Intensive Care Med (2000) 26: 501–507

ORIGINAL

G. Foti
M. Cereda
M. E. Sparacino
L. De Marchi
F. Villa
A. Pesenti

Effects of periodic lung recruitment maneuvers on gas exchange and respiratory mechanics in mechanically ventilated acute respiratory distress syndrome (ARDS) patients

Received: 31 May 1999
Final revision received: 19 October 1999
Accepted: 10 December 1999

This study was supported by departmental funds

A. Pesenti (✉) · G. Foti · M. Cereda · M. E. Sparacino · L. De Marchi · F. Villa
Department of Anesthesia and Intensive Care, Nuovo Ospedale S. Gerardo dei Tintori, via Donizetti 106, Monza, University of Milan, Milan 20052, Italy
e-mail: antonio.pesenti@unimib.it
Tel.: + 39-039-233290/233366
Fax: + 39-039-233297

Abstract *Objective:* We wished to investigate whether volume recruitment maneuvers (VRMs) could improve alveolar recruitment and oxygenation in acute respiratory distress syndrome (ARDS) patients, ventilated at relatively low positive end-expiratory pressure (PEEP).
Setting: General intensive care unit (ICU) located in a teaching hospital.
Patients: 15 PEEP responder ARDS patients undergoing continuous positive pressure ventilation (CPPV) with sedation and muscle paralysis.
Interventions: We identified a low (9.4 ± 3 cmH_2O) and a high (16.0 ± 2 cmH_2O) level of PEEP associated with target oxygenation values. Using a custom modified mechanical ventilator, we applied in random order three steps lasting 30 min: (1) CPPV at the low PEEP level (*CPPV LO*); (2) CPPV at the high PEEP level (*CPPV HI*); (3) CPPV at low PEEP with the superimposition of periodic VRMs (*CPPV VRM*). VRMs were performed twice a minute by increasing PEEP to the high level for two breaths. Each brace of two breaths was spaced 30 seconds from the preceding one.
Measurements and results: We measured gas exchange, hemodynamics, respiratory mechanics, and the end expiratory lung volume (EELV). Compared to CPPVLO, CPPVVRM resulted in higher PaO_2 (117.9 ± 40.6 vs 79.4 ± 13.6 mmHg, $P < 0.01$) and EELV (1.50 ± 0.62 vs 1.26 ± 0.50 l, $P < 0.05$), and in lower venous admixture (Q_{VA}/Q_T) (0.42 ± 0.07 vs 0.48 ± 0.07, $P < 0.01$). During CPPVHI, we observed significantly higher PaO_2 (139.3 ± 32.5 mmHg) and lower Q_{VA}/Q_T (0.37 ± 0.08) compared to CPPVLO ($P < 0.01$) and to CPPVVRM ($P < 0.05$).
Conclusions: VRMs can improve oxygenation and alveolar recruitment during CPPV at relatively low PEEP, but are relatively less effective than a continuous high PEEP level.

Key words Positive end-expiratory pressure · Mechanical ventilation · Barotrauma prevention · Alveolar recruitment · Acute respiratory distress syndrome (ARDS)

Introduction

Current suggestions for the management of acute respiratory distress syndrome (ARDS) patients propose limiting peak alveolar pressures to levels suggested as safe [1] while optimizing alveolar recruitment [2]. Pulmonary overdistension may result indeed in lung damage [3, 4], while unstable alveolar patency may lead to parenchymal lesions [5]. The use of low tidal volumes (V_T) and of relatively high positive end-expiratory pressure (PEEP) levels has therefore been proposed, while supra-normal levels of $PaCO_2$ are tolerated [6]. High PEEP acts in stabilizing alveolar recruitment and preventing the loss of lung volumes and compliance ob-

Table 1 Patient Population Characteristics. (*LIS,* lung injury score; *RR,* respiratory rate; *PEEP,* positive end expiratory pressure)

Pts	Diagnosis	Days from intubation	age (yrs)	Weight (kg)	LIS	PaO_2/FiO_2 (mm Hg)	RR (bpm)	PEEP (cm H_2O)
1	Neurogenic Pulmonary Edema	2	21	75	2.5	80	19	15
2	Pneumonia	4	22	90	3.5	91	13	19
3	Sepsis	1	63	60	2.5	85	11	10
4	Gastric inhalation	23	26	55	3.5	131	22	15
5	Trauma	6	19	80	2.75	169	10	13
6	Sepsis	9	28	55	3.25	125	14	14
7	Pneumonia	2	43	80	3.2	73	17	14
8	Sepsis	7	24	55	3.5	172	17	12
9	Pneumonia	3	34	83	3	133	17	12
10	Pneumonia	3	68	100	2.75	105	15	8
11	Pneumonia	3	37	79	3	190	15	12
12	Pneumonia	7	20	85	3	149	10	10
13	Gastric inhalation	7	51	70	3.5	80	20	15
14	Pneumonia	2	33	60	3	163	15	14
15	Sepsis	7	48	100	3.5	114	12	16
Mean		5.7	35.8	76	3.1	124	15.1	13.3
SD		5.4	15.7	16	0.4	38	3.6	2.7

