Prone Position Augments Recruitment and Prevents Alveolar Overinflation in Acute Lung Injury

Eftichia Galiatsou, Eleonora Kostanti, Eugenia Svarna, Athanasios Kitsakos, Vasilios Koulouras, Stauros C. Efremidis, and Georgios Nakos

Departments of Intensive Care Medicine and Clinical Radiology, University Hospital of Ioannina, Ioannina, Greece

Rationale: **Mechanical ventilation in the prone position may be an effective means of recruiting nonaerated alveolar units and minimizing ventilation-induced lung injury.**

Objectives: **To evaluate and quantify regional lung volume alterations when patients with lobar or diffuse acute lung injury (ALI) were turned prone after a recruitment maneuver.**

Methods: **In 21 patients with ALI, a recruitment maneuver was applied in the supine position followed by a multislice spiral computed tomography (CT) scan; then, patients were turned prone and a second CT scan was performed.**

Main Results: **Both the recruitment maneuver and prone position resulted in improved oxygenation in patients with lobar ALI. Prone position also resulted in increased respiratory system compliance and decreased Pa_{CO_2} in lobar ALI. In lobar ALI, the proportion of overinflated and nonaerated areas declined, whereas the proportion of well-aerated areas increased in the prone position. The decrease in overinflated areas was observed mainly in the ventral areas. The dorsal regions showed a decrease in nonaerated areas and an increase in well-aerated areas. Recruitment maneuver and prone position improved oxygenation but had no effect either on Pa_{CO_2} or on the respiratory system compliance of patients with diffuse ALI. These patients responded to prone position with a decrease in nonaerated areas.**

Conclusions: **Prone position recruited the edematous lung further than recruitment maneuvers and reversed overinflation, resulting in a more homogeneous distribution of aeration. The effects of the prone position were more pronounced in patients with lobar ALI.**

Keywords: acute lung injury; acute respiratory distress syndrome; computed tomography; prone position; recruitment maneuver

In acute respiratory distress syndrome (ARDS), the amount of normally aerated lung is strikingly reduced as a consequence of alveolar flooding and nonaeration. The majority of patients with acute lung injury (ALI) or its more severe form, ARDS, present with partially or normally aerated upper lobes and nonaerated lower lobes (1). In the supine position, the loss of functional lung volume predominates in the caudal and juxtadiaphragmatic regions and may result from cardiac and abdominal compression and from filling of alveoli and alveolar ducts by edematous fluid (2, 3). The "sponge lung" model, which has been recently challenged (3), describes how the increased lung mass due to edema and the increased superimposed pressure squeeze out the gas of the gravity-dependent lung regions, leading to loss of lung aeration (4, 5).

Recruitment is a dynamic, basically inspiratory process that refers to re-aeration of the previously nonaerated lung. Lung recruitment may be accomplished by periodically and briefly raising transpulmonary pressure to higher levels than those achieved during tidal ventilation (6), whereas positive end-expiratory pressure (PEEP) may prevent end-expiratory derecruitment. Although effective in recruiting the lung and reversing hypoxemia, recruitment maneuvers (RMs) have not shown a consistent and sustained effect in patients with ALI/ARDS (7). On the other hand, patients with ALI who demonstrate a distribution of hyperdensities in lower lobes and absence of a lower inflection point in pressure–volume curves are at risk of lung overinflation at high PEEP levels (8). In these patients with focal loss of aeration, compliance of the upper lobes remains normal, whereas compliance of the lower lobes is low; in this setting, the application of PEEP results in overinflation of the aerated lung areas (9). Overinflated lung regions are mainly found in the right middle lobe and lingula and in the anterior segments of lower lobes (10). Because high transpulmonary pressures for the nonaerated lung are, at the same time, "distending" pressures for the normally aerated lung, lung recruitment bears an inherent risk of alveolar overinflation (11). Alveolar overinflation is considered to be the most important factor related to ventilator-induced lung injury (VILI) (12).

Prone positioning is an adjunctive therapy that improves oxygenation in the majority of patients with ALI/ARDS (13, 14) and may be an effective means of recruiting nonaerated alveolar units and minimizing VILI when used early in the course of acute hypoxemic respiratory failure (15).

The purpose of this study was to evaluate and quantify regional lung volume alterations when patients with ALI/ARDS were turned prone after an RM.

Some of the results of these studies have been previously reported in the form of an abstract (16).

METHODS

Patients

This study was performed among patients admitted to the intensive care unit of the University Hospital of Ioannina, Greece, from May 2001 to October 2005. Of the 67 patients with ALI/ARDS admitted during that period, 22 consecutive patients with no contraindications to the prone position (17) who could safely be transported to the radiology department were eligible to be included in the study. One patient did not complete the study because of dislodgement of the endotracheal tube. Twenty-one patients were included in the analysis. ALI/ARDS was defined according to standard criteria (18). Cardiogenic pulmonary edema, chronic lung disease, and hemodynamic instability were considered as exclusion criteria. Patients were classified as having "lobar" ALI/ARDS if hyperattenuated areas had a lobar distribution with preserved aeration of the upper lobes or as having "diffuse" ALI/ARDS if loss of aeration was homogeneously distributed (19). The study protocol was approved by the local ethics committee, and informed consent was obtained from the next of kin of all patients.

Study Protocol

The timeline of study protocol is schematically displayed in Figure 1. Each patient was transferred to the radiology department by two physicians. Volume-controlled mechanical ventilation was provided using a Siemens

(*Received in original form June 10, 2005; accepted in final form April 24, 2006*)

Correspondence and requests for reprints should be addressed to Georgios Nakos, M.D., Associate Professor in Intensive Care, Director, Intensive Care Unit, University Hospital of Ioannina, University Street, 45500 Ioannina, Greece. E-mail: gnakos@cc.uoi.gr

Am J Respir Crit Care Med Vol 174. pp 187–197, 2006
Originally Published in Press as DOI: 10.1164/rccm.200506-899OC on April 27, 2006
Internet address: www.atsjournals.org

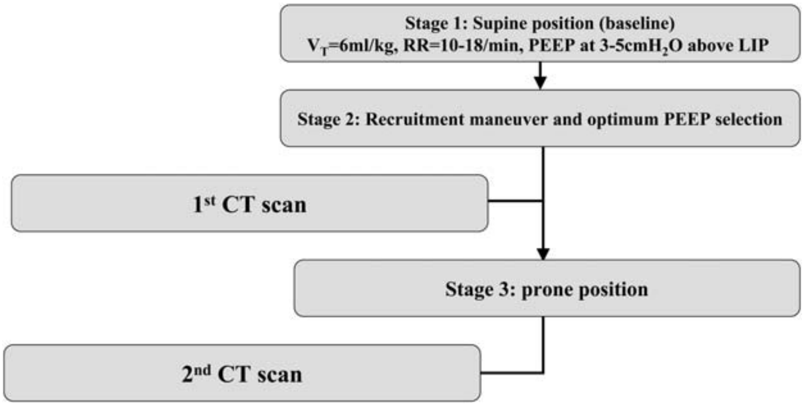

Figure 1. Schematic diagram of study protocol. At each stage, respiratory system compliance and blood gases were measured. The second computed tomography (CT) scan was performed after 30 min in the prone position. LIP = lower inflection point; PEEP = positive end-expiratory pressure.

Servo 300 ventilator (Siemens-Elemi, Solana, Sweden). Baseline respiratory variables were set as follows: frequency of 10 to 18 breaths/min and tidal volume of 6 ml/kg of ideal body weight. PEEP was set 3 to 5 cm H_2O above the lower inflection point. The pressure–volume curve was obtained using the quasistatic constant flow method. In cases where the lower inflection point was not identified, PEEP was set at 10 cm H_2O. $F_{I_{O_2}}$ was set at the minimal level at which an arterial oxygen saturation of 90% could be achieved.

Electrocardiogram, central venous pressure, arterial pressure, and pulse oximetry were monitored throughout the entire procedure using a Hewlett Packard M1166A monitor (Hewlett Packard, Andover, MA). Patients were sedated and paralyzed with intravenous midazolam and vecuronium bromide.

