

# Can the Tomographic Aspect Characteristics of Patients Presenting with Acute Respiratory Distress Syndrome Predict Improvement in Oxygenation-related Response to the Prone Position?

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**Background:** In some patients with acute respiratory distress syndrome, the prone position is able to improve oxygenation, whereas in others it is not. It could be hypothesized that the more opacities that are present in dependent regions of the lung when the patient is in the supine position, the better the improvement in oxygenation is observed when the patients are turned prone. Therefore, we conducted a prospective study to identify computed tomographic scan aspects that could accurately predict who will respond to the prone position.

**Methods:** We included 46 patients with acute respiratory distress syndrome (31 responders and 15 nonresponders). Computed tomographic scan was performed in the 6-h period preceding prone position. Blood gas analyses were performed before and at the end of the first 6-h period of prone position.

**Results:** Arterial oxygen partial pressure/fraction of inspired oxygen increased from  $117 \pm 42$  (mean  $\pm$  SD) in the supine position to  $200 \pm 76$  mmHg in the prone position ( $P < 0.001$ ). There were 31 responders and 15 nonresponders. There was a vertebral predominance of the opacities ( $P < 0.0001$ ). However, there was no difference between responders and nonresponders. When only the amount of consolidated lung located under the heart was evaluated, there was more consolidated tissue under the heart relative to total lung area in nonresponders than in responders ( $P = 0.01$ ).

**Conclusions:** There are no distinctive morphologic features in the pattern of lung disease measured by computed tomographic scanning performed with the patient in the supine position that can predict response to the prone position.

ACUTE respiratory distress syndrome (ARDS) has diverse causes and carries high morbidity and mortality rates.<sup>1</sup> It is characterized by profound hypoxemia, pulmonary hypertension, and poor lung compliance. In the absence of definitive therapy, management involves supportive care using mechanical ventilation with increased inspired oxygen concentration and positive end-expiratory pressure (PEEP). Prone positioning is one of the therapeutic strategies that has been recently proposed for ARDS patients, although the beneficial effects of prone positioning on

arterial oxygenation were already described by Bryan<sup>2</sup> more than 20 yr ago. Other investigators have confirmed these findings.<sup>3–9</sup> Prone positioning is now more commonly used to improve oxygenation in ARDS patients.

Computed tomographic (CT) appearances of ARDS are variable. CT typically shows symmetric ground-glass opacification with gravity-dependent opacities when the patient is in the supine position. However, the literature contains many contradictory descriptions that range from ground-glass opacification to consolidation, from focal to generalized disease, and from homogeneous to patchy opacities.<sup>10–17</sup> These parenchymal opacities predominating in the dependent portions of the lung are thought to result from the collapse of the lowermost alveoli under the weight of the uppermost edematous lung,<sup>6</sup> the heart,<sup>13</sup> as well as pressure exerted by the abdominal contents.<sup>7</sup> It could therefore be hypothesized that the more opacities that are present in dependent regions of the lung when the patient is in the supine position, the better the improvement in oxygenation observed when the patients are turned prone.

The mechanisms by which the prone position induces an increase in arterial oxygen partial pressure ( $P_{aO_2}$ ) are still controversial. Lamm *et al.*<sup>18</sup> showed that the prone position markedly improved dorsal lung ventilation and, accordingly, also improved dorsal lung ventilation-perfusion relations, with minimal if any compromise of ventral lung ventilation or ventral ventilation-perfusion relations. Therefore, as suggested by Albert and Hubmayr,<sup>19</sup> reversible airspace closure occurs in dorsal lung regions when patients with ARDS are supine, while turning them prone sufficiently alters dorsal lung transpulmonary pressures to reverse this closure without shifting the air-space closure to the ventral regions. A number of factors could contribute to this differential ability of the prone position to modify dorsal lung transpulmonary pressures. One of these factors is the direct transmission of the weight of the heart to the regions of the lung located beneath it.<sup>19–22</sup> Albert and Hubmayr,<sup>19</sup> studying CT scans of seven spontaneously ventilated patients, found that there was a dramatic decrease of the percent of both lungs located under the heart when the patients were turned prone. Moreover, Malbouisson *et al.*<sup>13</sup> showed, using a CT method, that the heart plays an important role in the loss of aeration of lung lobes in ARDS patients lying in the supine position.

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Finally, in some ARDS patients, the prone position improves oxygenation, whereas in others it does not. The main objective of the current study was therefore to identify CT scan characteristics in the supine position that could accurately predict who will respond and who will not respond to prone positioning. A secondary objective was to evaluate characteristics of the lung regions that could be subjected to the weight of the heart in ARDS patients lying in the supine position. Our hypothesis was that the more dependent opacities present with the patient in the supine position, the better improvement in oxygenation will be related to the prone position.

