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C. Guerin
M. Badet
S. Rosselli
L. Heyer
J.-M. Sab
B. Langevin
F. Philit
G. Fournier
D. Robert

Effects of prone position on alveolar recruitment and oxygenation in acute lung injury

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C. Guerin (✉) · M. Badet · L. Heyer · J.-M. Sab · B. Langevin · F. Philit · D. Robert
Service de Réanimation Médicale et Assistance Respiratoire,
Hôpital de la Croix-Rousse,
93 Grande Rue de la Croix-Rousse,
F-69004 Lyon, France
e-mail: c-guerin@cismsun.univ-lyon1.fr
Tel.: + 33-4-72 07 17 62
Fax: + 33-4-72 07 17 74

S. Rosselli · G. Fournier
Service de Réanimation Médicale,
Centre Hospitalier Lyon-Sud,
Chemin du Grand Revoyet,
F-69495 Pierre Benite Cedex, France

Abstract *Objective*: To investigate the effects of prone position (PP) on alveolar recruitment and oxygenation in acute respiratory failure.
Design: Prospective physiologic study.
Setting: Medical ICU two in a university hospital.
Patients: Twelve adult patients intubated and mechanically ventilated with medical primary acute lung injury/adult respiratory distress syndrome (ALI/ARDS) in whom PP was indicated.
Measurements and results: We constructed the static inflation volume-pressure curves (V-P) of the respiratory system in the 12 patients and differentiated between lung and chest wall in ten of them. We determined the difference between end-expiratory lung volume on positive end-expiratory pressure (PEEP) and relaxation volume of the respiratory system on zero PEEP (ΔFRC). The recruited alveolar volume was computed as the ΔFRC times the ratio of static elastance of the respiratory system to the lung. These measurements together with arterial blood gases determination were made in supine position (SP1), after 1 h of PP and after 1 h of supine repositioning (SP2) at the same level of PEEP. The PaO_2/FIO_2 ratio improved from SP1 to PP (136 ± 17 vs 204 ± 24 mm Hg; $p < 0.01$). An PP-induced alveolar recruitment was found in five patients. The change in oxygenation correlated to the recruited volume. The static elastance of the chest wall decreased from 4.62 ± 0.99 cmH_2O/l in SP1 to 6.26 ± 0.54 cmH_2O/l in PP ($p < 0.05$) without any correlation to the change in oxygenation.
Conclusions: Alveolar recruitment may be a mechanism of oxygenation improvement in some patients with acute hypoxemic respiratory failure. No correlation was found between change in oxygenation and chest wall elastic properties.

Key words Acute respiratory failure · Alveolar recruitment · Mechanical ventilation · Prone position · Respiratory mechanics

Introduction

Over the years, turning from supine (SP) to prone position (PP) during mechanical ventilation has emerged as a useful and simple tool to improve oxygenation of patients with acute respiratory failure (ARF) [1–5]. However, the knowledge of the mechanism by which this effect is obtained is not completely understood. From animal studies, PP seems to act essentially by reversing the regional pleural pressure gradient, and hence the transpulmonary pressure gradient, which becomes more homogeneously distributed throughout the lung [6]. In humans with adult respiratory distress syndrome (ARDS), computed tomography (CT) studies of the lungs showed that pulmonary densities mostly involved the dorsal regions in SP and moved toward the ventral regions in PP

Table 1 Anthropometric characteristics, cause of acute respiratory failure and ICU outcome of the 12 patients

Patient	Age (years)	Sex	Weight (kg)	Height (m)	BMI (kg/m^2)	Cause of acute respiratory failure; underlying condition of interest	ICU outcome
1	64	m	87	1.75	28.41	Pneumococcal pneumonia; alchool	D
2	35	m	80	1.70	27.68	Pseudomonas pneumonia; HIV positive	D
3	67	m	62	1.65	22.77	Pneumocystis carinii pneumonia; Wegener Granulomatosis	D
4	50	m	56	1.60	21.88	Aspiration; alchool	S
5	56	m	72	1.76	23.24	Aspergillosis; hepatic transplant	S
6	61	f	73	1.60	28.52	Aspiration	S
7	78	m	69	1.71	23.60	Aspiration	D
8	56	m	88	1.70	30.45	Undertermined pneumonia	S
9	65	f	76	1.55	31.63	Legionnaire's disease	S
10	62	f	53	1.50	23.56	Undertermined pneumonia; bone marrow transplant	D
11	75	m	77	1.75	25.14	Legionnaire's disease	S
12	60	f	94	1.64	34.95	Alveolar hemorrhage	S
Mean	61		72	1.66	26.08		
SEM	3		3	0.02	0.94		

BMI = body mass index; m = male; f = female; D = death; S = survival

[7]. Recently, Pelosi et al. showed very nicely that the improvement of oxygenation with PP correlated with the static chest wall compliance (Cst,w) in SP [8]. They found, indeed, that the higher the Cst,w in SP and the greater the reduction of Cst,w from SP to PP, the greater the gain in oxygenation with PP [8]. This study was carried out on a single inflation volume, namely the baseline inflation volume (ΔV). By constructing the static volume-pressure curves (V-P) of the respiratory system in SP and PP, Servillo et al. [9] observed that the improvement of oxygenation with PP correlated with an increase in static compliance of the respiratory system (Cst,rs).