The study protocol was as follows: an RM was applied in the supine position followed by a multislice spiral CT scan. After the RM, patients were turned prone. After 30 min, a second spiral CT scan in the prone position was performed (Figure 1). All CT scans were performed at end of expiration. In four patients, one more CT scan was performed in the prone position and at the end of inspiration. Arterial blood gases and respiratory system compliance (Crs) were measured before and after the RM in the supine position, and after 30 min in the prone position. Crs was calculated by dividing tidal volume by the difference between plateau pressure and the sum of extrinsic and intrinsic PEEP (20).

RM

An RM was applied using a pressure-control mode with a 40-cm H_2O peak pressure and a 20-cm H_2O PEEP for 30 s. PEEP was subsequently reduced by 2-cm H_2O increments until a decrease in compliance was observed. A second RM was then performed and PEEP was set one step above the level at which compliance declined (optimum PEEP). Pressure-control level was kept at 20 cm H_2O during the optimum PEEP determination.

CT Scan

The first two patients included in the study underwent CT scan with a Philips Secura scanner that was available at that time. All the subsequent scans were performed with with a 16-slice tomographer (Mx8000IDT; Philips Medical Systems, Nederland B.V., Eindhoven, The Netherlands). Scan parameters were set as follows: 16 × 1.5 mm collimation; 140-kV tube voltage with a tube current-time product of 180 mA·s; pitch, 0.9; rotation time was 0.75 s; field-of-view, 400 × 400 mm^2; matrix, 512 × 512. For the analysis of the images, CT software was used (Mx View; Philips Medical Systems Nederland B.V.). All images were observed and analyzed in a width of 1,250 Hounsfield units (HU) and at a −700-HU level. The CT scan images were acquired with the patient in apnea at functional residual capacity (FRC) and at optimum PEEP for 25 s. The apnea at FRC was achieved by clamping the endotracheal tube with a forceps at end expiration.

Volumetric Analysis of the CT Scan

The objective of this analysis was to measure volume, weight, and distribution of the different lung zones: overinflated, well aerated, poorly aerated, and nonaerated. Contiguous multislice CT scans of the whole lung were taken. In each slice, the roller ball was used to trace the outline of inner pleura after marking mediastinal structures, pleural fluid collections, and ribs (Figure 2). Each lung was divided into three equal compartments along the sternovertebral anteroposterior axis: ventral, middle, and dorsal (Figure 2). The axis was set at the level of the bronchus bifurcation after measuring the anteroposterior diameter of thorax. To define the three lung compartments, a specially designed grid was applied to each lung section. The volume of each section was calculated by measuring the number of CT units of volume (voxels). With the aforementioned scan protocol, the voxel volume was 0.91 mm^3. The X-ray attenuation of tissue (radiologic density) in each voxel is expressed by CT numbers in HU (21). The attenuation scale assigns air a value of −1,000 HU, water a value of 0 HU, and bone a value of +1,000 HU. Lung zones were classified in one of the four categories: below −900 HU as overinflated, between −900 and −500 HU as well aerated, −500 to −100 as poorly aerated, and −100 to +100 as nonaerated (4, 22). The weight of tissue in each compartment was calculated as

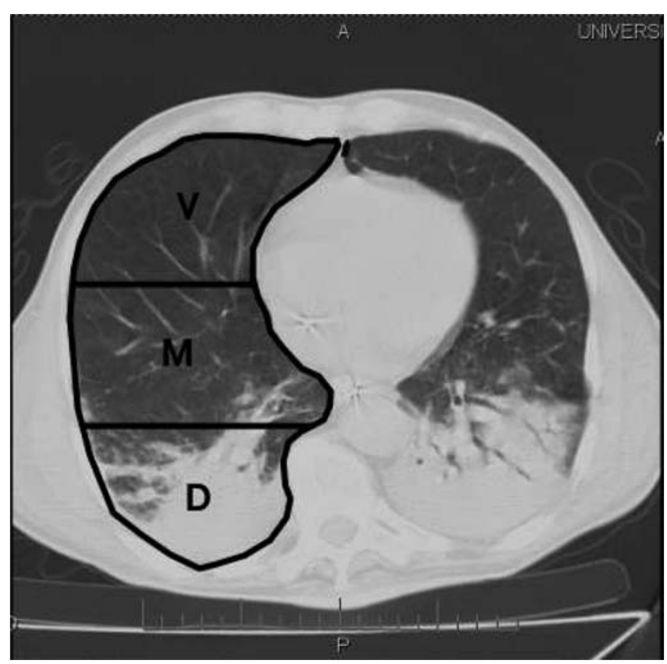

Figure 2. Volumetric analysis of CT scan. Each lung is divided into three equal sections along the anteroposterior axis: ventral (V), middle (M), and dorsal (D).

TABLE 1. DEMOGRAPHIC AND CLINICAL CHARACTERISTICS OF PATIENTS

Age, yr	43.15 ± 12.26*
Sex	7 F/14 M
Cause of admission	
Trauma	11
Stroke	7
Sepsis	3
ARDS lobar/diffuse	15/6
Duration of ICU stay, d	13.40 ± 8.03*
Duration of mechanical ventilation, d	11.27 ± 7.64*

Definition of abbreviations: ARDS = acute respiratory distress syndrome; F = female; ICU = intensive care unit; M = male.
* Values are expressed as mean ± SD.

volume of compartment × (1 − [average CT number of compartment/ −1.000]) (23).

Statistical Analysis

Statistical analysis was performed using the Statistical Package for Social Sciences version 12 for Windows (SPSS, Inc., Chicago, IL). Data were tested for normality using the Kolmogorov-Smirnov test and presented as means ± SD. Paired *t* tests or Wilcoxon matched pairs test were used to compare blood gases, respiratory compliance, and lung aeration between the study stages. Comparison between lobar and diffuse ARDS was made using a *t* test. A p value of less than 0.05 was considered statistically significant.

RESULTS

Twenty-one critically ill patients (7 female, 14 male) were included in this study (Table 1). Fifteen patients were classified as have lobar ALI/ARDS and six as having diffuse ALI/ARDS. The cause of admission was trauma in 11 patients, stroke in 7 patients, and sepsis in 3 patients. Mean age was 43.15 ± 12.26 yr. All patients had been mechanically ventilated on average for 11.27 ± 7.64 d at study entry.

Lobar ARDS

Crs and blood gases in the prone and supine positions are shown in Table 2. Both RM and prone position resulted in improved oxygenation ($P_{O_2}/F_{I_{O_2}}$: 106.25 ± 15.88 before vs. 143.00 ± 12.27 mm Hg after RM, p = 0.000, vs. 225.00 ± 37.82 mm Hg in prone position, p = 0.000). The Pa_{CO_2} remained practically at the same levels postrecruitment (44 ± 6.18 before vs. 42.7 ± 5.03 mm Hg after RM, p = 0.095), but declined in the prone position (42.7 ± 5.03 after RM vs. 36.25 ± 3.41 mm Hg prone, p = 0.001). Crs tended to increase post-RM, although this difference did not reach statistical significance (32.75 ± 4.23 before vs. 37.12 ± 6.31 mL/cm H_2O after, p = 0.061). A significant increase in Crs was noted in the prone position in comparison with the supine position post-RM (37.12 ± 6.31 supine vs. 43.12 ± 6.56 mL/cm H_2O prone, p = 0.019; Table 2).

The results of volumetric analysis are shown in Tables 3–8 and in Figures 3–5. Nonaerated lung compartments represented a substantial proportion, almost 50%, of both right and left lung weight in the supine position (47.95 ± 5.58 and 50.0 ± 2.72%, respectively). A nonuniform distribution of aeration was noted in the supine position along the sternovertebral axis, with predominance of poorly and nonaerated regions in the dorsal lung regions, whereas overinflated areas were observed mainly in the ventral regions (Tables 5–8). Overall, in the prone position, there was a significant reduction of nonaerated areas (51% for right and 59% for left lung weight), whereas the proportion of well-aerated and poorly aerated areas of both lungs increased in the prone position (Tables 3 and 4, Figure 3). The volume and weight of overinflated right lung and the volume of overinflated left lung decreased in the prone position (Table 3). When the same analysis was repeated for the three lung compartments, ventral, middle, and dorsal, it became obvious that, with the prone position, there was a decrease in overinflated areas in the ventral and middle areas of both lungs (Tables 5–8). The dorsal regions showed a predominant decrease in nonaerated areas and increase in well-aerated and poorly aerated areas (Tables 5–8). An increase in the volume of nonaerated areas of the ventral right lung was noted in the prone position (Table 5). This finding, however, was not consistent because when right lung weight was considered, no such redistribution of nonaerated areas toward the ventral regions was observed (Table 6). Similarly, there was no increase in the nonaerated ventral left lung weight or volume (Tables 7 and 8). Poorly aerated areas increased in the ventral and dorsal regions and tended to increase in the middle regions (Tables 5–8). We found no evidence of end-expiratory derecruitment in the prone position because the proportion of nonaerated regions and the overall distribution of aeration was unchanged between end inspiration and end expiration (Table 9).