served when a low V_T is used [7, 8]. This "lung protective" strategy has been reported to improve the outcome of ARDS patients [9]. However, elevated levels of PEEP can have harmful effects, such as hemodynamic impairment and decreased renal function [10]. Moreover, high PEEP may lead to dangerously high end-inspiratory airway pressures, implying an increased risk of barotrauma.

Lung opening maneuvers, such as deep breaths or sighs, are known to restore compliance and oxygenation in anesthetized subjects ventilated with low V_T [11]. In a recent study, sighs optimized oxygenation and alveolar recruitment in ARDS patients, when applied during "lung protective" ventilatory strategy [12]. Similar maneuvers could also be used as an alternative to high PEEP to increase lung recruitment in low V_T ventilated patients with ARDS.

We designed a ventilatory strategy that adds volume recruitment maneuvers (VRMs) to continuous positive pressure ventilation (CPPV). VRMs are periodically administered and consist of temporary increases of PEEP at constant V_T. The higher level of PEEP is maintained for two ventilatory cycles. In a population of selected ARDS patients, we tested the hypothesis that CPPV at relatively low PEEP, when complemented by VRMs, could result in improved alveolar recruitment and oxygenation.

Methods

Patients

We enrolled 15 patients with ARDS [13] according to the following criteria: (1) lung injury score [14] of at least 2.5; (2) no active air leak; (3) no history of chronic obstructive pulmonary disease; (4) no bronchospasm; (5) a significant oxygenation response to a PEEP increase trial (see below). At the time of enrollment, all patients were undergoing CPPV and were sedated with continuous infusions of fentanyl, propofol, or a combination of these drugs, while paralysis was maintained by pancuronium bromide in boluses. All patients already had an arterial and a pulmonary artery catheter in place. Relevant demographic and clinical data of the patient population are described in Table 1. On the day of the study, patients were ventilated at an FIO_2 of 0.89 ± 0.13 and with a V_T of 591 ± 153 ml (7.9 ± 1.8 ml/kg of body weight). Suctioning of tracheal secretions was performed when clinically indicated.

PEEP trial. Keeping all other ventilatory settings unchanged, we set PEEP to obtain a capillary oxygen saturation of approximately 90%, monitored by pulse oximetry. This level of PEEP ($PEEP_{LO}$) was noted and arterial blood gases were analyzed. We then increased PEEP, in steps of 2–3 cmH_2O maintained for about 15 min each, up to a maximum of 20 cmH_2O to identify a level ($PEEP_{HI}$) resulting in a PaO_2 increase of at least 30% of the value at $PEEP_{LO}$. Patients reaching this goal were declared PEEP responders and included in the study. The values of both $PEEP_{LO}$ and $PEEP_{HI}$ were adopted during the subsequent study protocol.

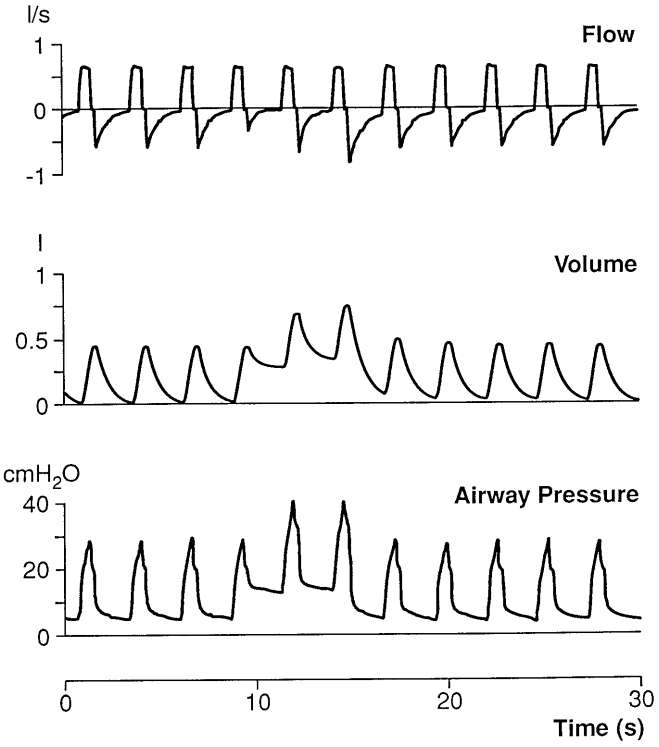

Fig. 1 Original recordings of flow, volume, and airway pressure during performance of a volume recruitment maneuver (VRM). VRM is obtained by transiently increasing PEEP from the baseline level for the duration of two ventilatory cycles. Tidal volume, respiratory rate, and inspiratory time are not modified during VRMs