In the present study, we addressed the issue of alveolar recruitment as a possible mechanism of the effects of PP on oxygenation. The lung densities on CT scan, which were found to redistribute down to the ventral dependent regions with PP, are comprised of tissue (atelectasis), edema (extravascular lung water) and blood. Gattinoni et al. [10] very elegantly proposed methods to distinguish between these different components. However, on this basis it is not clear whether or not alveolar recruitment, i. e. a reopening of previously atelectatic lung units, occurs with PP. The redistribution of CT densities does not systematically mean alveolar recruitment [7]; on the other hand the redistribution of lung densities did not correlate with the change in oxygenation, maybe because the measurements were made only 10 min after turning the patient to the PP [7]. Hence, in the present study, we attempted to identify and to quantify alveolar recruitment by using the static V-P curves and to correlate this, if any, with the change in oxygenation. In addition, we determined lung and chest wall mechanical properties in both the SP and PP.

Material and methods

Patients

Patients were included if they met all of the following criteria: (1) tracheal intubation and mechanical ventilation, (2) acute lung injury (ALI) [11], (3) prone positioning indicated by the clinician in charge, (4) informed consent obtained from the next of kin. Patients were excluded in cases of thoracic drainage, hemodynamic instability, continuous hemofiltration, colonization or infection of the lower respiratory tract with a multiple antibiotic-resistant bacteria or if informed consent was not obtained. We investigated 12 consecutive patients whose clinical characteristics are listed in Table 1. They were studied 1–8 days after initiation of mechanical ventilation (Table 2). Eleven of them met the criteria of ARDS and one those of ALI [11]. None of them had chronic lung disease or cardiogenic pulmonary edema. The PP trial was indicated by the clinician in charge essentially because of failure in oxygenation with high levels of FIO_2 (Table 2).

The patients were orotracheally intubated (Mallinckrodt cuffed-endotracheal tube of 7.0–8.5 mm internal diameter (ID); Mallinckrodt, Athlone, Ireland) and mechanically ventilated (Siemens-Elema 900 C Servo-Ventilator; Solna, Sweden). During the study all patients were sedated with midazolam (0.2 mg/kg) and paralyzed with atracurium (0.3–0.6 mg/kg). The baseline ventilatory settings are listed in Table 2. Airflow ($\dot{V}$) was measured with a heated pneumotachograph (Fleisch No.2; Fleisch, Lausanne, Switzerland) inserted between the endotracheal tube and the Y-piece of the ventilator. The pressure drop across the two ports of the pneumotachograph was measured with a differential piezoelectric pressure transducer (163PC01D36, ± 12.7 cmH_2O; Micro switch Freeport, Ill.). The response of the pneumotachograph was linear over the experimental range of $\dot{V}$. Pressure at the airway opening (Pao) was measured proximal to the endotracheal tube with a piezoelectric pressure transducer (143PC03D, ± 176 cmH_2O; Micro switch). Tracheal pressure (Ptr) was measured via a polyethylene catheter (1.5 mm ID) with multiple side holes and an occluded end hole, placed 2 cm past the carinal end of the endotracheal tube and connected to a piezoelectric pressure transducer (143PC03D, ± 176 cmH_2O; Micro switch). In addition, except for in patients 3 and 7, we measured esophageal pressure (Pes) with a thin-walled latex balloon (10 cm long, 3 cm in circumfer-

Table 2 Days of investigation and baseline ventilatory settings

Patient	Days from tracheal intubation	FIO_2	PEEP (cmH_2O)	ΔV (ml)	ΔV (ml/kg)	Flow (l/s)	Breathing frequency (breaths/min)	Ti (s)	Te (s)
1	7	1.00	12	760	8.74	0.77	20	0.99	2.01
2	5	0.90	14	800	10.00	0.52	18	1.67	1.67
3	1	1.00	9	580	9.35	0.62	21	0.94	1.92
4	5	0.80	6	450	8.04	0.30	20	1.50	1.50
5	6	1.00	8	610	8.47	0.55	18	1.11	2.22
6	1	1.00	3	580	7.95	0.29	15	2.00	2.00
7	8	0.65	13	640	9.28	0.40	15	1.60	2.40
8	6	0.80	12	700	7.95	0.34	14	2.06	2.23
9	2	1.00	11	800	10.53	0.53	10	1.50	4.50
10	1	0.50	11	600	11.32	0.43	14	1.41	2.87
11	8	1.00	11	750	9.74	0.55	25	0.79	1.61
12	4	0.80	0	760	8.09	0.89	15	1.00	3.00
Mean	4.5	0.87	9	669	9.12	0.52	17	1.38	2.33
SEM	0.8	0.05	1	32	0.32	0.05	1	0.12	0.24