TABLE 2. RESPIRATORY SYSTEM COMPLIANCE AND BLOOD GASES AT BASELINE, AFTER RECRUITMENT, AND IN PRONE POSITION

			Statistical Significance*			Statistical Significance†	
	Baseline (supine)	Post-RM (supine)	p Value	95% CI of the Difference	Prone Position	p Value	95% CI of the Difference
Lobar ARDS							
Crs	32.75 ± 4.23	37.12 ± 6.31	0.061	−9.01, 0.27	43.12 ± 6.56	0.019	−10.69, −1.31
P_{CO_2}	44 ± 6.18	42.7 ± 5.03	0.095	−0.28, 2.78	36.25 ± 3.41	0.01	3.56, 9.4
$P_{O_2}/F_{I_{O_2}}$	106.25 ± 15.88	143.00 ± 12.27	0.000	−43.42, −30.08	225.00 ± 37.82	0.000	−112.86, −1.14
Diffuse ARDS							
Crs	29.20 ± 4.44	32.60 ± 4.39	0.15	−5.283, −1.517	31.40 ± 4.28	0.31	0.64 to 1.75
P_{CO_2}	43.60 ± 5.59	43.00 ± 5.48	0.07	−0.08, 1.28	41.20 ± 4.15	0.09	−0.42, 4.02
$P_{O_2}/F_{I_{O_2}}$	117.8 ± 25.99	149.6 ± 20.38	0.04	−60.32, −3.28	180.4 ± 17.87	0.0003	−38.11, −23.49

Definition of abbreviations: ARDS = acute respiratory distress syndrome; CI = confidence interval; Crs = respiratory system compliance, RM = recruitment maneuver.
Values are expressed as mean ± SD.
* Comparison between baseline and post-RM.
† Comparison between post-RM and prone position.

TABLE 3. LOBAR ACUTE RESPIRATORY DISTRESS SYNDROME: PERCENTAGES OF RIGHT LUNG COMPARTMENTS ACCORDING TO AERATION

			Statistical Significance*	
	Post-RM Supine	Prone	p Value	95% CI of the Difference
		Right Lung Mass (n = 15)		
Overinflated	1.4 ± 0.69	0.29 ± 0.28	0.0031	0.5112, 1.767
Well aerated	35.6 ± 7,99	42.63 ± 7.26	0.0189	−12.40, −1.488
Poorly aerated	16.4 ± 3.77	32.14 ± 7.04	0.0002	−21.19, −10.21
Nonaerated	47.9 ± 5.58	23.20 ± 5.20	0.0000	19.43, 30.08
		Right Lung Volume (n = 15)		
Overinflated	9.9 ± 3.8	2.1 ± 1.7	0.000	4.72, 10.73
Well aerated	46.5 ± 7.9	65.2 ± 13.9	0.000	−22.78, −8.85
Poorly aerated	18.3 ± 13.2	18.0 ± 8.0	0.729	−9.53, 13.17
Nonaerated	25.3 ± 9.8	14.7 ± 3.7	0.001	6.97, 18.29

Definition of abbreviations: CI = confidence interval; RM = recruitment maneuver.
Values are expressed as mean ± SD.
* Comparison between supine (post-RM) and prone positions is made with paired t test.

TABLE 4. LOBAR ACUTE RESPIRATORY DISTRESS SYNDROME: PERCENTAGES OF LEFT LUNG COMPARTMENTS ACCORDING TO AERATION

			Statistical Significance*	
	Post-RM Supine	Prone	p Value	95% CI of the Difference
		Left Lung Mass (n = 15)		
Overinflated	1.46 ± 0.17	1.21 ± 1.75	0.683	−1.093, 1.584
Well aerated	33.69 ± 4.55	44.34 ± 6.29	0.0000	−13.60, −7.705
Poorly aerated	15.26 ± 2.28	35.86 ± 6.84	0.0000	−25.48, −15.73
Nonaerated	50.01 ± 2.72	20.42 ± 8.192	0.0000	21.82, 37.36
		Left Lung Volume (n = 15)		
Overinflated	10.40 ± 1.26	2.10 ± 1.28	0.000	7.54, 9.05
Well aerated	44.50 ± 5.48	66.50 ± 11.97	0.000	−29.15, −14.85
Poorly aerated	19.00 ± 13.71	15.20 ± 8.56	0.526	−9.23, 16.83
Nonaerated	26.10 ± 8.69	10.50 ± 4.37	0.000	9.22, 21.97

For definition of abbreviations, *see* Table 3.
Values are expressed as mean ± SD.
* Comparison between prone and supine positions is made with paired t test.

TABLE 5. LOBAR ACUTE RESPIRATORY DISTRESS SYNDROME: PERCENTAGES OF VENTRAL, MIDDLE, AND DORSAL RIGHT LUNG VOLUME ACCORDING TO AERATION

	Ventral				Middle				Dorsal			
			Statistical Significance*				Statistical significance*				Statistical Significance*	
	Post-RM Supine	Prone	p Value	95% CI of the Difference	Post-RM Supine	Prone	p Value	95% CI of the Difference	Post-RM Supine	Prone	p Value	95% CI of the Difference
OI	6.73 ± 2.24	1.09 ± 1.04	0.000	3.83, 7.45	1.91 ± 1.37	0.00 ±	0.001	0.98, 2.83	1.18 ± 1.40	1.00 ±	0.774	−1.18, 1.55
WA	21.09 ± 3.01	19.00 ± 5.19	0.055	−1.71, 5.91	19.18 ± 5.17	20.36 ± 9.91	0.250	−5.73, 3.37	6.18 ± 2.36	22.81 ± 9.90	0.000	−23.02, −10.25
PA	2.73 ± 1.95	3.63 ± 2.41	0.351	−2.97, 1.16	7.63 ± 4.73	5.00 ± 2.14	0.114	−0.75, 6.03	8.27 ± 7.55	8.55 ± 5.97	0.938	−7.93, 7.39
NA	1.82 ± 1.77	4.63 ± 3.26	0.017	−5.02, −0.61	4.18 ± 3.37	1.27 ± 0.90	0.007	0.99, 4.82	19.27 ± 6.82	6.36 ± 2.15	0.000	7.76, 17.51

Definition of abbreviations: CI = confidence interval; NA = nonaerated areas; OI = overinflated areas; PA = poorly aerated areas; RM = recruitment maneuver; WA = well-aerated areas.
Values are expressed as mean ± SD; n = 15, right lung.
* Comparison between prone and supine position is made with paired t test.

Diffuse ARDS

Both the RM and prone position resulted in improved oxygenation in patients with diffuse ARDS and had a neutral effect on P_{CO_2} (Table 2). Crs was not affected by either RM or prone position (Table 2).