Protocol

The protocol was approved by the local ethical committee, and informed consent was obtained from the patient's next of kin. The investigation was conducted according to the "Helsinki Declaration". After enrollment, the patients were connected to an EVA ventilator (Dräger, Lübeck, Germany) modified to perform periodic VRMs (see below). The ventilator was set in volume controlled mode delivered through square wave flow profile with V_T, respiratory rate (RR), FIO_2, inspiratory flow, and inspiratory time (T_I) as previously selected by the attending physician. These settings were kept unchanged during the whole experiment. The study consisted of three 30 min experimental periods in each patient, applied in random order: (1) CPPV at constant PEEP set at $PEEP_{LO}$ ($CPPV_{LO}$); (2) CPPV at constant PEEP set at $PEEP_{HI}$ ($CPPV_{HI}$); (3) CPPV at $PEEP_{LO}$ with the adjunct of VRMs ($CPPV_{VRM}$).

Volume recruitment maneuvers

VRMs were effected by periodic increases of PEEP. When a special button is pressed, the EVA ventilator increases PEEP from the baseline level to the level set by the "intermittent PEEP/ASB" knob (Dräger EVA manual) for the duration of two consecutive ventilatory cycles. During $CPPV_{VRM}$, this level of PEEP was set at $PEEP_{HI}$. V_T, RR, inspiratory flow, and T_I were unchanged during the performance of VRMs. An increase in peak inspiratory pressure and volume is therefore obtained (Fig. 1). Using an external controller provided by Dräger, we could deliver VRMs at a preselected frequency of 2 per minute.

Physiologic measurements

Gas exchange and hemodynamics

We took all measurements at the end of each 30 min experimental period. We collected arterial and mixed venous blood samples for the measurement of PO_2, PCO_2, pH, hemoglobin concentration, and saturation (HbO_2). We measured mean systemic arterial pressure (MAP), mean pulmonary artery pressure (PAP), central venous pressure (CVP), pulmonary artery wedge pressure (WP), and cardiac output (CO). CO was measured in triplicate by the thermodilution technique injecting 10 ml of 5% dextrose at room temperature. Venous admixture (Q_{VA}/Q_T) and oxygen delivery were obtained using standard formulas [15]. During $CPPV_{VRM}$, we took care to draw the blood samples slowly over a period of 30 s, thus including one VRM and a period of ventilation at $PEEP_{LO}$. All hemodynamic parameters were measured in the time between two subsequent VRMs.

Expired gas was collected for 2 min using a 40 l airtight bag connected to the expiratory outlet of the ventilator. The fraction of mixed expired CO_2 was measured by a Normocap capnometer (Datex, Helsinki, Finland) and the physiologic dead space volume to tidal volume ratio (V_D/V_T) was computed using Enghoff's modification of Bohr's equation [15]. Ventilatory circuit dead space and compressible volume were minimized and resulted in 25 ml and 1.9 ml/cmH_2O, respectively.

Respiratory mechanics

We measured airway pressure and flow using a Bicore CP100 pulmonary monitor (Bicore Monitoring Systems, Irvine, Calif.). The flow transducer was inserted between the Y piece of the ventilator circuit and the proximal end of the endotracheal tube. The digital output of the pulmonary monitor was connected to a personal computer. One 6 min set of airway pressure and flow signals, sampled at 50 Hz, was recorded on the computer memory for subsequent offline analysis. During recording, we performed 3 end-inspiratory airway occlusions using the hold button of the ventilator, and 3 end-expiratory airway occlusions acting on a manual valve inserted in the ventilator circuit. Airway occlusions lasted at least 3 s. During $CPPV_{VRM}$, airway occlusions were performed at the end of the $PEEP_{LO}$ period between two consecutive VRMs.

We then analyzed the recorded tracings using a dedicated software (Computo, Elekton, Agliano Terme, Italy), obtaining RR, V_T by integration of the flow signal, and minute ventilation (V_E) as V_T*RR. Mean airway pressure (Paw) was measured as the average of the airway pressure signal during a 60 s period containing no occluded breaths. From the analysis of occluded breaths, we obtained: peak inspiratory airway pressure (PIP), end-inspiratory elastic recoil pressure (Pel,i), end-expiratory elastic recoil pressure (Pel,e), and the inspiratory flow at the time of occlusion (V'I). We computed the compliance of the respiratory system (Crs) as $Crs = V_T/(Pel,i–Pel,e)$, the total inspiratory resistance of the respiratory system (Rtot) as $Rtot = (PIP–Pel,i)/V'I$, and intrinsic PEEP (PEEPi) as $PEEPi = Pel,e–PEEP$ [16]. In the recordings obtained during $CPPV_{VRM}$, data were obtained by the analysis of the breaths at $PEEP_{LO}$. Additionally, we obtained PEEP ($PEEP_{VRM}$) and PIP (PIP_{VRM}) reached during VRM breaths. We used the mean value of three breaths for each ventilatory and respiratory mechanics variable.