FIO_2 = fraction of inspired oxygen; PEEP = Positive End Expiratory Pressure; ΔV = inflation volume; Ti = duration of inspiration; Te = duration of expiration

ence) sealed over one end of a polyethylene catheter (2 mm ID, 120 cm long), inflated with 0.6–1 ml of air, and connected to a solid-state pressure transducer (143PC03D, ± 176 cmH_2O; Micro switch).

The correct position of the esophageal balloon was ascertained by the occlusion test before sedation paralysis [12]. With the system used to measure Pao, Ptr and Pes there was no appreciable shift or alteration in amplitude up to 20 Hz. The equipment dead space (not including the endotracheal tube) was 150 ml. All variables were recorded on an IBM compatible computer by a 12 bit analog digital board (DT2801-A) interfaced with a data acquisition software (Labdat, RHT-Infodat, Montreal, Canada) at a sample frequency of 100 Hz. Subsequent data analysis was made with Anadat (RHT-Infodat). In this analysis ΔV was obtained by digital integration of the $\dot{V}$ signal. Special care was taken to avoid gas leaks in the equipment and around the tracheal cuff. To reduce the effects of the compliance and resistance of the system connecting the subjects to the ventilator on the mechanics measurements, we used a single length of standard adult low compliance tubing supplied with the machine (2 cm ID, 110 cm long) and omitted the humidifier during the experiment.

Arterial blood gases were measured with an ABL 500 blood gas analyzer (Radiometer, Copenhagen, Denmark). Before the experiment, PaO_2 averaged 131 ± 14 mm Hg, $PaCO_2$ 46 ± 1 mm Hg and pH 7.37 ± 0.02 under the baseline ventilatory settings listed in Table 2. Heart rate and arterial oxygen saturation (SpO_2) (HPM1020 A; Hewlett Packard) were continuously monitored.

At first, V-P curves were constructed in the SP after PEEP was withdrawn for 20 min. For safety reasons (rapid drop of SpO_2 on ZEEP), this step was not completed in patients 7 and 11. In patient 12, the baseline PEEP was in fact ZEEP. The level of PEEP set by the clinician was then resumed for 20 min. Measurements of arterial blood gases and respiratory mechanics (see below) were made in the supine (SP1), PP and supine positions (SP2) with 1 h period of stabilization after each turn. In these three conditions, the bed was positioned horizontally. In PP, the head was turned to one side, the arms of the patient at his sides and the abdomen was not supported in any way. Before measurements, the trachea was gently suctioned. The ventilatory settings were kept unchanged throughout the experiment (Table 2). During the study a physician and a nurse not involved in the experiment were always present to provide patient care.

Procedure and data analysis

Respiratory mechanics

Respiratory mechanics were assessed by the constant $\dot{V}$ rapid airway occlusion method previously described in detail [13]. Whilst baseline $\dot{V}$ was kept constant (Table 2), ΔV was changed randomly from 0.1 to 1 l for single test breaths by changing the frequency of the ventilator. The end-inspiratory occlusions, obtained by pressing the end-inspiratory hold knob on the ventilator, lasted 5 s. Before each test breath, an end-expiratory occlusion was performed by pressing the end-expiratory hold button on the ventilator. This allowed quantification of PEEPi and the initiation of the test breath from a fixed static elastic equilibrium condition. When PEEP was applied, the end-expiratory occlusion pressure was the sum of the PEEP set by the ventilator and PEEPi. This sum was termed total PEEP (PEEPt). It should be noted that on ZEEP the ventilator generated a slightly positive end-expiratory pressure, averaging 0.9 ± 0.2 cmH_2O, so that PEEPt was also measured on ZEEP. We also measured the difference between the end-expiratory lung volume (EELV) and the relaxation volume of the respiratory system (Vr) by reducing the ventilator frequency to its lowest value during baseline expiration, while removing PEEP when present, thus prolonging the expiratory duration to allow the patient to exhale to Vr: Vr was achieved when expiratory flow became nil and end-expiratory occlusion resulted in no change in airway pressure (i.e. no PEEPi). This difference was termed ΔFRC. After each test breath, the baseline ventilation was resumed until ΔV, $\dot{V}$, Pao and Ptr returned to their baseline values (usually in a few breaths). Each measurement was made twice.