Nonaerated areas represented one-third of both right and left lung mass in patients with diffuse ARDS in the supine position (29.33 ± 12.91 and 36.21 ± 14.12%, respectively; Tables 10 and 11). Nonaerated areas were located mainly in dorsal regions of both lungs in the supine position (Tables 12 and 13). In the prone position, nonaerated areas significantly decreased and well-aerated areas tended to increase, although this did not reach statistical significance (Tables 10 and 11). When analysis

TABLE 6. LOBAR ACUTE RESPIRATORY DISTRESS SYNDROME: PERCENTAGES OF VENTRAL, MIDDLE, AND DORSAL RIGHT LUNG MASS ACCORDING TO AERATION

	Ventral				Middle				Dorsal			
			Statistical Significance*				Statistical Significance*				Statistical Significance*	
	Post-RM Supine	Prone	p Value	95% CI of the Difference	Post-RM Supine	Prone	p Value	Prone	Post-RM Supine		p Value	95% CI of the Difference
OI	0.95 ± 0.39	0.15 ± 0.16	0.000	0.44, 1.16	0.30 ± 0.20	0.00 ± 0.00	0.002	0.15, 0.46	0.17 ± 0.25	0.14 ± 0.16	0.790	−0.24, 0.30
WA	15.99 ± 3,54	13.56 ± 4.83	0.120	−0.79, 5.65	15.04 ± 4.39	16.21 ± 3.71	0.440	−4.47, 2.14	4.73 ± 1.99	12.86 ± 3.20	0.000	−10.75, −5.50
PA	2.65 ± 1,.8	6.611 ± 3.01	0.001	−5.88, −2.05	7.16 ± 2.53	8.75 ± 3.26	0,323	−5.09, 1.90	6.32 ± 1.92	17.47 ± 6.96	0.001	−16.67, −5.62
NA	3.85 ± 2.95	8.51 ± 6.20	0.067	−9.73, 0.40	7.86 ± 4.63	2.67 ± 1.29	0.005	2.05, 8.33	36.40 ± 5.05	11.62 ± 4.05	0.000	19.58, 29.98

For definition of abbreviations, *see* Table 5.
Values are expressed as mean ± SD; right lung, n = 15.
* Comparison between prone and supine position is made with paired *t* test.

TABLE 7. LOBAR ACUTE RESPIRATORY DISTRESS SYNDROME: PERCENTAGES OF VENTRAL, MIDDLE, AND DORSAL LEFT LUNG VOLUME ACCORDING TO AERATION

	Ventral				Middle				Dorsal			
			Statistical Significance*				Statistical Significance*				Statistical Significance*	
	Post-RM Supine	Prone	p Value	95% CI of the Difference	Post-RM Supine	Prone	p Value	95% CI of the Difference	Post-RM Supine	Prone	p Value	95% CI of the Difference
OI	6.27 ± 0.90	1.18 ± 0.98	0.000	4.38, 5.79	2.91 ± 1.57	0.09 ± 0.30	0.000	1.70, 3.94	1.37 ± 1.12	0.09 ± 0.30	0.005	0.47, 2.07
WA	21.18 ± 8.58	16.55 ± 7.51	0.182	−2.56, 11.83	18.91 ± 4.52	15.63 ± 5.62	0.004	1.32, 5.22	7.36 ± 3.69	30.36 ± 12.01	0.000	−31.68, −14.32
PA	1.73 ± 1.55	4.91 ± 3.20	0.028	−5.93, −0.43	7.00 ± 5.03	4.00 ± 2.75	0.085	−0.49, 6.49	9.45 ± 7.21	7.27 ± 5.33	0.516	−5.04, 9.41
NA	2.00 ± 1.09	3.18 ± 2.40	0.103	−2.65, 0.28	3.82 ± 2.22	1.64 ± 1.43	0.001	1.06, 3.29	20.64 ± 6.90	6.09 ± 2.77	0.000	9.27, 19.81

For definition of abbreviations, *see* Table 5.
Values are expressed as mean ± SD; left lung, n = 15.
* Comparison between prone and supine position is made with paired *t* test.

TABLE 8. LOBAR ACUTE RESPIRATORY DISTRESS SYNDROME: PERCENTAGES OF VENTRAL, MIDDLE, AND DORSAL LEFT LUNG MASS ACCORDING TO AERATION

	Ventral				Middle				Dorsal			
			Statistical Significance*				Statistical Significance*				Statistical Significance*	
	Supine	Prone	p Value	95% CI of the Difference	Supine	Prone	p Value	95% CI of the Difference	Supine	Prone	p Value	95% CI of the Difference
OI	0.86 ± 0.13	0.16 ± 0.14	0.000	0.58, 0.82	0.44 ± 0.20	0.02 ± 0.05	0.000	0.2440, 0.59	0.17 ± 0.16	0.63 ± 1.02	0.212	−1.24, 0.323
WA	14.68 ± 5.20	12.62 ± 6.37	0.202	−1.37, 5.50	14.06 ± 1.67	15.80 ± 7.98	0.568	−8.50, 5.02	4.87 ± 2.13	17.76 ± 3.63	0.000	−16.06, −9.73
PA	1.65 ± 1.52	8.44 ± 4.38	0.004	−10.74, −2.826	5.93 ± 1.21	9.34 ± 5.09	0.07	−7.188, 0.36	7.83 ± 2.49	18,09 ± 5,10	0.000	−13.94, −6.59
NA	3.90 ± 1.53	6.00 ± 4.37	0.157	−5.217, 1.010	7.13 ± 3.49	3,57 ± 2.53	0.008	1.19, 5.93	38.99 ± 4.14	10.85 ± 5.56	0.000	21.20, 35.09

For definition of abbreviations, *see* Table 5.
Values are expressed as mean ± SD; left lung, n = 15.
* Comparison between prone and supine position is made with paired *t* test.

was repeated for the three lung areas (ventral, middle, and dorsal), it appeared that dorsal well-aerated areas increased in the prone position (Tables 12 and 13). Dorsal nonaerated areas decreased (27–44% for right and left lung, respectively), although this difference was statistically significant only when lung volume was considered (Tables 12 and 13). There was no redistribution of nonaerated areas toward the ventral compartment (Tables 12 and 13).

Comparison between Lobar and Diffuse ARDS

We compared the differential response of the two subsets of patients to the prone position. The diffuse ARDS group presented with a smaller amount of nonaerated lung in the supine position (Tables 3, 4, 10, and 11). The lobar ARDS group displayed a greater response because the reduction in nonaerated areas of both right and left lung was greater than in the diffuse group (25 vs. 12% reduction for the right lung, at p = 0.019, and 30 vs. 13% reduction for the left lung, at p = 0.0062, respectively; Figures 6 and 7). Although the amount of overinflated lung was similar in lobar and diffuse ARDS (approximately 9% of lung volume in both groups), a greater reduction in overinflated areas of right lung was observed for patients in the lobar ARDS group in comparison with the diffuse ARDS group (1.2 vs. 0.2%, p = 0.0285), whereas no such difference was noted in the left lung (p = 0.98; Figures 6 and 7).

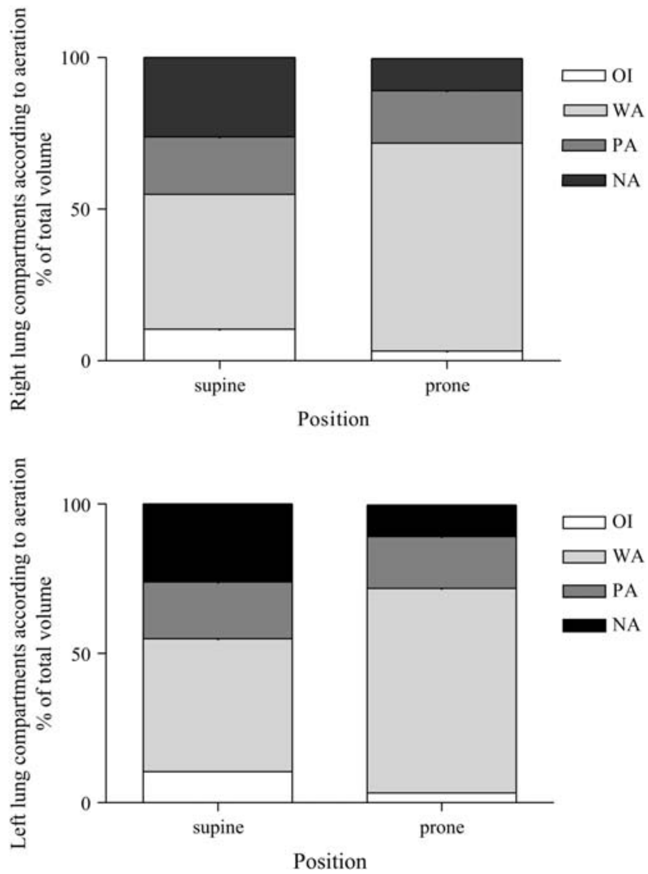

Figure 3. Distribution of the differently aerated areas of the right and left lung volume in lobar acute lung injury (ALI)/acute respiratory distress syndrome (ARDS). Comparison between the supine (post-recruitment) and prone positions. , NA = nonaerated; OI = overinflated; PA = poorly aerated; WA = well aerated.