Table 2 Gas Exchange Data. Values are mean ± SD. (*pHa,* arterial blood pH; *HbO_2a*, arterial blood oxygen saturation; *HbO_2v,* mixed venous blood oxygen saturation; *Q_{VA}/Q_T*, venous admixture; *V_D/V_T*, physiologic dead space to tidal volume ratio)

	CPPV$_{LO}$	*CPPV$_{HI}$*	*CPPV$_{VRM}$*
PaO_2 (mm Hg)	79.4 ± 13.6	139.3 ± 32.5[a]	117.9 ± 40.6[ab]
$PaCO_2$ (mm Hg)	58.8 ± 12.3	58.4 ± 12.4	57.5 ± 13.1
pHa	7.36 ± 0.07	7.36 ± 0.07	7.35 ± 0.07
HbO_2a (%)	91.5 ± 3.6	95.6 ± 1.2[a]	94.3 ± 2.6[ab]
HbO_2v (%)	71.5 ± 7.8	76.9 ± 8.0[c]	74.7 ± 7.1
Q_{VA}/Q_T	0.48 ± 0.7	0.37 ± 0.8[a]	0.42 ± 0.7[ab]
V_D/V_T	0.56 ± 0.11	0.55 ± 0.10	0.53 ± 0.11

[a] $p < 0.01$ vs (*CPPV$_{LO}$*); [b] $p < 0.05$ vs (*CPPV$_{HI}$*); [c] $p < 0.05$ vs (*CPPV$_{LO}$*)

Lung volumes and alveolar recruitment

To evaluate the effects of VRMs on lung volumes, we measured the functional residual capacity (FRC) and the end-expiratory lung volume (EELV). EELV is the total lung gas volume at end expiration when PEEP is applied and was obtained as the sum of FRC and the volume exhaled (Vex) following PEEP withdrawal [17]. Therefore, we abruptly released PEEP at the end of an expiration and measured Vex by the pneumotachograph. Then, we disconnected the patient from the ventilator and measured FRC by a simplified closed circuit Helium dilution technique [17]. During CPPVVRM, measurement of FRC and of EELV was performed immediately following the last or the second last breath preceding VRMs.

Statistical analysis

Values are expressed as mean ± SD. Data obtained during the 3 steps were compared using two-way ANOVA. When a statistically significant effect was detected, post hoc comparisons were performed using the Newman-Keuls method to identify significant differences between pairs of single steps [18]. For all comparisons, a *P* level lower than 0.05 was considered significant.

Results

Gas exchange

Gas exchange data are shown in Table 2. CPPVVRM resulted in significantly higher PaO_2 and HbO_2a, compared to CPPVLO. During CPPVVRM, we also observed significantly lower Q_{VA}/Q_T values than during CPPVLO. We found no significant differences between CPPVLO and CPPVVRM in $PaCO_2$, V_D/V_T and pHa. During CPPVHI, PaO_2 and HbO_2a significantly increased, while Q_{VA}/Q_T significantly decreased, compared to CPPVLO. CPPVHI resulted in higher PaO_2 and HbO_2a, and also in lower Q_{VA}/Q_T when compared to CPPVVRM. Compared to the other two steps, CPPVHI showed no significant difference in $PaCO_2$, V_D/V_T, and pHa.

Table 3 Respiratory Mechanics and Lung Volumes Data. Values are mean ± SD. (*PIP,* peak inspiratory airway pressure; *Pel,i,* end inspiratory elastic recoil pressure; *Paw,* mean airway pressure; *Crs,* compliance of the respiratory system; *Rtot,* total resistance of the respiratory system; *FRC,* functional residual capacity; *EELV,* end-expiratory lung volume). *PIP* and *Pel,i* during *CPPV$_{VRM}$* refer to those measured at end inspiration of tidal volumes starting from PEEPLO