## Materials and Methods

### Study Population

During a 2-yr period (from August 1998 to July 2000), 748 patients were admitted in the medical and surgical intensive care unit (15 beds) of Sainte-Marguerite University Hospital in Marseille, France. During this period, 95 patients met the American-European Consensus Conference criteria for ARDS.<sup>23</sup> The protocol was approved by the institutional review board (Comité Consultatif de Protection des Personnes dans la Recherche Biomédicale, Marseille, France). Correction of hypoxemia related to ARDS was based on the first-line use of inhaled nitric oxide or almitrine bismesylate before initiating prone positioning. The prone position was used in 71 patients when  $Pao_2$ /fraction of inspired oxygen ( $Fio_2$ ) during nitric oxide (1–20 ppm) or almitrine bismesylate ( $2\text{--}16\text{ }\mu\text{g}\cdot\text{kg}^{-1}\cdot\text{min}^{-1}$ ) was lower than 200 mmHg. CT scan was performed in 46 of the 71 potentially eligible patients. Therefore, 25 patients were not included in the current study. These 25 patients presented the following characteristics: age  $50 \pm 17$  yr; SAPS II on admission:  $39 \pm 17$ ; Logistic Organ Dysfunction System score:  $5.5 \pm 3.4$ ; Lung Injury Score<sup>24</sup>:  $3.3 \pm 0.5$ ; ARDS of pulmonary causes: 88%. Seven of these 25 patients were included in other studies. We excluded the remaining 18 patients because they had concurrent cerebral edema ( $n = 10$ ), imminent death ( $n = 5$ ), or major medical contraindications to being transported ( $n = 2$ ). The remaining 46 patients (36 males, 10 females; age  $50 \pm 16$  yr; SAPS II on admission:  $39 \pm 12$ ) were prospectively investigated after written informed consent was obtained from each patient's next of kin. ARDS was related to pulmonary causes in 74% of the cases (pneumonia,  $n = 15$ ; lung contusion,  $n = 12$ ; aspiration,  $n = 6$ ; miscellaneous,  $n = 1$ ), and to extrapulmonary causes in 26% of the cases. On the day of ARDS diagnosis, Lung Injury Score was  $3.1 \pm 0.4$ , whereas Logistic Organ Dysfunction System was  $4.8 \pm 2.4$ . Prone positioning was initiated  $3.1 \pm 2.1$  days after the beginning of ARDS. On inclusion into the study, respiratory parameters were as follows: tidal volume,  $8.1 \pm 1.9$  ml/kg;  $Fio_2$ ,  $0.78 \pm$

$0.18$ ; respiratory rate,  $21.5 \pm 4.5$  breaths/min; and PEEP,  $10.7 \pm 2.3$  cm  $H_2O$ . The selection of appropriate PEEP level was performed by increasing PEEP in steps of 2 cm  $H_2O$ . A blood gas analysis was performed after a 30-min period of stabilization of oxygen saturation. Finally, the lowest level of PEEP giving the greatest improvement of oxygenation was chosen. When no improvement was found while increasing PEEP, the level was set at 8 cm  $H_2O$ . A recruitment maneuver was never performed. All patients were tracheostomized, sedated, and paralyzed with a continuous infusion of sufentanil, midazolam, and vecuronium bromide, and the lungs were ventilated using conventional volume-controlled mechanical ventilation (Puritan Bennett 7200 series; Mallinckrodt, Carlsbad, CA).

### The Prone Position

All patients were positioned on special mattresses using a dynamic flotation system incorporating a sensor pad (Nimbus Prone Nursing®; Huntleigh Healthcare, Luton, United Kingdom). Change of position was manually performed by 3 nurses and 2 staff members. With the patient in the prone position, the arms were laid parallel to the body. Pillows were not used in order to increase abdomen kinetics. Care was taken to avoid eye damage or any nonphysiologic movements of the limbs during posture changes.

### Instrumentation and Measurements

**Blood Gas Analyses.** Arterial pH,  $Pao_2$ , and arterial carbon dioxide partial pressure were measured using a blood gas analyzer (278-blood gas system; Ciba Corning, Medfield, MA).

**Respiratory Parameters.** The following respiratory parameters were recorded: exhaled tidal volume, peak inspiratory pressure, and respiratory rate were evaluated using a pneumotachograph (Spiro +; Saime, Savigny-le-Temple, France) and were recorded on a data acquisition and analysis system (Spiroscope 2.01; Saime).

**Computed Tomographic Scanning.** Images were obtained by a Siemens Somaris tomograph (Siemens, Munich, Germany), with exposures taken at 120 kV and 250 mAs. An intravenous injection of 80 ml contrast medium was used to differentiate pleural effusions from nonaerated lung parenchyma. CT scans were obtained at a constant PEEP level during apnea. High-definition 1-mm-thick sections obtained at intervals of 10 mm and selected by means of a thoracic scout view were performed.

**Computed Tomography Evaluation.** All indices were evaluated jointly by two radiologists (O. D. and S. G.) independent of the intensive care unit and while unaware of the clinical condition of the patients. As previously proposed,<sup>25</sup> the scans were evaluated at three representative levels: the apex (top of the upper aortic arch), the hilum (first section below the carina), and the base (2 cm above the highest diaphragm). Each trans-