DISCUSSION

This study, which has examined the effects of proning applied after an RM on the distribution of lung aeration in ALI/ARDS, has produced five findings:

1. Patients with diffuse and lobar ALI/ARDS presented with a significant amount of nonaerated lung and a high potential for recruitment soon after an RM in the supine position.
2. Prone position and RM had an additive effect on oxygenation. The prone position recruited the edematous lung in dependent areas more than the RM had achieved, and reversed overinflation of ventral areas.
3. These effects of the prone position were more pronounced in lobar ALI/ARDS. Patients with the diffuse pattern responded to the prone position with recruitment of nonaerated areas but showed no reversal of ventral overinflation.
4. There was no redistribution of nonaerated areas toward the ventral compartment in the prone position.
5. There was no evidence of end-expiratory "de-recruitment" in the prone position. In other words, the prone position resulted in decreased "dispersion" of aeration and decreased alveolar overinflation, an effect that is possibly protective against ventilator-induced lung injury.

To our knowledge, there is still limited and rather indirect support of such an effect of the prone position in human studies (24, 25), whereas some animal studies have shown that the prone position may alleviate VILI. In experimental animal models, the prone position resulted in less lung edema and less severe histologic abnormality than did the supine position (18), or delayed the progression of VILI, possibly by inducing a more uniform distribution of lung strain (26). A recent randomized study has shown that prone position but not PEEP improved oxygenation in ARDS with localized infiltrates, whereas patients with diffuse infiltrates responded to PEEP, whatever their position (25). We have shown that diffuse ALI/ARDS also

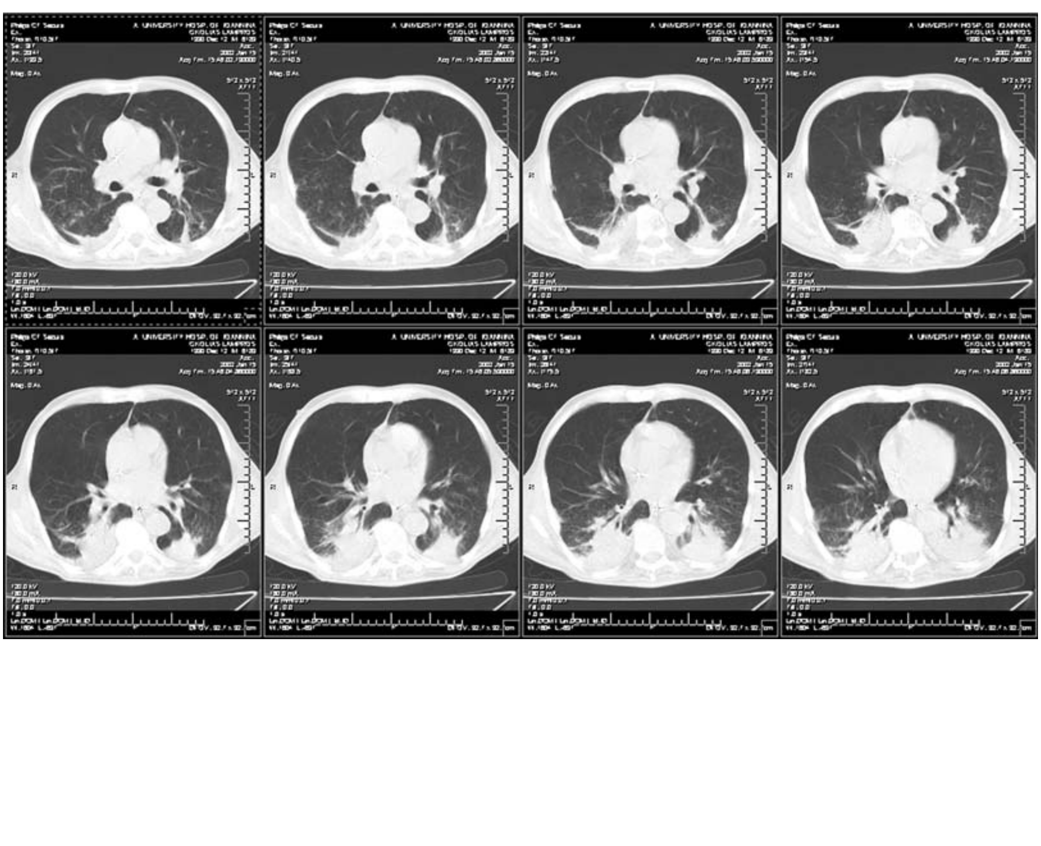

Figure 4. A thoracic CT scan obtained at end expiration in the supine position shows bilateral nonaerated dorsal areas.

Figure 5. The thoracic CT scan of the same patient as shown in Figure 4 obtained at end expiration in the prone position shows the dramatic decrease of the dorsal nonaerated areas.

responds to prone positioning albeit to a lesser degree and without reversing overinflation. In patients with ARDS and dynamic hyperinflation, the prone position has improved alveolar ventilation and gas exchange without increasing overinflation (24). In our patients with lobar ALI/ARDS, the parallel increase in Pa_{O_2} and decrease in Pa_{CO_2} after prone positioning may reflect the reduction in overinflated areas and physiologic dead space or an optimization of ventilation–perfusion matching. CO_2 exchange is of great prognostic significance in early ARDS, as elevated values of dead-space fraction are associated with increased risk of death (27). Patients with ALI/ARDS who respond to prone positioning with reduction of the Pa_{CO_2} have a better outcome than the patients who do not (28). It is not yet clear whether this effect of prone position on CO_2 exchange is due to blood flow redistribution from nonaerated to aerated areas of the lung, or to recruitment of previously nonaerated and perfused regions. In healthy experimental animals, PEEP in the prone position results in a more uniform distribution of pulmonary blood flow, than in the supine position (29). When supine, application of PEEP resulted in accentuation of the gravity dependence of blood flow. In the prone position with the same amount of PEEP, blood flow was kept more uniform, possibly as a result of more uniform transalveolar pressures.

TABLE 9. LOBAR ACUTE RESPIRATORY DISTRESS SYNDROME: DIFFERENCES IN AERATION AT END EXPIRATION VERSUS END INSPIRATION

	End Expiration	End Inspiration	p Value*
		Right Lung (n = 4)	
Overinflated	0.34 ± 0.27	0.41 ± 0.24	0.1250
Well aerated	42.48 ± 6.16	43.85 ± 4.12	0.3750
Poorly aerated	33.38 ± 3.10	35.00 ± 4.79	0.3750
Nonaerated	23.70 ± 6.47	25.18 ± 7.84	0.6250
		Left Lung (n = 4)	
Overinflated	1.33 ± 1.68	0.58 ± 0.14	0.8750
Well aerated	45.94 ± 3.51	49.65 ± 5.04	0.1250
Poorly aerated	35.41 ± 6.72	38.50 ± 10.41	0.3750
Nonaerated	17.36 ± 6.84	17.62 ± 4.23	1.1250

Values are expressed as mean ± SD.

* Comparison between prone and supine position is made with a Wilcoxon matched pairs test.

The bulk of studies analyzing the physiologic effects of prone positioning refer to the early stages of ARDS. ARDS is a syndrome that includes patients with diverse pathologic and functional characteristics and with different reactions to therapeutic maneuvers. The lung pathology of ARDS involves alveolar flooding, interstitial inflammation, and edema, with lung nonaeration that predominates in the caudal and juxtadiaphragmatic regions (4). Lung protective modes of mechanical ventilation with low tidal volumes might further increase the loss of lung aeration. Although effective in recruiting the lung and reversing hypoxemia, RMs have not shown a consistent and sustained effect in patients with ALI/ARDS (7). Previous studies have revealed that combining the prone position with cyclic sighs as RMs may provide optimal recruitment in early ALI/ARDS (30).