	CPPV$_{LO}$	*CPPV$_{HI}$*	*CPPV$_{VRM}$*
PIP (cmH_2O)	35.9 ± 5.6	44 ± 4.6[a]	35.5 ± 5.4[d]
Pel,i (cmH_2O)	25.4 ± 7.0	35.0 ± 5.7[a]	24.8 ± 6.4[d]
PEEP (cmH_2O)	9.4 ± 3	16.0 ± 2[a]	9.4 ± 3.0[d]
Paw (cmH_2O)	17.4 ± 4.2	24.3 ± 3.1[a]	19.1 ± 3.9[ad]
Crs (ml/cmH_2O)	33.7 ± 9.4	30.3 ± 6.9[c]	35.7 ± 10.4[d]
Rtot (cmH_2O/l/s)	12.9 ± 2.1	13.5 ± 3.3	13.4 ± 2.4
FRC (l)	0.78 ± 0.33	1.01 ± 0.54[a]	0.92 ± 0.43[c]
EELV (l)	1.26 ± 0.50	1.92 ± 0.83[a]	1.50 ± 0.62[cd]

[a] $p < 0.01$ vs (*CPPV$_{LO}$*); [b] $p < 0.05$ vs (*CPPV$_{HI}$*); [c] $p < 0.05$ vs (*CPPV$_{LO}$*); [d] $p < 0.01$ vs (*CPPV$_{HI}$*)

Respiratory mechanics and ventilatory variables

Ventilatory variables and respiratory mechanics data are shown in Table 3. During the CPPVVRM step, values of PIP and Pel,i measured at PEEPLO were not significantly different from CPPVLO. Paw was slightly but significantly higher during CPPVVRM than during CPPVLO. Compared to CPPVHI, we observed significantly lower PIP, Pel,i, and Paw in both the CPPVVRM and the CPPVLO steps. We did not observe any significant intrinsic PEEP in any of our patients.

During the delivery of VRMs, an average PEEPVRM level of 16.2 ± 1.9 cmH_2O was applied while PIPVRM reached a mean value of 44.5 ± 6.2 cmH_2O. PEEPVRM and PIPVRM did not differ significantly from the values of PEEP and PIP observed during the CPPVHI step.

During CPPVHI, Crs was significantly lower than during both the CPPVVRM and the CPPVLO step. No significant difference in Crs was detected between CPPVVRM and CPPVLO.

Lung volumes

During CPPVVRM, we observed higher lung volumes than during CPPVLO. In fact, FRC and EELV were both significantly higher during the former step. CPPVVRM resulted in an average EELV increase of 0.24 ± 0.20 l from the value observed during CPPVLO. Also during CPPVHI, FRC and EELV were higher than during CPPVLO.

Hemodynamics data are summarized in Table 4; no significant changes were observed among the three ventilatory modalities.

Table 4 Hemodynamics Data. Values are mean ± SD. (*CO,* cardiac output; *MAP,* mean systemic arterial pressure; *PAP,* mean pulmonary artery pressure, *CVP,* central venous pressure; *WP,* wedge pressure, *DO2,* oxygen delivery)

	CPPV$_{LO}$	*CPPV$_{HI}$*	*CPPV$_{VRM}$*
CO (l/min)	10.2 ± 3.3	9.6 ± 3.4	10 ± 3.5
MAP (mm Hg)	76.6 ± 10.8	78 ± 11	77.3 ± 6.5
PAP (mm Hg)	28.5 ± 5.5	29.5 ± 4.9	28.1 ± 5.8
CVP (mm Hg)	10.4 ± 3.7	11.8 ± 3.2	10.8 ± 3.3
WP (mm Hg)	13.3 ± 6.2	14.8 ± 4.9	14.2 ± 4.9
DO2 (ml/min)	120 ± 43	120 ± 46	123.1 ± 46

Discussion

We applied CPPV$_{VRM}$ in PEEP responder patients with ARDS and obtained significantly improved oxygenation and alveolar recruitment compared to CPPV$_{LO}$. Even though it did not reach the efficacy on oxygenation of CPPV$_{HI}$, CPPV$_{VRM}$ allowed the use of a lower Paw and time-limited the exposure to high peak inflation pressures.

Effects of VRMs on gas exchange and lung volumes

CPPV$_{VRM}$ effectively improved oxygenation, compared to CPPV$_{LO}$. The improvement in oxygenation was accompanied by an increase in FRC and EELV. EELV was obtained at the same end-expiratory airway pressure level during the CPPV$_{VRM}$ and the CPPV$_{LO}$ steps. Therefore, the higher EELV values observed during CPPV$_{VRM}$ are probably due to recruitment of collapsed alveoli [19]. The higher FRC measured at the end of this step suggests that part of the alveoli recruited by VRMs were still open after PEEP withdrawal and disconnection from the ventilator.

