ventilation – the volume actually delivered varies with both respiratory system compliance and resistance. Furthermore, the ventilatory volume depends on the intrinsic PEEP created. On the other hand, as with any volume-controlled ventilation mode, end-inspiratory airway pressures (and hence peak alveolar pressures) can vary with changes in ventilator mechanics, frequency and flow settings. Thus the tidal/minute volumes may inadvertently exceed the desired level. Both ventilatory approaches – the volume-controlled, as well as the pressure-controlled method for implementing inverse ratio ventilation – have their advantages and disadvantages. By using the pressure-regulated volume-controlled (PRVC) modality of the Servo Ventilator 300, we could control both end-inspiratory pressures and delivered volumes.

In summary, we conclude that in the surfactant deficient piglet pressure-regulated volume-controlled ventilation (PRVC) with I : E ratio up to 2 : 1 produces better oxygen delivery at reduced risk of barotrauma compared to volume-controlled ventilation at the same level of MPAW. By reducing I : E ratio to 1.5 : 1 with PRVC – without interfering with gas exchange – oxygen delivery further improves at reduced airway pressures.

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