Approximately one-third of patients with ARDS present with bilateral attenuations almost exclusively in the lower lobes (1). ARDS in these patients is more frequently of secondary origin and pressure–volume curves show a lower inflection point that is either absent or less than 5 cm H_2O. The lungs of patients with lobar CT attenuations can be described as a bicompartmental model composed of a compliant and a stiff compartment. Because of the interdependence between these two compartments, PEEP-induced overinflation in the compliant compartment prevents recruitment of the other (9). Prone position reduces lobar interdependence and promotes the recruitment of juxtadiaphragmatic lung regions by decreasing the chest wall compliance through a limitation of the expansion of the cephalic parts of the thorax (31). Our patients with lobar ARDS fulfill the criteria for ARDS definition (32) and present lower lobar distribution of densities with preserved aeration of the upper lobes (1). Arterial oxygenation impairment in these patients was severe, in contrast to the lack of extensive diffuse radiologic abnormalities. They apparently responded partially to the RM but have shown an impressive reversal of nonaeration and an increase of the well-aerated and poorly aerated compartments in the prone position. This was combined with increased Crs in the prone position. The re-aeration of the injured lung involves

TABLE 10. DIFFUSE ACUTE RESPIRATORY DISTRESS SYNDROME: PERCENTAGES OF RIGHT LUNG ACCORDING TO AERATION

			Statistical Significance*	
	Post-RM Supine	Prone	p Value	95% CI of the Difference
		Right Lung Mass (n = 6)		
Overinflated	1.65 ± 2.45	1.47 ± 2.21	0.236	−0.1825, 0.5505
Well aerated	39.81 ± 5,48	48.38 ± 10.75	0.058	−17.59, 0.4458
Poorly aerated	29.02 ± 14.75	34.20 ± 14.85	0.314	−17.69, 7.321
Nonaerated	29.33 ± 12.91	15.96 ± 12.48	0.026	2.657, 24.09
		Right Lung Volume (n = 6)		
Overinflated	8.60 ± 11.26	6.86 ± 9.16	0.1751	−1.195, 4.675
Well aerated	55.80 ± 5.67	62.00 ± 4.36	0,0579	−12.73, 0.3339
Poorly aerated	20.80 ± 12.15	23.20 ± 12.40	0.50	−11.46, 6.664
Nonaerated	14.80 ± 7.56	8.00 ± 5.61	0.0299	1.084, 12.52

For definition of abbreviations, *see* Table 3.
Values are expressed as mean ± SD.
* Comparison between prone and supine position is made with paired t test.

TABLE 11. DIFFUSE ACUTE RESPIRATORY DISTRESS SYNDROME: PERCENTAGES OF LEFT LUNG ACCORDING TO AERATION

			Statistical Significance*	
	Supine	Prone	p Value	95% CI of the Difference
		Left Lung Mass (n = 6)		
Overinflated	1.68 ± 2.64	1.95 ± 0.87	0.407	− 0.58, 1.15
Well aerated	37.03 ± 8.15	44.09 ± 12.79	0.072	−15.17, 1.03
Poorly aerated	25.47 ± 6.7 8	31.61 ± 10.14	0.124	−14.92, 2.64
Nonaerated	36.21 ± 14.12	23.03 ± 15.07	0.006	6.133, 20.22
		Left Lung Volume (n = 6)		
Overinflated	8.60 ± 11.80	7.00 ± 8.72	0,317	−2.286, 5.486
Well aerated	52.80 ± 7.22	58.60 ± 9.74	0.145	−14.73, 3.126
Poorly aerated	18.40 ± 5.46	22.20 ± 9.31	0.185	−10.39, 2.793
Nonaerated	19.40 ± 9.66	12.00 ± 9.06	0.012	2.705, 12.09

For definition of abbreviations, *see* Table 3.
Values are expressed as mean ± SD.
* Comparison between prone and supine position is made with paired t test.

TABLE 12. DIFFUSE ACUTE RESPIRATORY DISTRESS SYNDROME: PERCENTAGES OF VENTRAL, MIDDLE, AND DORSAL RIGHT LUNG ACCORDING TO AERATION

	Ventral				Middle				Dorsal			
			Statistical Significance*				Statistical Significance*				Statistical Significance*	
	Supine	Prone	p Value	95% CI of the Difference	Supine	Prone	p Value	95% CI of the Difference	Supine	Prone	p Value	95% CI of the Difference
					Right Lung Mass (n = 6)							
OI	1.27 ± 1.93	1.07 ± 1.86	0.121	−0.083, 0.48	0.34 ± 0.45	0.29 ± 0.39	0.233	−0.04, 0.14	0.04 ± 0.09	0.10 ± 0.22	0.648	−0.38, 0.27
WA	15.15 ± 3.22	14.78 ± 4.84	0.881	−5.99, 6.72	15.47 ± 3.64	18.10 ± 4.79	0.129	−6.48, 1.21	9.19 ± 2.32	15.64 ± 3.72	0.017	−11.02, −1.88
PA	6.98 ± 2.18	10.12 ± 4.50	0.077	−6.84, 0.55	11.28 ± 7.87	9.49 ± 5.78	0.394	−3.43, 7.01	10.76 ± 6.17	14.59 ± 7.58	0.356	−14.05, 6.39
NA	3.17 ± 2.72	1.85 ± 1.85	0.110	−0.47, 3.12	6.97 ± 5.83	4.93 ± 2.59	0.266	−2.35, 6.42	19.19 ± 5.55	13.91 ± 7.51	0.075	−0.87, 11.44
					Right Lung Volume							
OI	6.60 ± 8.82	4.86 ± 7.69	0.084	−0.37, 3.85	1.80 ± 2.17	1.40 ± 1.67	0.177	−0.28, 1.08	0.20 ± 0.44	0.60 ± 1.34	0.587	−2.283, 1.48
WA	21.40 ± 5.13	18.80 ± 4.32	0.392	−4.93, 10.13	21.40 ± 1.95	23.20 ± 3.42	0.410	−7.24, 3.64	13.00 ± 3.67	20.20 ± 4.27	0.024	−12.85, −1.552
PA	5.00 ± 1.87	7.00 ± 3.74	0.102	−4.63, 0.63	8.20 ± 6.38	6.60 ± 4.67	0.305	−2.19, 5.39	7.60 ± 4.77	9.60 ± 5.46	0.494	−9.397, 5.397
NA	1.60 ± 1.52	0.80 ± 0.84	0.099	−0.24, 1.84	3.60 ± 3.21	2.30 ± 1.30	0.229	−1.24, 3.84	9.60 ± 3.36	6.70 ± 3.74	0.032	0.4016, 5.398

For definition of abbreviations, *see* Table 5.
Values are expressed as mean ± SD.
* Comparison between prone and supine position is made with paired t test.

TABLE 13. DIFFUSE ACUTE RESPIRATORY DISTRESS SYNDROME: PERCENTAGES OF VENTRAL, MIDDLE, AND DORSAL LEFT LUNG ACCORDING TO AERATION

	Ventral				Middle				Dorsal			
			Statistical Significance*				Statistical Significance*				Statistical Significance*	
	Supine	Prone	p Value	95% CI of the Difference	Supine	Prone	p Value	95% CI of the Difference	Supine	Prone	p Value	95% CI of the Difference
					Left Lung Mass (n = *6*)							
OI	1.18 ± 1.93	0.98 ± 1.66	0.220	−0.18, 0.59	0.26 ± 0.36	0.25 ± 0.17	0.946	−0.30, 0.3187	0,23 ± 0.36	0.07 ± 0.15	0.423	−0.35, 0.67
WA	12.06 ± 4.68	12.49 ± 5.56	0.853	−6.45, 5.60	15.90 ± 1.90	18.50 ± 5.81	0.286	−8.44, 3.260	9.06 ± 3.47	13.64 ± 4.00	0.000	−5.89, −3.27
PA	6.48 ± 2.09	10.11 ± 4.06	0.025	−6.52, −0.73	10.88 ± 3.02	11.20 ± 5.76	0.888	−6.16, 5.53	8.10 ± 3.65	10.30 ± 0.83	0.262	−6.90, 2.49
NA	3.29 ± 4.58	2.93 ± 3.23	0.799	−3.28, 3.99	11.15 ± 8.76	7.95 ± 4.12	0.394	−6.12, 12.53	21.76 ± 11.48	12.14 ± 10.95	0.051	−0.07, 19.31
					Left Lung Volume (n = *5*)							
OI	6.00 ± 8.60	4.80 ± 7.46	0.178	−0.84, 3.24	1.40 ± 1.67	1.40 ± 0.89	1.00	−1.52, 1.52	3.60 ± 4.50	0.40 ± 0.89	0.405	−1.59, 3.19
WA	16.80 ± 3.83	16.40 ± 5.32	0.897	−7.67, 8.47	23.30 ± 4.27	24.80 ± 6.38	0.587	−9.13, 5.93	12.80 ± 4.44	18.20 ± 3.90	0.000	−6.81, −3.98
PA	4.80 ± 2.05	7.20 ± 3.83	0.051	−4.82, 0.02	8.00 ± 2.83	7.80 ± 4.32	0.897	−3.86, 4.26	5.60 ± 1.67	7.20 ± 1.79	0.242	−4.84, 1.64
NA	1.80 ± 2.49	1.40 ± 1.67	0.587	−1.48, 2.28	5.80, 5.07	4.00, 2.35	0.415	−3.71, 7.31	11.80 ± 7.40	6.60 ± 6.65	0.039	0.44, 9.96