Paw was higher during CPPV$_{VRM}$ than during CPPV$_{LO}$ and it could be argued that this difference could account for the observed increases in oxygenation and lung volumes. However, the difference in Paw was minor and it seems unlikely that the same effects as CPPV$_{VRM}$ could have been obtained by just increasing PEEP (and therefore Paw) to a similar extent (2 cmH_2O). Moreover, the higher Paw value obtained during CPPV$_{VRM}$ was due to the fact that Paw was measured during 1 min recordings and that, during this step, two PEEP increase maneuvers were included in this time. Yet, we measured FRC and EELV at the end of the period between two VRMs, when airway pressures were similar between CPPV$_{LO}$ and CPPV$_{VRM}$. We therefore speculate that alveolar recruitment was obtained during the intermittent PEEP increases and was, at least partially, maintained during the subsequent period at low PEEP. Loss of alveolar patency occurs in ARDS patients when PEEP is decreased following lung recruitment [8], but it does not seem to occur instantaneously, requiring a relatively long time to complete [20].

Periodic deep breaths, or sighs, are known to improve gas exchange and recruit lung volume during anesthesia and mechanical ventilation [11, 21]. General anesthesia [22], ventilation at low V_T [23], and muscle paralysis [24] enhance progressive decrease in PaO_2 and lung compliance, due to the onset of atelectasis [25]. Despite their proven effectiveness in reopening atelectatic lung tissue in anesthetized healthy subjects, lung inflation maneuvers have been reported to have no beneficial effects in patients with respiratory failure [26, 27], and are not part of current clinical practice. Probably, the routine use of high V_T, common in the past years, made sigh maneuvers redundant and non-effective, as alveoli can already be recruited by high V_T inflation [28]. However, the recent use of lower V_T (< 10 ml/kg) increases the probability of loss of compliance and lung volume [7]. In our study, the use of a mildly reduced V_T (7.9 ± 1.8 ml/kg) probably unmasked the effects of VRMs on oxygenation and alveolar recruitment. It is possible that a lower V_T might have resulted in an even bigger efficacy of VRMs, but the effects of different V_T were not addressed in this study.

We decided to add VRMs to CPPV at a relatively low level of PEEP. With these settings, VRMs limited loss of lung volume related to the combined use of low PEEP and of low V_T [7, 8]. Recent work by Pelosi et al. [12] suggests that alveolar recruitment may be incomplete even when PEEP is set to optimize lung opening and that sighs can also be beneficial in these conditions.

While sighs are usually administered as periodically increased V_T [11, 12, 21], our VRMs consisted of transient increases in PEEP lasting for the duration of two ventilatory cycles (Fig. 1). We do not know the relative effectiveness of VRMs obtained by increasing PEEP at constant V_T compared to sighs reaching similar inspiratory plateau pressures, but without increasing PEEP. Further investigation is needed to clarify whether our VRMs are more effective than periodic sighs delivered at constant PEEP.

Effect of VRMs compared to high PEEP

We selected a population of PEEP responder patients and, as expected, oxygenation and alveolar recruitment were increased during CPPV$_{HI}$ compared to CPPV$_{LO}$. The comparison between CPPV$_{HI}$ and CPPV$_{VRM}$ shows that the latter was slightly less effective on oxygenation. These data suggest that, although effective in obtaining lung reopening, periodic increases of PEEP do not reach the full effect of a constantly applied high PEEP. This could be ascribed to the fact that the high level of PEEP was sustained for a shorter total time, during

VRMs (four ventilatory cycles per min vs a total respiratory rate of 15.1 ± 3.6 bpm). Alveolar recruitment seems to be a time-dependent mechanism, and increased levels of PEEP may require prolonged application for full effect on lung volumes to occur [29]. When PEEP is periodically increased for a brief period of time, as during CPPVVRM, it is likely that full lung opening is never reached, or else, that substantial derecruitment takes place between VRMs.

It has been suggested that two kinds of atelectasis may coexist in ARDS lung: compression atelectasis and reabsorption atelectasis [12].

As shown by CT studies [30], compression atelectasis develop very rapidly and are mainly due to small airways collapse at end expiration. This mechanism is related to increased lung weight and is probably counterbalanced by PEEP. Reabsorption atelectasis develops more slowly and is due to an imbalance between the amount of gas delivered to the alveoli by each inspiration and gas uptake by the bloodstream. Low Va/Q and high FiO_2 favor reabsorption atelectasis.

The two mechanisms may coexist when airways collapse at end expiration due to compression atelectasis. The gas left behind the collapse then undergoes the slower process of reabsorption by the bloodstream. If a new VRM takes place before complete atelectasis, the cycle may start all over, preserving oxygenation.

Information about the effects of increased lung weight, PEEP and high FiO_2 upon reabsorption atelectasis in the ARDS lung is scanty. We cannot therefore speculate about the relative importance of reabsorption vs compression in causing atelectasis. We can only conclude that VRMs applied by periodically increased PEEP substantially improves oxygenation, at least in this selected population of PEEP responders ARDS patients.