verse scan was divided into three sections: an anterior third (sternal), posterior third (vertebral), and middle third (central). The left and right lungs were analyzed individually. The final analysis consisted of 18 anatomic locations: three transverse levels (apex, hilum, and base), each of which was analyzed at three positions (sternal, central, and vertebral) in the left and right lungs. According to the Fleischner Society Nomenclature Committee,<sup>26</sup> CT attenuations were classified in CT consolidations (markedly increased attenuation, no visible vessels) and ground-glass opacifications (mild increased attenuation, visible vessels). At each of the 18 locations, the lung was scored as follows: normal lung (NL), ground-glass opacification (GG), and consolidation. For each location, a 0 was assigned when the morphologic features were essentially absent, a 1 was assigned when the morphologic features occupied one third or less of the subsection, a 2 was assigned when the morphologic features occupied one or two thirds of the subsection, and a 3 was assigned when the morphologic features occupied more than two thirds of the subsection. The sum of the subsection had to equal three. Because the cross-sectional areas of the hilar and basilar regions of the lung are greater than the area of the apical region, correction factors of 1.7 and 1.8, respectively, were used.<sup>27</sup> These corrections were applied to calculate the total disease score for each morphologic category as follows: total GG = GG apex + 1.7 GG hilum + 1.8 GG base (range, 0–81); total consolidation = consolidation apex + 1.7 consolidation hilum + 1.8 consolidation base (range, 0–81); total NL = NL apex + 1.7 NL hilum + 1.8 NL base (range, 0–81); and total lung disease = total GG + total consolidation (range, 0–81).

To evaluate the possible effect of the heart on lung function, four sections were studied as proposed by Albert and Hubmayr.<sup>19</sup> Briefly, these sections must be approximately evenly spaced from the carina to the most cephalad portion of the diaphragm. The cardiac and pleural margins were traced on 10 × 10-mm/cm graph paper. Perpendicular lines were drawn from the right and left lateral cardiac margins to the posterior chest wall. In each section, the relative volume of lung parenchyma beneath the heart was determined by counting the number of square millimeter boxes located medial to these lines in each hemithorax and expressing this as a percentage of the total number of square millimeter boxes present in each hemithorax. The percentage of consolidated lung located under the heart relative to total lung area or relative to the lung area located under the heart was evaluated using the same methodology. To evaluate the incidence of the shape of the lung on the improvement of oxygenation related to the prone position, the lung area (evaluated on the section above the diaphragm) was divided into two compartments (at 50% of the ventral–dorsal distance), the upper and the lower compartments.

**Procedure.** Computed tomographic scan was performed in the 6-h period preceding the first trial of prone positioning. Baseline measurements (blood gas analysis and respiratory parameters) were evaluated with the patient in the supine position just before turning the patients prone. Blood gas analyses and respiratory parameters were then measured at the end of the 6-h period of prone positioning. Therefore, arterial blood gases were analyzed within the 12 h following CT examination.

**Definitions.** A response to prone positioning was defined by at least a 33% increase in the  $P_{aO_2}/F_{iO_2}$  ratio when compared with supine position.

### Statistical Methods

Data are expressed as mean ± SD. Statistical calculations were performed using the SPSS 8.0 package (SPSS Inc., Chicago, IL). Statistically significant differences were analyzed using the Student *t* test for continuous variables and the chi-square test for categorical variables. The Mann-Whitney rank sum test or the Kruskal-Wallis test was used when variables were unequal among the groups. Two-way analyses of variance (with the factors being responders *vs.* nonresponders and spatial location) were performed to evaluate the degree of lung injury. When appropriate, a *post hoc* analysis was performed using a pairwise multicomparison procedure (Tukey test). *P* < 0.05 indicated significance.

## Results

### Effect of Prone Positioning on Oxygenation

Transport and performance of CT scanning were not associated with relevant adverse effects necessitating a modification of ventilatory parameters or vasoactive agent requirements. Moreover, we did not observe adverse renal effects. When all 46 patients were considered, the  $P_{aO_2}/F_{iO_2}$  ratio increased from  $117 \pm 42$  while in the supine position to  $200 \pm 76$  mmHg while in the prone position (*P* < 0.001 by Student paired *t* test). There were 31 responders and 15 nonresponders. In the 31 responders, the  $P_{aO_2}/F_{iO_2}$  ratio increased from  $116 \pm 44$  mmHg while in the supine position to  $228 \pm 67$  mmHg when they were turned prone. In the 15 nonresponders,  $P_{aO_2}/F_{iO_2}$  ratio increased from  $120 \pm 39$  while in the supine position to  $141 \pm 57$  mmHg when turned prone (nonsignificant). Only 2 of the 15 nonresponders had a decrease in  $P_{aO_2}/F_{iO_2}$  ratio when turned prone. The characteristics of responders and nonresponders are summarized in table 1.

### Total Lung Disease

The mean total lung disease scores in responders and in nonresponders were similar ( $47.4 \pm 17.4$  for responders *vs.*  $51.8 \pm 20.5$  for nonresponders), meaning that in



Table 1. Characteristics of Responders and Nonresponders

Characteristic	Responders (n = 31)	Nonresponders (n = 15)	P Value
Pao <sub>2</sub> /Fio <sub>2</sub> on inclusion (mmHg)	116 ± 44	120 ± 39	NS
Increase of Pao <sub>2</sub> /Fio <sub>2</sub> related to prone position	115 ± 86%	15 ± 19%	0.001
Age (yr)	53 ± 18	44 ± 10	NS
SAPS II	37 ± 12	42 ± 13	NS
LIS	3.10 ± 0.39	3.06 ± 0.38	NS
LODS	4.26 ± 1.59	5.93 ± 3.30	0.024
PEEP (cm H <sub>2</sub> O)	11.0 ± 2.5	10.0 ± 1.7	NS
Onset of ARDS (d)	3.0 ± 1.9	3.4 ± 2.3	NS
Tidal volume (ml/kg)	7.9 ± 2.0	8.2 ± 1.7	NS
Pulmonary causes of ARDS	74%	73%	NS
Under NO and/or almitrine on inclusion	61%	47%	NS

Pao<sub>2</sub> = arterial oxygen tension; Fio<sub>2</sub> = fraction of inspired oxygen; SAPS II = Simplified Acute Physiology Score; LIS = Lung Injury Score; LODS = Logistic Organ Dysfunction System; PEEP = positive end-expiratory pressure; ARDS = adult respiratory distress syndrome; NO = nitric oxide; NS = not statistically significant.

both groups, approximately 60% of the lung was abnormal (58.5% in responders; 64.0% in nonresponders).