After end-inspiratory airway occlusions, Ptr and Pao, but not Pes, exhibited an initial rapid drop (Pmax-P1) followed by a slow decline to an apparent plateau pressure. During this period, the contribution of reduction in pressure due to volume loss by continuing gas exchange should be negligible. Ptr, Pes and transpulmo-

Table 3 Pressure (cmH_2O) at lower inflection points in supine position on ZEEP and values of PEEP applied by the primary physician in supine and prone positions

Patient	LIP,rs	LIP,L	LIP,w	PEEP SP1	PEEP PP	PEEP SP2
1	7.0	3.4	3.7	12.4	12.5	13.0
2	14.2	12.8	a	14.4	15.5	15.5
3	8.0	a	a	9.2	10.5	10.0
4	a	a	a	6.4	7.2	7.3
5	7.1	6.8	a	7.9	6.0	6.8
6	a	a	a	3.2	4.3	4.2
7	b, c	b, c	b, c	13.0	13.3	14.5
8	9.9	7.9	c	12.4	12.9	12.7
9	a	a	a	10.7	10.4	10.2
10	a	a	a	11.5	11.8	11.2
11	c	a	a	11.0	12.2	11.6
12	a	a	a	0.4	0.3	0.0
Mean	9.2	7.7		9.4	9.8	9.7
SEM	1.3	1.9		1.2	1.3	1.3

ZEEP = zero end-expiratory pressure; PEEP = positive end-expiratory pressure; LIP,rs, LIP,L, LIP,w = lower inflection points of the respiratory system, lung and chest wall, respectively; SP1 = supine position before prone position; PP = prone position; SP2 = supine position after PP
a not detected
b esophageal pressure not measured
c zero end-expiratory pressure not applied

nary (P_L) pressures measured at 5 s were taken to represent the static end-inspiratory elastic recoil pressure of the respiratory system (Pst,rs), chest wall (Pst,w) and lung (Pst,L), respectively. Dividing Pmax,tr-Pst,tr and Pmax,tr-P1,tr by the $\dot{V}$ immediately preceding the occlusion, Rrs and Rint,rs were obtained. ΔRrs was calculated as the difference between Rrs and Rint,rs.

In computation of Rint, the errors caused by the closing time of the ventilator valve were corrected as previously described [13]. By dividing Pmax,es-Pst,w by the $\dot{V}$ immediately preceding the occlusion, the total resistance of the chest wall (Rw) was obtained. Because Pes did not exhibit an immediate drop after end-inspiratory occlusion, Rw represents the additional resistance of the chest wall (ΔRw). Total (RL), interrupter (Rint,L) and additional (ΔRL) resistances of the lung were obtained by subtracting the corresponding values of the chest wall from those pertaining to the respiratory system. The static elastances of the respiratory system (Est,rs), chest wall (Est,w) and lung (Est,L) were computed by dividing the corresponding values of Pst-PEEPt by ΔV. To obtain the static inflation V-P curves of the respiratory system, chest wall and lung, the values of ΔV relative to Vr were plotted against those of Pst,rs, Pst,w and Pst,L, respectively.

Assessment of alveolar recruitment between the different positions was made according to the method described by Ranieri and co-workers [14], by computing the difference of ΔV between SP1 and PP or SP1 and SP2 for the same Pst,rs of 20 cmH_2O from the static inflation V-Pst,rs relationships obtained in the corresponding conditions. However, this method should underestimate alveolar recruitment. In fact, the actual recruited alveolar volume should approximate [15]

$$\text{Recruited alveolar volume} = \text{change in } \Delta FRC \times Est,rs/Est,L \quad (1)$$

where Est,rs and Est,L pertain to PP and change in ΔFRC is the difference of ΔRFC between the two positions. This assumes that there were no changes in thoracic blood volume [15]. Detection of lower (LIP) or of upper (UIP) inflection points were made by visual inspection of the V-Pst,rs, V-Pst,L and V-Pst,w curves on ZEEP. The investigators who performed the post-sampling analysis were blinded to the postural sequence.

Statistical analysis

Linear regression analysis was made by the least squares method. Values obtained in three different positions (SP1, PP and SP2) at a similar level of applied PEEP were compared using the one-way analysis of variance (ANOVA) for repeated measurements. Values are mean ± SEM. For our statistics, we used SPPS 7.5 software for Windows 95.

Results

As shown in Table 3, LIP was present on the V-P curve of the respiratory system (LIP,rs) on ZEEP in five patients out of the ten who underwent this step. In patient 1, the chest wall contributed to a large extent to this phenomenon. In patients 1, 2, 5 and 8, PEEP was set above the value of LIP detected on the V-P curve of the lung (LIP,L). PEEP was greater than the pressure corresponding to LIP,rs in all instances. Only in patient 5 was PEEP at PP and SP2 slightly lower than the pressure corresponding to LIP,rs.