Cyclically fluctuating PEEP with constant V_T has been previously used in animal models of lung injury, and, unlike our study, it was more effective on oxygenation than constant high PEEP [31]. However, the benefits of fluctuating PEEP were observed in unilateral lung injury only, while no advantage over continuous high PEEP was shown when lung injury was bilateral.

We chose to deliver VRMs at a rate of two per min based on preliminary experiences. Similarly, the choice of PEEP during VRMs was empirical, while we do not know whether the duration of each VRM can affect its efficacy on alveolar recruitment. Further investigation is needed to optimize VRM settings with the goal of improving its effectiveness.

Mechanical ventilation at high PEEP may result in elevated peak alveolar pressures and lead to overdistension of patent alveolar units [32]. This finding can be associated to a decrease in Crs, compared to lower PEEP levels [8]. Therefore, alveolar overdistension can explain why Crs was significantly lower during CPPVHI than during both CPPVLO and CPPVVRM.

In the population studied no changes in hemodynamics were observed, possibly because of the relatively minor PEEP changes. In the presence of a larger shift in the PEEP level, depression of cardiac output may be anticipated; the effect on hemodynamics of CPPVVRM in such circumstances needs further investigation.

Clinical implications

In recent years, "lung protective strategies" have been suggested in the ventilatory treatment of ARDS [1, 2]. Such strategies include the use of reduced V_T (< 10 ml/kg) to limit peak alveolar pressures while maximizing alveolar recruitment [9]. Therefore, it is often necessary to tolerate values of $PaCO_2$ well above normal [6], and high PEEP levels to maintain oxygenation. In these settings, periodic VRMs could allow the use of lower PEEP and the application of elevated distending pressures only for a limited time.

In our study, CPPVHI was more effective than CPPVVRM on oxygenation, but it resulted in continuous lung overdistension, as suggested by the decreased Crs. Compared to CPPVHI, CPPVVRM achieved significant alveolar recruitment at lower baseline PEEP by increasing airway pressures for a shorter time. We suggest that reducing the time in which the lung is overdistended might limit the occurrence of barotrauma, compared to the application of continuously high airway pressures. This hypothesis is only speculative and experimental data are warranted to address this issue.

The extent of alveolar patency instability during ventilation with VRMs should also be investigated, together with strategies to optimize lung volume recruitment through these maneuvers. Alveolar instability and suboptimal lung recruitment are in fact a suggested cause of iatrogenic lung injury [5] and should, therefore, be avoided. However, the results obtained by Pelosi et al. [12] indicate that atelectasis may take place even when PEEP is optimized according to the "lung protective" strategy. The use of a high PEEP, together with limitation of peak alveolar pressure, may not adequately prevent alveolar instability.

Acknowledgements We would like to thank Dr. D. Weismann of the Dräger Company (Lübeck, Germany) for providing the external controller we used in the study.