### Types of Parenchymal Abnormalities

In responders, ground-glass opacification was as extensive as consolidation (mean total GG, 23.9 ± 15.4; mean total consolidation, 23.4 ± 10.8). In nonresponders, ground-glass opacification was also as extensive as consolidation (mean total GG, 26.2 ± 17.2; mean total consolidation, 25.6 ± 8.3). When the type of opacification (GG or consolidation) was compared, there was no difference between responders and nonresponders.

### Regional Distribution

A two-way analysis of variance showed that there was no difference between responders and nonresponders concerning ground-glass opacifications. However, there was an effect of the spatial location ( $P = 0.004$ ; fig. 1). No interaction was found between the two factors (responders *vs.* nonresponders and spatial location). In responders, ground-glass opacification was equally distributed among an anterior-posterior axis, whereas in nonresponders there was a predominance of ground-glass opacification in the central (hilar) one third of the

lung as compared with the vertebral third (fig. 1). Concerning the consolidations, a two-way analysis of variance showed that there was no difference between responders and nonresponders. However, as for ground-glass opacifications, there was an effect of spatial location ( $P < 0.001$ ; fig. 2). No interaction was found between the two factors (responders *vs.* nonresponders and spatial location). Consolidation predominated in the vertebral one third of the lung in both responders and nonresponders to the prone position (fig. 2).

When total lung disease was considered, there was no difference between responders and nonresponders. In contrast, the two-way analysis of variance showed that there was a significant effect of the level (sternal, central, vertebral;  $P < 0.001$ ) with a vertebral predominance of these abnormalities (fig. 3). No interaction was found between the two factors (responders *vs.* nonresponders and spatial location).

When both sides (right lung, left lung) were considered separately, there was no predominance of ground-glass opacification or consolidation in responders when compared with nonresponders. The total lung disease was almost evenly distributed between the left and right lungs in both responders and nonresponders (fig. 4).

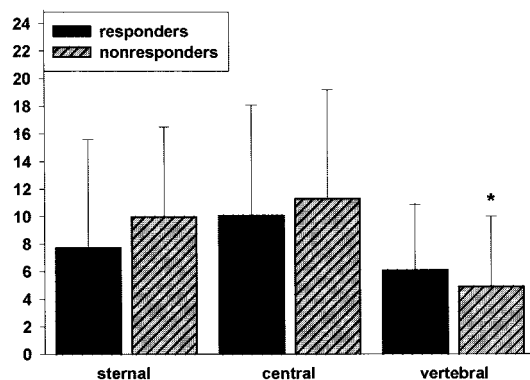


Fig. 1. Distribution of ground-glass opacification according to the anteroposterior level (mean ± SD). \* $P < 0.05$  versus central one third in nonresponders by Tukey test.

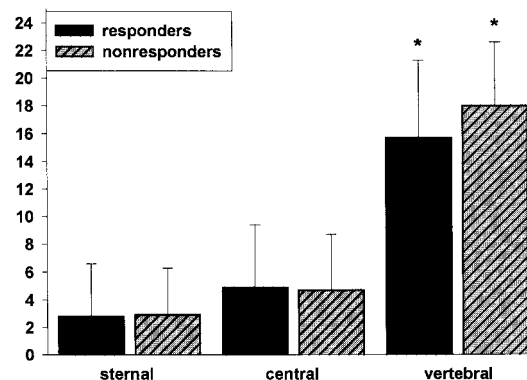


Fig. 2. Distribution of consolidation according to the anteroposterior level (mean ± SD). \* $P < 0.001$  versus sternal one third and central one third.

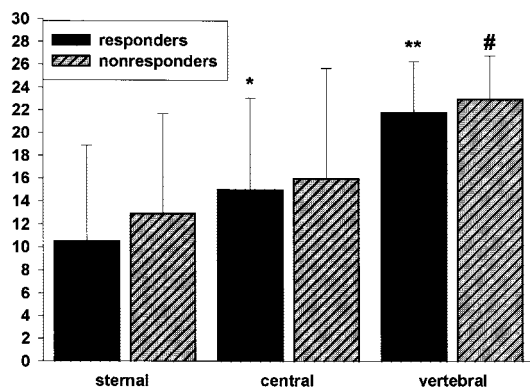


Fig. 3. Distribution of total lung disease according to the antero-posterior level (mean  $\pm$  SD). \* $P < 0.05$  versus sternal one third in responders by Tukey test; \*\* $P < 0.001$  versus sternal one third and central one third in nonresponders by Tukey test; # $P < 0.05$  versus central one third and  $P < 0.001$  versus sternal one third in nonresponders by Tukey test.