For definition of abbreviations, *see* Table 5.
Values are expressed as mean ± SD.
* Comparison between prone and supine position is made with paired t test.

first an increase in alveolar volume and displacement of the gas–liquid interface from the alveolar ducts to the alveolus, and subsequent translocation of the edematous fluid to the interstitium (33). Given that the time required for fluid transfer from the alveoli to the pulmonary interstitium is a few minutes, we hypothesize that the increase of poorly and well-aerated areas in combination with the improved Crs after 30 min in the prone position could be attributed to transformation of alveolar edema to interstitial and to amplified edema clearance (3, 33). Cardiac and abdominal compression appear to be the main factors causing loss of dorsal and caudal lung aeration (2, 34, 35). Decrease of intra-abdominal pressure and relief of abdominal compression in the prone position could possibly be an additional factor associated with increased edema clearance in the prone position (36, 37). Prone position in animals improves oxygenation and gas exchange to a greater degree in the presence of, versus the absence of, abdominal distension and decreases intragastric pressure in the presence of abdominal distension (36). In experimental ALI, a rise in intraabdominal pressure increased the amount of lung edema mainly in the base lung regions, and this was possibly due to a combination of increased edema formation and decreased clearance (37). All our patients were turned prone with the abdomen suspended, but we were not monitoring esophageal and intraabdominal pressure throughout the procedure and this is a limitation of our method.

Another potential methodologic limitation of this study involves the risk of underestimating lung aeration by CT, particularly when lung morphology displays a focal loss of aeration (38). In this case, thick (10-mm) CT sections may lead to a significant underestimation of overinflated, poorly aerated, nonaerated compartments. Except in the first two patients included in this study, we have used 1.5-mm CT sections that allow an accurate assessment of lung overinflation. Radiologic density does not measure "aeration" but rather a combination of aeration, blood volume, and fluid volume. For example, the average CT attenuation in each "well aerated" voxel can be composed of either well-aerated alveoli or an equal amount of overinflated and nonaerated alveoli. Thus, decreasing voxel size allows a greater degree of precision. The volume of an acinus at FRC is 16 to 22 mm^3, which contains approximately 2,000 alveoli (23). The voxel volume in this study was 0.91 mm^3 (i.e., it contained 83–114 alveoli at FRC).

Prone positioning is currently used as an adjunctive therapy during mechanical ventilation to improve oxygenation, although no randomized controlled study has demonstrated a favorable effect of prone positioning *per se* on the outcome of patients with acute respiratory failure (14, 39). Several possible mechanisms of benefit have been proposed, such as increase in FRC, more uniform distribution of regional ventilation, and more efficient drainage of secretions. Our small-scale study supports the idea that the prone position, when performed after an RM, is an

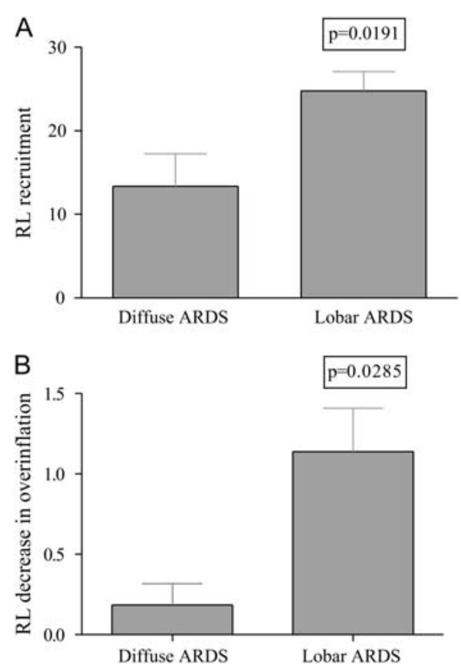

Figure 6. Differential response of diffuse and lobar ARDS to the prone position. Decrease in the mass of nonaerated areas of right lung (= RL recruitment) is greater for lobar ARDS (*A*). Decrease in overinflated areas of right lung (RL) is also greater for lobar ARDS (*B*).

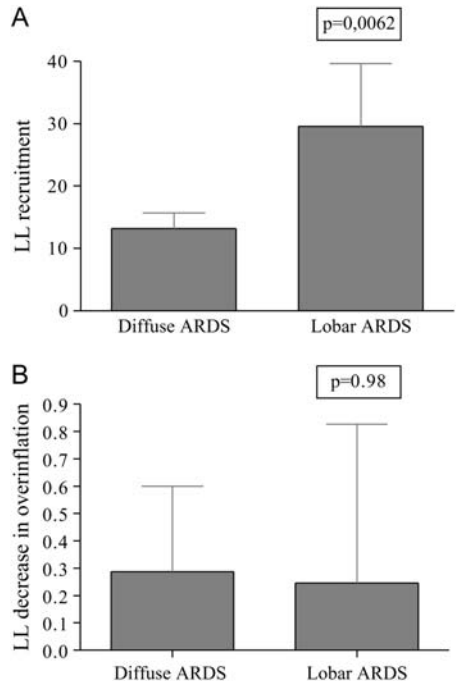

Figure 7. Differential response of diffuse and lobar ARDS to the prone position. Decrease in the mass of nonaerated areas of left lung (= LL recruitment) is greater for lobar ARDS (*A*). Decrease in overinflated areas of left lung (LL) is similar for lobar and diffuse ARDS (*B*).

effective method of recruiting nonaerated alveolar units and preventing overinflation—in this way, part of a lung protective strategy that could possibly alleviate VILI, especially in lobar ALI/ARDS.

***Conflict of Interest Statement*:** None of the authors has a financial relationship with a commercial entity that has an interest in the subject of this manuscript.