References

1. Marini J (1996) Tidal volume, PEEP, and barotrauma. An open and shut case? Chest 109: 302–04
2. Lachmann B (1992) Open up the lung and keep the lung open. Intensive Care Med 18: 319–21
3. Kolobow T, Moretti MP, Fumagalli R, Mascheroni D, Prato P, Chen V, Joris M (1987) Severe impairment in lung function induced by high peak airway pressure during mechanical ventilation. An experimental study. Am Rev Respir Dis 135: 312–15
4. Dreyfuss D, Soler P, Basset G, Saumon G (1988) High inflation pressure pulmonary edema. Respective effects of high airway pressure, high tidal volume, and positive end-expiratory airway pressure. Am Rev Respir Dis 137: 1159–64
5. Muscedere JG, Mullen JBM, Gan K, Slutsky AS (1994) Tidal ventilation at low airway pressures can augment lung injury. Am J Respir Crit Care Med 149: 1327–34
6. Hickling KG (1990) Ventilatory management of ARDS: can it affect the outcome? Intensive Care Med 16: 219–26
7. Suter PM, Fairley HB, Isenberg MD (1978) Effect of tidal volume and positive end-expiratory pressure on compliance during mechanical ventilation. Chest 73: 158–62
8. Cereda M, Foti G, Musch G, Sparacino ME, Pesenti A (1996) Positive end-expiratory pressure prevents the loss of respiratory compliance during low tidal volume mechanical ventilation. Chest 109: 480–85
9. Amato MBP, Barbas CSV, Medeiros DM, Magaldi RB, Schettino GPP, Lorenzi-Filho G, Kairalla RA, Deheinzelin D, Munoz C, Oliveira R, Takagaki TY, Carvalho CRR (1998) Effect of a protective-ventilation strategy on mortality in the acute respiratory distress syndrome. N Engl J Med 338: 347–54
10. Petty TL (1988) The use, abuse, and mystique of positive end-expiratory pressure. Am Rev Respir Dis 138: 475–8
11. Egbert LD, Laver MB, Bendixen HH (1963) Intermittent deep breaths and compliance during anesthesia in man. Anesthesiology 24: 57–60
12. Pelosi P, Cadringher P, Bottino N, Panigada M, Carrieri F, Riva E, Lissoni A, Gattinoni L (1999) Sigh in acute respiratory distress syndrome. Am J Respir Crit Care Med 159: 872–880
13. Bernard GR, Artigas A, Brigham KL, Carlet J, Falke K, Hudson L, Lamy M, Morris A, Spragg R (1994) The American-European Consensus Conference of ARDS: definitions, mechanisms, relevant outcomes, and clinical trial coordination. Am J Respir Crit Care Med 149: 818–24
14. Murray JF, Matthay MA, Luce JM, et al (1988) An expanded definition of the adult respiratory distress syndrome. Am Rev Respir Dis 138: 720–723
15. Nunn JF (1993) Nunn's applied respiratory physiology. Butterworth-Heinemann, Oxford
16. Broseghini C, Brandolese R, Poggi R, Bernasconi M, Manzin E, Rossi A (1988) Respiratory resistance and intrinsic positive end-expiratory pressure (PEEP) in patients with the adult respiratory distress syndrome (ARDS). Eur Respir J 1: 726–31
17. Pelosi P, Cereda M, Foti G, Giacomini M, Pesenti A (1995) Alterations of lung and chest wall mechanics in patients with acute lung injury: effects of positive end-expiratory pressure. Am J Respir Crit Care Med 152: 531–7
18. Altman DG (1991) Practical statistics for medical research. First Edition. Chapman and Hall, London
19. Valta P, Takala J, Eissa T, Milic-Emili J (1993) Does alveolar recruitment occur with positive end-expiratory pressure in adult respiratory distress syndrome patients? J Crit Care 8: 34–42
20. Lichtwarck-Aschoff M, Guttmann J, Eberhard L, Fabry B, Birle J, Adolph M (1997) Delayed derecruitment after removal of PEEP in patients with acute lung injury. Acta Anaesthesiol Scand 41: 675–84
21. Mead J, Collier J (1958) Relation of volume history to respiratory mechanics in anesthetized dogs. J Appl Physiol 14: 669–78
22. Bendixen HH, Hedley-White J, Laver MB (1963) Impaired oxygenation in surgical patients during general anesthesia with controlled ventilation: a concept of atelectasis. N Engl J Med 269: 991–6
23. Sykes MK, Young WE, Robinson BE (1965) Oxygenation during anaesthesia with controlled ventilation. Brit J Anaesth 37: 314–25
24. Putensen C, Rasanen J, Lopez FA (1994) Ventilation-perfusion distributions during mechanical ventilation with superimposed spontaneous breathing in canine lung injury. Am J Respir Crit Care Med 150: 101–8
25. Brismar B, Hedenstierna G, Lundquist H, Strandberg A, Svensson L, Tokics L (1985) Pulmonary densities during anesthesia with muscular relaxation. A proposal of atelectasis. Anesthesiology 62: 422–824
26. Housley E, Louzada N, Becklake MR (1970) To sigh or not to sigh. Am Rev Respir Dis 101: 611–4
27. Fairley HB (1976) The mechanical ventilation sigh is a dodo. Respir Care 21: 1127–30
28. Ranieri VM, Mascia L, Fiore T, Bruno F, Brienza A, Giuliani R (1995) Cardiorespiratory effects of positive end-expiratory pressure during progressive tidal volume reduction (permissive hypercapnia) in patients with acute respiratory distress syndrome. Anesthesiology 83: 710–20
29. Katz JA, Ozanne GM, Zinn SE, Fairley HB (1981) Time course and mechanisms of lung-volume increase with PEEP in acute pulmonary failure. Anesthesiology 1981 54: 9–16
30. Gattinoni L, Pelosi P, Crotti S, Valenza F (1995) Effect of positive end expiratory pressure on tidal volume and recruitment in adult respiratory distress syndrome. Am J Respir Crit Care Med 151: 1807–1814
31. Uchida H, Inaba H, Sato J, Sakurada M, Mizuguchi T (1988) Fluctuating PEEP versus conventional PEEP in diffuse and unilateral lung injury induced by oleic acid. Acta Anesthesiol Scand 32: 420–5
32. Ranieri VM, Eissa T, Corbeil C, Chasse' M, Braidy J, Matar N, Milic-Emili J (1991) Effects of positive end-expiratory pressure on alveolar recruitment and gas exchange in patients with the adult respiratory distress syndrome. Am Rev Respir Dis 144: 544–51