Ground-glass opacification and consolidation were also both evenly distributed according to the cranio-caudal direction in both responders and nonresponders. When total lung disease was analyzed according to the cranio-caudal direction, there was no difference between responders and nonresponders (fig. 5).

#### *Compression of the Lungs by the Heart and Response to Prone Positioning*

The cardiothoracic ratio measured on standard posterior-anterior chest roentgenograms was  $0.51 \pm 0.06$  in responders and  $0.49 \pm 0.07$  in nonresponders (nonsignificant). There was no correlation between cardiothoracic ratio and the improvement in oxygenation related to prone positioning.

The percentage of the lung located under the heart increased only for the left lung from section 1 (subcarinal level) to section 4 (sudsiaphragmatic level) for both responders and nonresponders ( $P < 0.001$  by Kruskal-Wallis one-way analysis of variance on ranks; fig. 6). However, there was no difference between responders and nonresponders. When the percentage of consoli-

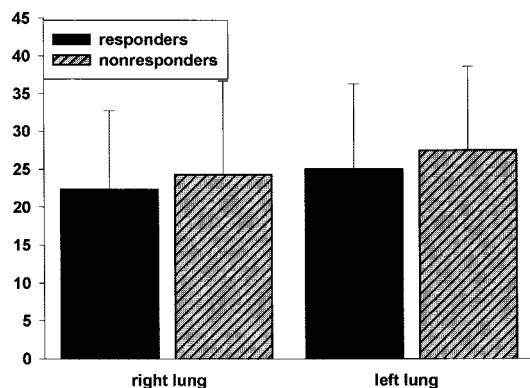


Fig. 4. Distribution of total lung disease according to the lung side (mean  $\pm$  SD).

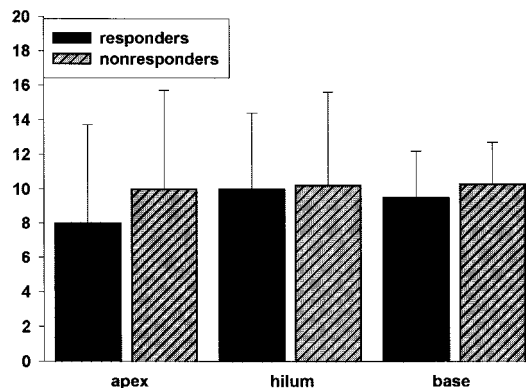


Fig. 5. Distribution of total lung disease according to the cranio-caudal direction (mean  $\pm$  SD).

dated lung located under the heart relative to total lung area was considered, there was more consolidated tissue in nonresponders than in responders ( $P = 0.01$  by analysis of variance; fig. 7). There was also a progressive increase in consolidated tissue from section 1 to section 4 for both responders and nonresponders ( $P < 0.001$  by analysis of variance; fig. 7). When the dependence of consolidated tissue located under the heart relative to lung area on cephalocaudal distance was compared for the two lungs, there was an increase from section 1 to section 4 only for the left lung for responders and nonresponders ( $P < 0.001$  by Kruskal-Wallis one-way analysis of variance on ranks; fig. 7).

When only the part of the lung located under the heart was analyzed, there was more consolidated tissue in nonresponders than in responders ( $P = 0.001$  by a two-way analysis of variance; fig. 8). However, the two-way analysis of variance showed that there was no effect of the section level and that there was no interaction between the presence or absence of a response and the section level.

#### *Effect of the Lung Shape*

A two-way analysis of variance (with the factors being responders *vs.* nonresponders and upper *vs.* lower compartments) showed that there was no difference between responders and nonresponders concerning the upper and lower compartments relative areas (fig. 9). However, a difference was found between the two compartments ( $P < 0.001$ ).

When the amount of consolidated lung tissue relative to total lung area was evaluated, no difference was found between responders and nonresponders, whereas the two-way analysis of variance identified a significant effect of the compartment ( $P < 0.001$ ). No interaction was found between the two factors (responders *vs.* nonresponders and upper *vs.* lower compartments) concerning the amount of consolidated lung tissue relative to total lung area.