References

1. Rouby JJ, Puybasset L, Cluzel P, Richecoeur J, Lu Q, Grenier P. Regional distribution of gas and tissue in acute respiratory distress syndrome: II. Physiological correlations and definition of an ARDS severity score. *Intensive Care Med* 2000;26:1046–1056.
2. Rouby JJ, Constantin JM. Roberto de A Girardi C, Zhang M, Lu Q. Mechanical ventilation in patients with acute respiratory distress syndrome. *Anesthesiology* 2004;101:228–234.
3. Hubmayr RD. Perspective on lung injury and recruitment: a sceptical look at the opening and collapse story. *Am J Respir Crit Care Med* 2002;165:1647–1653.
4. Rouby JJ, Puybasset L, Nieszkowska A, Lu Q. Acute respiratory distress syndrome: lessons from computed tomography of the whole lung. *Crit Care Med* 2003;3:S285–S295.
5. Gattinoni L, Caironi P, Pelosi P, Goodman LR. What has computed tomography taught us about the acute respiratory distress syndrome? *Am J Respir Crit Care Med* 2001;164:1701–1711.
6. Amato MBP, Barbas CSV, Medeiros DM, Magaldi RB, Schettino GP, Lorenzi-Filho G, Kairalla RA, Deheinzelin D, Munoz C, Oliveira R, *et al.* Effect of a protective-ventilation strategy on mortality in the acute respiratory distress syndrome. *N Engl J Med* 1998;338:347–354.
7. The ARDS Clinical Trials Network, National Heart, Lung, and Blood Institute, National Institutes of Health. Effects of recruitment maneuvers in patients with acute lung injury and acute respiratory distress syndrome ventilated with high positive end-expiratory pressure. *Crit Care Med* 2003;31:2592–2597.
8. Vieira RR, Puybasset L, Lu Q, Richecoeur J, Cluzel P, Coriat P, Rouby JJ. A scanographic assessment of pulmonary morphology in acute lung injury: significance of the lower inflection point detected on the lung pressure-volume curve. *Am J Respir Crit Care Med* 1999;159:1612–1623.
9. Puybasset L, Gusman P, Muller J-C, Cluzel P, Coriat P, Rouby JJ. Regional distribution of gas and tissue in acute respiratory distress syndrome: III. Consequences for the effects of positive end-expiratory pressure. *Intensive Care Med* 2000;26:1215–1227.
10. Nieszkowska A, Lu Q, Vieira S, Elman M, Fetita C, Rouby JJ. Incidence and regional distribution of lung overinflation during mechanical ventilation with positive end-expiratory pressure. *Crit Care Med* 2004;32: 1496–1503.
11. Rouby JJ. Lung overinflation: the hidden face of alveolar recruitment. *Anesthesiology* 2003;99:2–4.
12. American Thoracic Society. International Consensus Conferences in Intensive Care Medicine: ventilator-associated lung injury in ARDS. *Am J Respir Crit Care Med* 1999;160:2118–2124.
13. Nakos G, Tsangaris I, Kostanti E, Nathanail C, Lachana A, Koulouras V, Kastani D. Effect of the prone position on patients with hydrostatic pulmonary edema compared with patients with acute respiratory distress syndrome and pulmonary fibrosis. *Am J Respir Crit Care Med* 2000;161:360–368.
14. Gattinoni L, Tognoni G, Pesenti A, Taccone P, Mascheroni D, Labarta V, Malacrida R, Di Giulio P, Fumagalli R, Pelosi P, *et al.*; Prone-Supine Study Group. Effect of prone positioning on the survival of patients with acute respiratory failure. *N Engl J Med* 2001;345:568–573.
15. Pelosi P, Brazzi L, Gattinoni L. Prone position in acute respiratory distress syndrome. *Eur Respir J* 2002;20:1017–1028.
16. Nakos G, Svarna E, Kitsakos A, Koulouras V, Kostandi E, Metaphragi E, Galiatsou E, Efremidis S. Prone position opens the lung further than the recruitment maneuver and reduces overdistention. Sixth State of the Art Interdisciplinary Review Course on Pulmonary Diseases, Critical Care, Emergency Medicine, and Nursing Care, Athens; 2002.
17. Messerole E, Peine P, Wittkopp S, Marini JJ, Albert RK. The pragmatics of prone positioning. *Am J Respir Crit Care Med* 2002;165:1359–1363.
18. Broccard A, Shapiro RS, Schmitz LL, Adams AB, Nahum A, Marini JJ. Prone position attenuates and redistributes ventilator-induced lung injury in dogs. *Crit Care Med* 2000;28:295–303.
19. Puybasset L, Cluzel P, Gusman P, Grenier P, Preteux F, Rouby JJ. Regional distribution of gas and tissue in acute respiratory distress syndrome: I. Consequences for lung morphology. *Intensive Care Med* 2000;26:857–869.
20. Gattinoni L, Pesenti A, Avalli L, Rossi F, Bombino M. Pressure-volume curve of the total respiratory system in acute respiratory failure: computed tomographic scan study. *Am Rev Respir Dis* 1987;136:730–736.
21. Hounsfield GN. Computerized transverse axial scanning (tomography): part I. Description of system. *Br J Radiol* 1973;46:1016–1022.
22. Gattinoni L, Pesenti A, Bombino M, Baglioni S, Rivolta M, Rossi F, Rossi G, Fumagalli R, Marcolin R, Mascheroni D, *et al.* Relationships between lung computed tomographic density, gas exchange, and PEEP in acute respiratory failure. *Anesthesiology* 1988;69:824–832.
23. Gattinoni L, Chiumello D, Cressoni M, Valenza F. Pulmonary computed tomography and adult respiratory distress syndrome. *Swiss Med Wkly* 2005;135:169–174.
24. Vieillard-Baron A, Rabiller A, Chergui K, Peyrouset O, Page B, Beauchet A, Jardin F. Prone position improves mechanics and alveolar ventilation in acute respiratory distress syndrome. *Intensive Care Med* 2005;31:220–226.
25. Gainnier M, Michelet P, Thirion X, Arnal JM, Sainty JM, Papazian L. Prone position and positive end-expiratory pressure in acute respiratory distress syndrome. *Crit Care Med* 2003;31:2719–2726.
26. Valenza F, Guglielmi M, Maffioletti M, Tedesco C, Maccagni P, Fossali T, Aletti G, Porro GA, Irace M, Carlesco E, *et al.* Prone position delays the progression of ventilator-induced lung injury in rats: does lung strain distribution play a role? *Crit Care Med* 2005;33:361–367.
27. Nuckton TJ, Alonso JA, Kallet RH, Daniel BM, Pittet JF, Eisner MD, Matthay MA. Pulmonary dead-space fraction as a risk factor for death in the acute respiratory distress syndrome. *N Engl J Med* 2002;346: 1281–1286.
28. Gattinoni L, Vagginelli F, Carlesco E, Taccone P, Conte V, Chiumello D, Valenza F, Caironi P, Pesenti A; Prone-Supine Study Group. Decrease in $PaCO_2$ with prone position is predictive of improved outcome in acute respiratory distress syndrome. *Crit Care Med* 2003;31:2727–2733.
29. Walther SM, Domino KB, Glenny RW, Hlastala MP. Positive end-expiratory pressure redistributes perfusion to dependent lung regions in supine but not in prone lambs. *Crit Care Med* 1999;27:37–45.
30. Pelosi P, Bottino N, Chiumello D, Caironi P, Panigada M, Gamberoni C, Colombo G, Bigatello LM, Gattinoni L. Sigh in supine and prone position during acute respiratory distress syndrome. *Am J Respir Crit Care Med* 2002;167:521–527.

31. Cakar N, Van der Kloot T, Youngblood M, Adams A, Nahum A. Oxygenation response to a recruitment maneuver during supine and prone positions in an oleic acid-induced lung injury model. *Am J Respir Crit Care Med* 2000;161:1949–1956.
32. Bernard GR, Artigas A, Brigham KL, Carlet J, Falke K, Hudson L, Lamy M, Legall JR, Morris A, Spragg R. Report of the American-European Consensus Conference on ARDS: definitions, relevant outcomes, and clinical trial coordination. *Am J Respir Crit Care Med* 1994;20:225–232.
33. Martynowicz MA, Walters BJ, Hubmayr RD. Mechanisms of recruitment in oleic acid-injured lungs. *J Appl Physiol* 2000;90:1744–1753.
34. Malbouisson LM, Busch CJ, Puybasset L, Lu Q, Cluzel P, Rouby JJ; CT Scan ARDS Study Group. Role of the heart in the loss of aeration characterizing lower lobes in acute respiratory distress syndrome. *Am J Respir Crit Care Med* 2000;161:2005–2012.
35. Albert RK, Hubmayr RD. The prone position eliminates compression of the lungs by the heart. *Am J Respir Crit Care Med* 2000;161:1660–1665.
36. Mure M, Glenny RW, Domino KB, Hlastala MP. Pulmonary gas exchange improves in the prone position with abdominal distension. *Am J Respir Crit Care Med* 1998;157:1785–1790.
37. Quintel M, Pelosi P, Caironi J, Meinhardt JP, Luecke T, Herrmann P, Taccone P, Rylander C, Valenza F, Carlesso E, *et al.* An increase of abdominal pressure increases pulmonary edema in oleic acid-induced lung injury. *Am J Respir Crit Care Med* 2004;169:534–541.
38. Vieira S, Nieszkowska A, Lu Q, Elman M, Sartorius A, Rouby JJ. Low spatial resolution computed tomography underestimates lung overinflation resulting from positive pressure ventilation. *Crit Care Med* 2005;33:741–747.
39. Guerin C, Gaillard S, Lemasson S, Ayzac L, Girard R, Beuret P, Palmier B, Le QV, Sirodot M, Rosselli S, *et al.* Effects of sytematic prone positioning in hypoxemic acute respiratory failure: a randomized controlled trial. *JAMA* 2004;292:2379–2387.