Table 4 shows the values of respiratory mechanics at baseline ventilatory settings obtained in the three positions for a similar level of applied PEEP. As compared with SP1, the values of ΔFRC were lower in PP, those of Est,rs lower in SP2 and those of Est,w higher in PP. No other variable reached significance.

Figure 1 depicts the static inflation V-P curves of the respiratory system obtained in SP1, PP and SP2 in two patients (2 and 11). In patient 2, the V-P curve obtained in PP was shifted upward as compared with SP1, i.e. for a given Pst,rs of 20 cmH_2O the volume increased from SP1 to PP, indicating that there was recruitment of previously atelectatic lung units with PP. This increase in lung volume, termed recruited volume by Ranieri et al. [14], amounted to 0.85 l in this patient. The recruited volume was much less in patient 11. Three other patients (4, 5, 6) exhibited such alveolar recruitment from PP to SP1 (Table 5). In the remaining five patients in whom Eq. 1 could be computed, there was a derecruitment of previously open lung units with PP (Table 5).

In Fig. 1 it can also be seen that both V-P curves are shifted upward with SP2 compared to PP, indicating an overall recruitment volume of 0.48 l and 0.12 l, respectively, relative to SP1. This was also observed in patients 3, 5, 7, 8 and 10 (Table 5) In the remaining patients the opposite was true.

The value of PaO_2/FIO_2 increased significantly from 136 ± 17 in SP1 to 204 ± 24 mmHg in PP ($p < 0.01$) and

Table 4 Baseline respiratory mechanics of the 12 patients in the supine and prone positions[a]

	SP1	PP	SP2	*p* value SP1 vs *pp*	P value SP1 vs SP2
PEEPt (cmH_2O)	10.9 ± 1.0	11.1 ± 1.2	11.5 ± 1.1	0.75	0.14
PEEPi (cmH_2O)	1.6 ± 0.5	1.3 ± 0.3	1.8 ± 0.6	0.38	0.58
ΔFRC (L)	0.81 ± 0.14	0.75 ± 0.15	0.76 ± 0.15	0.59	0.67
Rint, rs (cmH_2O/L/s)	6.3 ± 1.2	5.7 ± 1.1	5.2 ± 1.0	0.47	0.20
ΔRrs (cmH_2O/L/s)	10.3 ± 1.3	9.6 ± 1.1	10.2 ± 1.1	0.22	0.96
Rrs (cmH_2O/L/s)	16.5 ± 1.6	15.2 ± 1.3	15.4 ± 1.4	0.30	0.34
ΔRL (cmH_2O/L/s)	8.7 ± 1.6	8.2 ± 1.3	8.6 ± 1.2	0.23	0.85
RL (cmH_2O/L/s)	14.7 ± 2.0	13.1 ± 1.4	13.5 ± 1.6	0.24	0.45
ΔRw (cmH_2O/L/s)	2.1 ± 0.6	1.7 ± 0.3	1.8 ± 0.4	0.46	0.62
Est, rs (cmH_2O/L)	20.5 ± 2.0	21.0 ± 1.8	18.9 ± 1.8	0.57	0.02
Est, L (cmH_2O/L)	15.1 ± 2.1	14.1 ± 1.7	13.9 ± 1.9	0.53	0.16
Est, w (cmH_2O/L)	4.6 ± 0.9	6.3 ± 0.5	4.7 ± 0.7	0.03	0.90

SP1 supine position before prone position; PP prone position; SP2 supine position after PP; PEEPt total positive end-expiratory pressure; PEEPi intrinsic positive and expiratory pressure; ΔFRC difference between end-expiratory lung volume during mechanical ventilation and relaxation volume of the respiratory system on ZEEP; Rint, rs, ΔRrs, Rrs interrupter, additional and total resistance, respectively, of the respiratory system; ΔRL, RL additional and total lung resistance; ΔRw additional resistance of the chest wall; Est, rs, Est, L, Est, w static elastance of the respiratory system, lung and chest wall, respectively