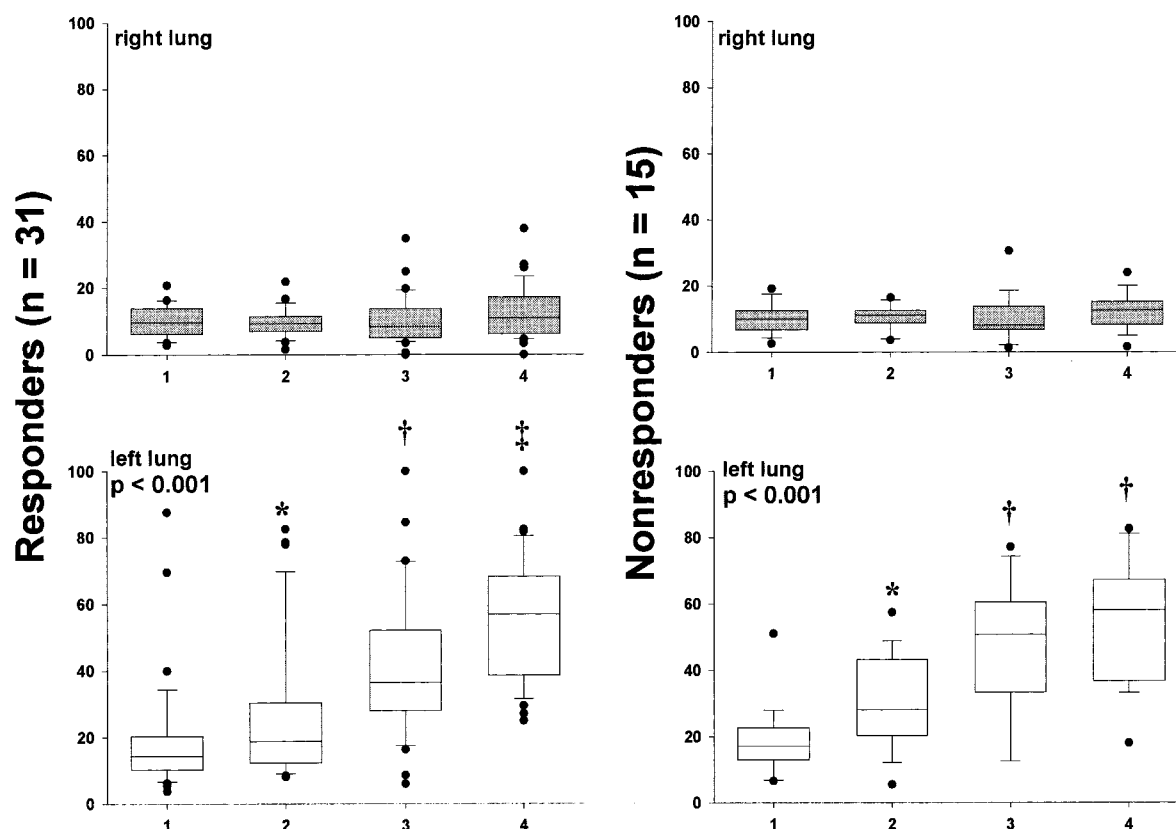


Fig. 6. Percentage of lung located under the heart relative to total lung area. Median values (25th, 50th, and 75th percentiles) and largest and smallest values that are not outliers are reported. Outliers (cases with values between 1.5 and 3 box lengths from the upper or lower edge of the box) are presented as closed circles. \* $P < 0.05$  versus section 1, † $P < 0.05$  versus sections 1 and 2, ‡ $P < 0.05$  versus sections 1, 2, and 3, all by Student-Newman-Keuls method.

## Discussion

The primary finding of this study was that there was no predictive factor of response to prone positioning except a greater amount of consolidated tissue under the heart in nonresponders in the supine position than in responders in the prone position. Indeed, the predominance of posterior hyperattenuated lung areas on CT scan performed with patients in the supine position was not predictive of an improvement in oxygenation in response to the prone position. Therefore, we can speculate that the influence of the weight of the heart on the lung located beneath it when the patients are in the supine position is not a major contributing factor in the improvement in oxygenation observed in responders to prone positioning.

Based on roentgenographic studies, it has been thought that ARDS produces a diffuse and homogeneous increase in lung stiffness, resulting in decreased lung volume. However, research conducted by a number of groups has now shown that the effects of ARDS on the lungs are far from homogeneous, particularly in the early stages.<sup>14,15,28,29</sup> Indeed, from the available data, it appears that lung lesions are inhomogeneous, with mor-

phologically intact areas coexisting with areas of abnormal lung density.<sup>29,30</sup> Using CT technology, it has been shown that radiographic densities predominate in the dependent (vertebral) lung regions while patients are in the supine position. In contrast, the nondependent (sternal) regions appear normal when patients are in the supine position.<sup>29,31</sup> The morphology of lung in patients with ARDS as determined by CT scanning in the current study appeared consistent with previous reports,<sup>14,15,29,31-33</sup> with dense regions located in the dependent regions of both lungs. The weight of the abdominal contents, acting against the diaphragmatic wall, generated an increase in the abdominal pressure, which is predominantly transmitted to the caudal and dependent lung regions and in turn leads to a cephalic displacement of posterior regions of the diaphragm. Froese and Bryan<sup>34</sup> found that, in supine, awake, spontaneously breathing humans, the dependent parts of the diaphragm moved more in a cephalocaudal direction than did the nondependent parts. They also observed that, during anesthesia with paralysis and mechanical ventilation, the pattern of diaphragm displacement was reversed, with more motion occurring in nondependent than in dependent regions, and that a cephalad shift of the end-expiratory position of the diaphragm occurred.

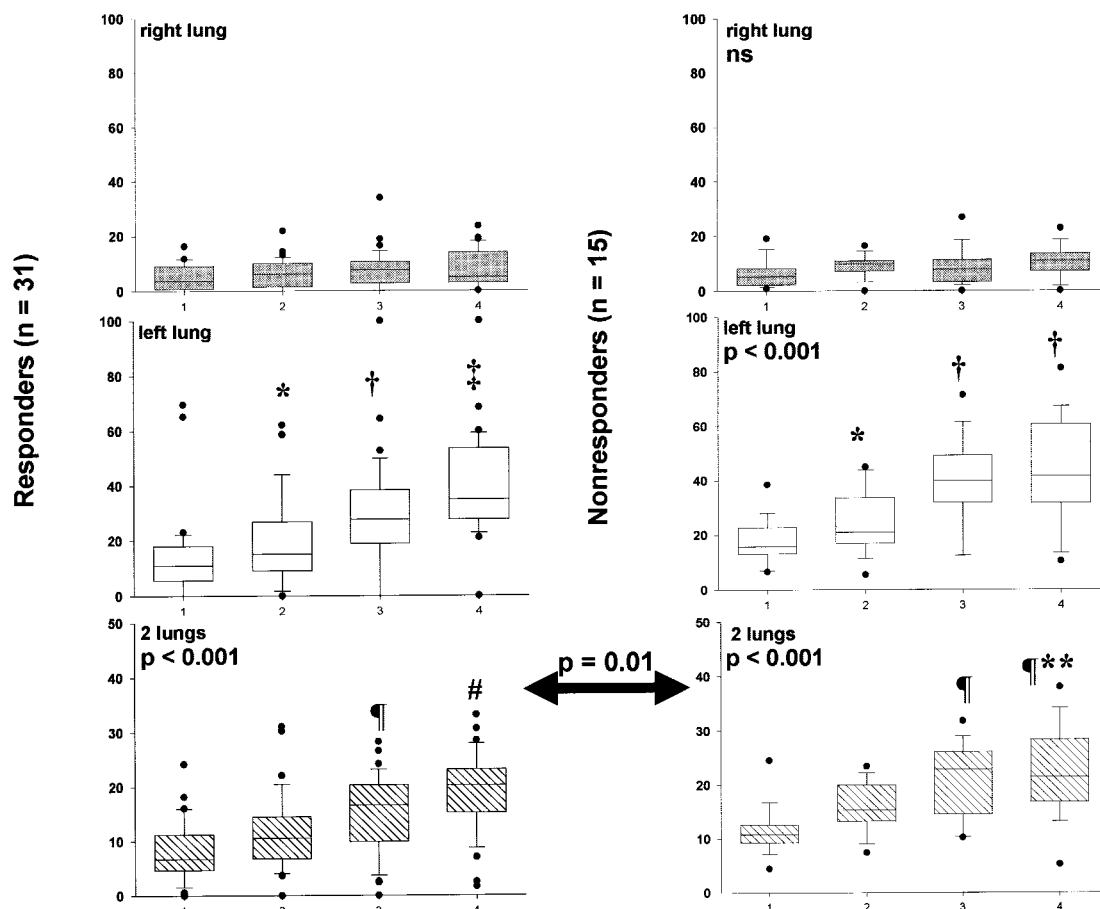


Fig. 7. Percentage of consolidated lung tissue located under the heart relative to total lung area. Median values (25th, 50th, and 75th percentiles) and largest and smallest values that are not outliers are reported. Outliers (cases with values between 1.5 and 3 box lengths from the upper or lower edge of the box) are presented as closed circles. \* $P < 0.05$  versus section 1, † $P < 0.05$  versus sections 1 and 2, ‡ $P < 0.05$  versus sections 1, 2, and 3, all by Student-Newman-Keuls method; § $P < 0.001$  versus section 1, # $P < 0.001$  versus sections 1 and 2, \*\* $P < 0.02$  versus section 2, all by Tukey test.

It has been reported that turning a patient from the supine to the prone position decreases dorsal consolidation and increases ventral consolidation within minutes.<sup>35</sup> Indeed, Gattinoni *et al.*<sup>6</sup> reported that there was

a density redistribution by gravity when changing from the supine to the prone position: the nondependent regions tended to clear, whereas the dependent regions increased their density in either position. Gattinoni *et al.*<sup>6</sup> hypothesized that, in patients with ARDS, the decreased transpulmonary pressure along the vertical axis

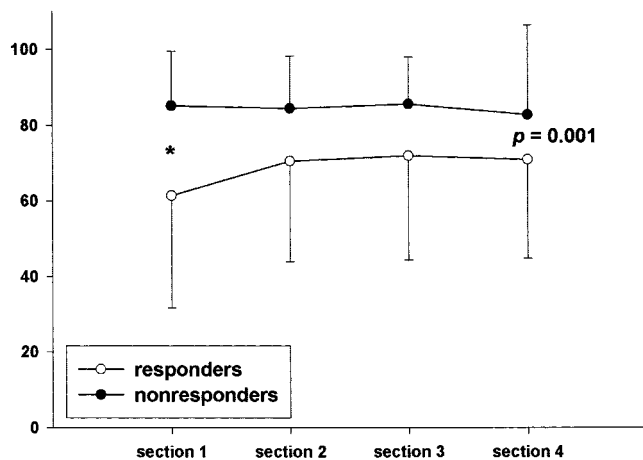


Fig. 8. Percentage of consolidated tissue relative to lung area located under the heart (mean  $\pm$  SD). \* $P < 0.01$  versus nonresponders by Tukey test.