[a] values are mean ± SEM

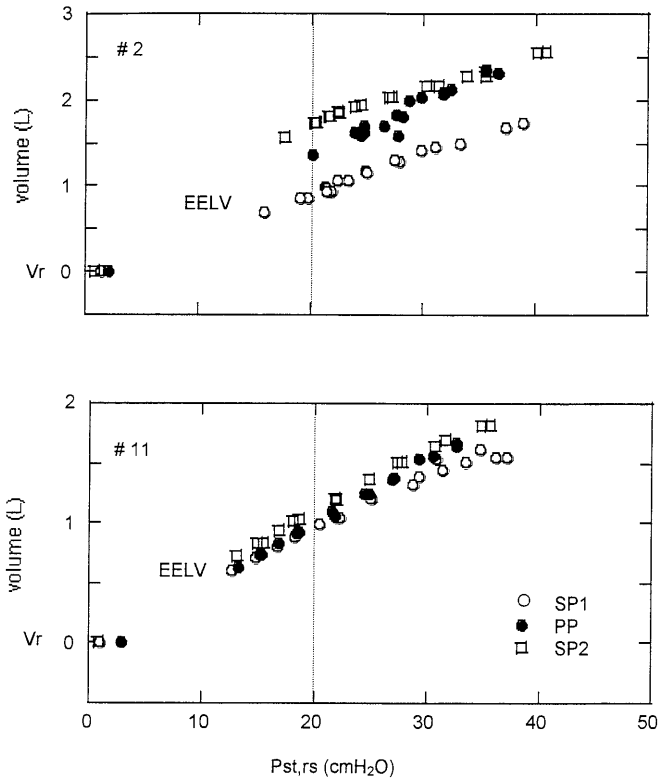

Fig. 1 Relationships of lung volume to static inspiratory pressures of the respiratory system in the three positions in two representative patients (*SP1* supine position before prone position, *PP* prone position, *SP2* supine position after PP, *Vr* relaxation volume of the respiratory system, *EELV* end-expiratory lung volume) The vertical distance between Vr and EELV is ΔFRC. There is no lower inflection point in the relationships. *Vertical broken lines*: lines of isostatic pressures used for the computations of the alveolar recruitment

decreased to 157 ± 21 mmHg in SP2, a value not significantly different from that obtained at SP1 (Table 5). Figure 2 depicts the significant relationships of the change in PaO_2 to the change in both V_{20} and ΔFRC among the different positions. In these relationships, we used the values of V_{20} as actual recruited volume computed from Eq. 1. No significant correlation was found between the change of the PaO_2/FIO_2 ratio or PaO_2 and any of the respiratory mechanics variables; the same was true for the alveolar recruitment.

Discussion

The results of this study are that: (1) turning patients from SP to PP resulted in an alveolar recruitment in five patients and alveolar derecruitment in five, (2) the change in oxygenation was slightly, but significantly, correlated with the amount of recruited volume, (3) Est,w increased in the PP without any significant correlation with the change in oxygenation and (4) Est,rs decreased when the patients were shifted again to the SP.

Before discussing these, a critique of our methodology is required. First, our estimates of the alveolar recruitment are based upon the assumption that the relaxation volume of the respiratory system does not change with PP. In normal awake subjects, the functional residual capacity (FRC) may be either increased or decreased in PP, as compared to SP, depending on whether the weight of the abdomen is supported or not [16]. In normal anesthetized paralyzed humans, FRC increased from 1.9 to 2.9 l between SP and PP [17]. In human adults with ARF, however, Pelosi et al. [8] showed that FRC (helium) did not change with PP. Hence, on the ba-