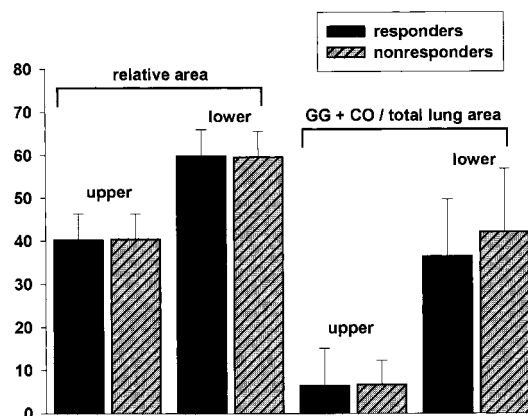


Fig. 9. Relative lung area of upper and lower compartments (mean  $\pm$  SD).



reduces alveolar size and induces collapse of potentially recruitable lung units. By performing two CT scans in the supine position separated by a 4-h period of prone positioning, Priolet *et al.*<sup>36</sup> showed that there was a 27.1% increase of normal lung segments on the second CT scan. However, Guérin *et al.*,<sup>37</sup> comparing pressure-volume curves, reported that there was no correlation between the improvement in  $\text{PaO}_2/\text{FiO}_2$  related to the prone position and the alveolar recruitment. The weight of the heart on the dorsal lung is supposed to contribute to this problem,<sup>38-40</sup> as are the effects of the supine position on chest wall shape.<sup>39,40</sup> Indeed, alterations in lung shape going from the prone to supine position are likely to be associated with changes in the pattern of lung expansion. We tested the hypothesis suggesting that patients presenting a more triangular shape of the lung (*i.e.*, upper lung area smaller than the lower lung area) respond better to the prone position than the patients with a more rectangular shape (*i.e.*, upper area similar to the lower area). However, in the current study we did not find any difference between responders and nonresponders, even when the amount of consolidated lung tissue was taken into account. The CT scans in the majority of patients with ARDS caused by pulmonary disease have areas of consolidation that are presumably a result of the initial direct lung injury. In the current study, ARDS was related to a pneumonia or lung contusion in 59% of the 46 patients. Therefore, pneumonia and lung contusion could not be recruited as atelectasis, explaining in part the fact that there was no correlation between the amount of vertebral opacities and the response to the prone position. In the present study, we did not perform a second CT scan at end-inspiration, which could help to differentiate atelectasis from consolidation. However, we did not find any relation between the type of ARDS (pulmonary or extrapulmonary), the localization of the opacities, and the response to the prone position. However, one limit of the present conclusion is the relatively small number of patients<sup>18</sup> free of pneumonia or lung contusion. It is also possible that when lung tissue is fully diseased, no recruitment is possible when the patients are turned from the supine to the prone position. Moreover, it is also possible that three or four transverse images do not give a true sample of the lung. Another explanation is that PEEP acts differently when ARDS is related to a direct lung injury than when it is a result of an extrapulmonary cause. Indeed, as suggested by Rouby *et al.*,<sup>41</sup> PEEP could induce overdistension of ventral lung regions in supine patients presenting lung injuries predominating in the posterior part of the lungs (and not in those presenting diffuse infiltrates). Therefore, when these patients are turned prone, it is conceivable that a more uniform pressure regimen across a vertical axis resulted in a better recruitment when increasing PEEP. It is also possible that improvement in  $\text{PaO}_2$  on switching from the supine to the

prone position occurs when a more homogenous distribution of alveolar inflation is present. Further studies are needed to test this hypothesis.

The compressive force exerted by the heart on the lungs was suggested by a study performed by Milic-Emili *et al.*,<sup>42</sup> who found that esophageal pressure measured in the region of the heart in normal subjects averaged approximately 5 cm  $\text{H}_2\text{O}$  more when patients were in the supine compared with the prone position. The compressive force of the heart would be greater in patients with cardiomegaly, as suggested by Wiener *et al.*,<sup>38</sup> and would probably be reduced in those with the smaller hearts associated with lung distension. However, in the study by Wiener *et al.*,<sup>38</sup> the mean cardiothoracic ratio was 0.66, whereas in the present study it was 0.51. This difference could partly explain the lack of correlation between responders and nonresponders for prone positioning concerning the percentage of the lung located under the heart reported in the current study. Using positron emission tomography, no difference in right-to-left lung density or lung expansion were seen in supine normal subjects at the midheart level.<sup>43</sup> A reasonable hypothesis would be that the effect of the heart on supine-prone differences in regional lung expansion would be present when the volume and weight of the heart is increased. In the study by Nakos *et al.*,<sup>44</sup> the patients with congestive heart failure and cardiomegaly exhibited a significant, rapid, and persistent improvement in oxygenation. This improvement could be partly related to the decompression of the left lower lobe by the enlarged heart during prone positioning. However, the investigators observed a persisting improvement after turning the patients to the supine position. Moreover, they observed that oxygenation increased faster in responder-ARDS group than in patients presenting an hydrostatic pulmonary edema, suggesting that heart volume did not affect significantly response to prone positioning.

Even if Gattinoni *et al.*<sup>45</sup> recently reported that the prone position did not modify outcome, it is important to identify subsets of patients who should respond to the prone position, especially severely hypoxemic patients. Indeed, in the latter study,<sup>45</sup> mortality was reduced using the prone position in this subgroup of patients. The current study showed that there is no tomodensitometric predictive factor of response to the prone position. Further studies are required to find predictive factors of response to the prone position that are easy to routinely assess.

In conclusion, the preponderance of radiologic opacities in the dorsal territories of ARDS patients does not influence the improvement in oxygenation related to the prone position. There are no distinctive morphologic features in the pattern of lung disease measured by CT



scanning performed with patients in the supine position that can predict response to the prone position.

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