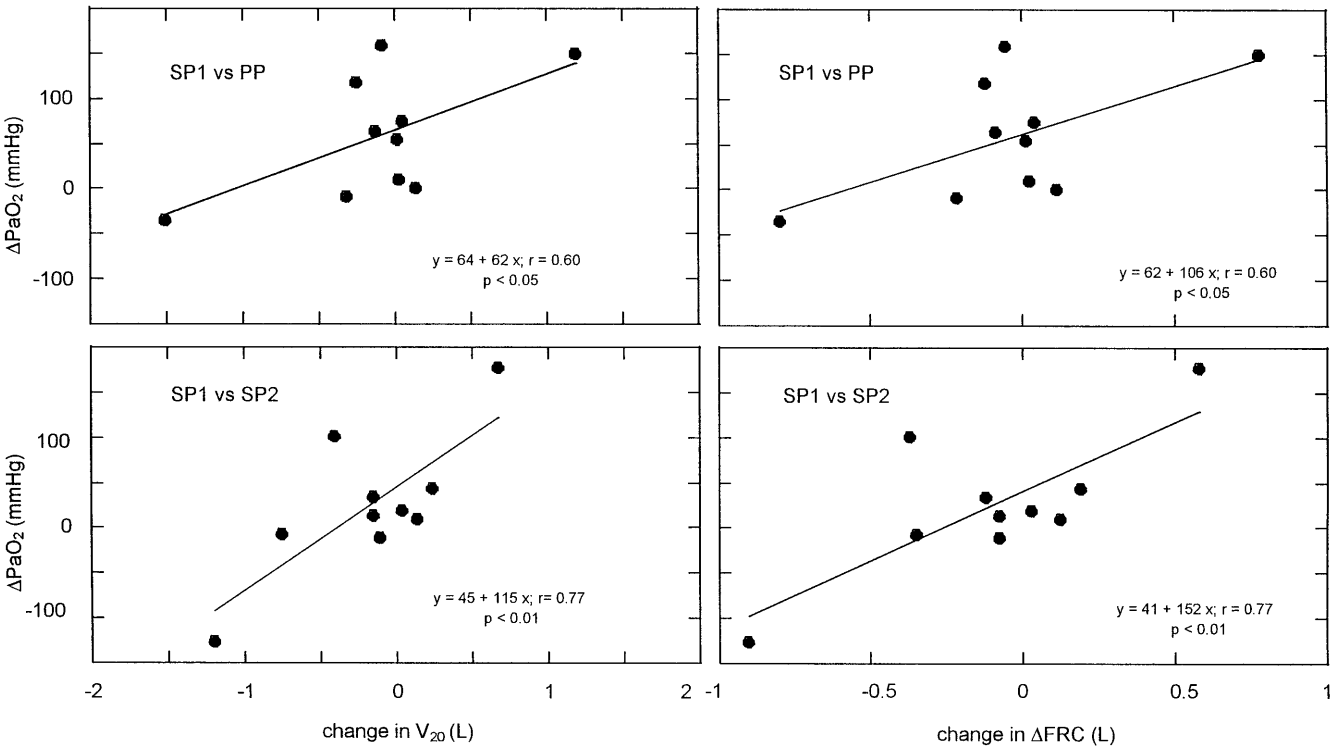

Fig. 2 Relationships of the changes in PaO_2 and the changes in V_{20} (*left panels*) and the changes in ΔFRC (*right panels*) between supine and prone positions (*SP1* supine position before prone position, *PP* prone position, *SP2* supine position after PP) The changes in V_{20} are computed according to Eq. 1. ΔFRC is the vertical line between Vr and EELV on Fig 1. Regression lines are shown

Table 5 Oxygenation and recruited alveolar volume

Patients	PaO_2 (mm Hg)			Recruited alveolar volume (l)	
	SP1	PP	SP2	SP1-PP	SP1-SP2
1	120	239	154	–0.25	–0.16
2	121	271	298	1.19	0.67
3	190	228	107		
4	90	144	104	0.01	–0.16
5	150	151	193	0.14	0.23
6	83	158	184	0.05	–0.41
7	77	111	102		
8	84	243	73	–0.09	–0.11
9	286	251	160	–1.51	–1.20
10	90	154	110	–0.14	0.04
11	69	79	80	0.03	0.13
12	68	60	62	–0.32	–0.76
Mean	119[a,b]	174	135	–0.09	–0.17
SEM	18	20	19	0.21	0.17

SP1 = supine position before prone position; PP = prone position; SP2 = supine position after PP.
Recruited alveolar volume was computed according to equation 1.
[a] p = 0.01 vs PP
[b] p = 0.47 vs SP2

sis of the FRC measurement made by Pelosi et al. [8], our assumption of a fixed Vr between supine and prone positions in the present patients could be valid. However, the comparison of the V-P curves between SP1 and SP2 cannot be criticized on this basis because one could reasonably assume that Vr did not change between SP before, and SP after, the PP trial. Secondly, the accuracy of the measurement of Pes in PP can be questioned. This method, which is the only one currently available in humans to assess the pleural pressure, has already been used in normal prone subjects [18] and in patients intubated and mechanically ventilated [8, 17]. Third, we investigated only a few patients, so that any conclusion is difficult. Finally, our measurements did not investigate the effects of PP beyond a 1-h trial.

The level of PEEP applied to our patients was not standardized but that set by the clinician. This, like the other ventilatory settings, was kept unchanged between the different conditions. Because we were primarily interested in investigating the correlation between alveolar recruitment and oxygenation we did not apply ZEEP in PP in order to avoid any confounding factor which could influence gas exchange. Indeed, it has been reported that PP has a time-dependent effect on oxygenation [5]. However, in SP we first studied the V-P curves on ZEEP. Mergoni et al. [19] have shown that setting PEEP upon LIP,rs on ZEEP could be erroneous because the chest wall can contribute to it. The presence of LIP,rs was observed in five of our ten patients in whom esophageal balloons were inserted. The chest wall contributed

to LIP,rs in only one of them. In all of these ten patients PEEP was above LIP,L. The values of PEEP between the four patients with, and the eight without, LIP,L, though substantial (12 ± 1 vs 8 ± 1 cmH_2O), were not significant. In the study of Mergoni et al. [19], LIP,rs on ZEEP was detected in all of the 12 patients studied. The difference of prevalence of LIP,rs on ZEEP between the two studies may be due to the method used to construct the V-P relationships [20].

Turning from supine to prone position

In our study we attempted to investigate the alveolar recruitment as a possible mechanism of oxygenation improvement with PP. Stemming from animal studies, several factors have been proposed to explain how PP may affect oxygenation. It was first suggested that oxygenation improvement could be related to an increase in FRC, after turning the patient to the prone position. As discussed above, available measurements of FRC in children [21] and adults [8] showed no significant differences between SP and PP and no correlation with oxygenation either. In dog lungs injured with oleic acid, the gain in oxygenation was largely due to a PP-induced shunt reduction [22], which resulted from neither a reduction of cardiac output nor a change in the regional distribution of lung perfusion [23]. Lamm et al. [6] showed, in dog oleic acid-induced lung injury, that after turning the dogs to PP the regional ventilation improved in dorsal regions more than it decreased in ventral regions without significant changes in the distribution of regional perfusion. This probably occurred because PP resulted in a more homogenous distribution of the pleural pressure gradient [24].

Whether or not this mechanism operates in human lungs with ARF has not yet been established. The change of the gravitational Pst,L gradient we could expect from the PP-induced change in pleural pressure gradient should promote the rationale for atelectatic dorsal lung units to reopen on turning prone, i.e. of an alveolar recruitment in PP. In our study, the marked patient-to-patient variability in both oxygenation and alveolar recruitment between the different positions renders it difficult to draw a conclusion from the data. With the above limitations in mind, we have found that alveolar recruitment was observed in five patients only and that a pattern, which could be referred to as alveolar derecruitment, occurred in the remaining patients. Alveolar recruitment should imply an increase in the overall FRC. On the other hand, overall FRC could remain unchanged whereas regional FRCs might change in opposite directions. One could imagine that dorsal regions are atelectatic and ventral regions overdistended.

By placing the patients in the PP, the dorsal regions reopen and increase their regional FRC while the ventral regions' becoming less distended counterbalance the recruitment, leaving the overall FRC unchanged. What we measured, however, was the change in ΔFRC from PEEP to ZEEP in the different positions. On average, the change in ΔFRC significantly decreased in PP compared to SP1. We found that both change in ΔFRC and recruited volume correlated with the change in oxygenation. The correlation was better when using PaO_2 values rather than PaO_2/FIO_2 ratio values (Fig. 2). The change in ΔFRC correlated with the recruited volume ($r = 0.92$; $p < 0.001$). The values of ΔFRC and recruited volume were not different. Hence, the changes of ΔFRC can be used as an index of alveolar recruitment (Fig. 2, right panels). Assuming no significant change in Vr between SP and PP, it is likely that the changes of lung volume observed with the changes in position reflect an alveolar recruitment/derecruitment phenomenon caused by PP. That means that turning to PP may have resulted in a loss of lung volume in some patients.

The correlation between oxygenation and alveolar recruitment, even though significant, was weak in our study. This suggests that PP acts through other mechanisms or that we underestimated the true amount of recruitment with our methods or that recruitment is occurring in regions receiving pulmonary perfusion while the same amount of lung derecruitment is occurring in regions not receiving much blood flow. Obviously, our methods cannot distinguish between these two mechanisms.

In line with Pelosi et al. [8], we found that Est,w increased significantly when the patients were turned prone. This was obtained, contrary to the study of Pelosi et al. [8], without attempting to support the abdomen. However, we did not find any significant correlation between the change in Est,w and the change in oxygenation between SP and PP. In humans [3] and animals [24] the improvement in oxygenation with PP was also obtained with an unsupported abdominal wall. Moreover, in the study of Mutoh et al. [24] in pigs, the abdominal wall compliance was reduced after infusion in the SP but remained unchanged after turning the animals prone. Very recently, Gattinoni et al. [25] reported that the respiratory mechanics were markedly different between ARDS originating from pulmonary and extrapulmonary disease. Specifically, Est,w was lower in the former group that in the latter. All our present patients suffered from a pulmonary ARDS and, indeed, exhibited values of Est,w in the range of those of Gattinoni et al. [25]. According to Pelosi et al. [8], given the relationship between supine Cst,w and further change in oxygenation with PP, one would expect that oxygenation would not improve in our prone patients. This, however, was absolutely not the case. Taken together, these data suggest that while the chest wall compliance may play a role, this is not the sole factor to explain why oxygenation did better with PP.

Turning from prone to supine

What happened to the lung and chest wall mechanics when the patients were repositioned supine was also interesting. One hour after SP2 oxygenation and Est,w returned to near their values observed in SP1. On the other hand, Est,rs during SP2 was significantly lower than during SP1. Similar results were reported by Pelosi et al. [8] although the values of Cst,L in SP2 were significantly higher than those in SP1. Of interest is that in three of our patients the increase in EELV with PP was preserved during SP2. Hence, in some patients PP can act as a recruitment maneuver whose efficiency may persist after the patients are again in SP.

In short, this is the first study that systematically describes the lung and chest wall inflation volume-static pressure relationships in humans with prone positioning in acute hypoxemic respiratory failure. With the limitations we discussed, we have observed that alveolar recruitment may be one of the mechanisms by which PP can improve oxygenation in some patients and that it may persist after the SP has been resumed. Further studies on a larger number of patients are required to confirm this finding.

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