

Prone Positioning Unloads the Right Ventricle in Severe ARDS*

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Background: Despite airway pressure limitation, acute cor pulmonale persists in a minority of ARDS patients. Insufficient airway pressure limitation, hypercapnia, or both may be responsible. Because prone positioning (PP) has been shown to be a safe way to reduce airway pressure and to improve alveolar ventilation, we decided to assess its effect on right ventricular (RV) pressure overload in ARDS patients.

Methods: Between January 1998 and December 2006, we studied 42 ARDS patients treated by PP to correct severe oxygenation impairment ($\text{PaO}_2/\text{fraction of inspired oxygen ratio}$, < 100 mm Hg). RV function was evaluated by bedside transesophageal echocardiography, before and after 18 h of prone-position ventilation. RV enlargement was measured by RV/left ventricular (LV) end-diastolic area ratio in the long axis. Septal dyskinesia was quantified by measuring short-axis systolic eccentricity of the LV.

Results: Before PP, 21 patients (50%) had acute cor pulmonale, defined by RV enlargement associated with septal dyskinesia (group 1), whereas 21 patients had a normal RV (group 2). PP was accompanied by a significant decrease in airway pressure and PaCO_2 . In group 1, this produced a significant decrease in mean ($\pm$ SD) RV enlargement (from 0.91 ± 0.22 to 0.61 ± 0.21) after 18 h of PP ($p = 0.000$) and a significant reduction in mean septal dyskinesia (from 1.5 ± 0.2 to 1.1 ± 0.1) after 18 h of PP ($p = 0.000$).

Conclusion: In the most severe forms of ARDS, PP was an efficient means of controlling RV pressure overload. (CHEST 2007; 132:1440–1446)

Key words: acute cor pulmonale; ARDS; echocardiography; prone position; right ventricle

Abbreviations: ED = end-diastole, diastolic; ES = end-systole, systolic; FIO_2 = fraction of inspired oxygen; LV = left ventricle, ventricular; LVEDA = left ventricular end-diastolic area; PEEP = positive end-expiratory pressure; PP = prone positioning; RV = right ventricle, ventricular; RVEDA = right ventricular end-diastolic area; TR = tricuspid regurgitation

From a physiologic point of view, there is a major mismatch between lung ventilation and lung perfusion in ARDS patients.¹ From a clinical point of

view, extensive lung damage in ARDS patients produces severe hypoxemia, which is difficult to control by mechanical ventilation. In the supine position, this lung damage mainly concerns dependent areas of the lung.² Prone positioning (PP), a respiratory strategy employed for > 20 years,³ has repeatedly proven to be an efficient way to improve oxygenation in ARDS patients. A possible mechanism of this improvement can be summarized as follows. In the supine position, the posterior part of the chest wall, lying on the plane of the bed, is less compliant, and ventilation is thus mainly distributed to the anterior, and nondependent, lung areas. At the same time, lung perfusion is affected by a vertical hydrostatic pressure gradient, favoring blood flow in the depen-

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dent lung areas. The net result of both combined is a tendency for the dependent areas to be underventilated and overperfused (shunt), whereas the non-dependent areas have a tendency to be overventilated and underperfused (dead space). In the prone position, the compliance of the anterior part of the chest wall, lying now on the plane of the bed, is reduced, favoring a better distribution of the ventilation to the posterior areas of the lung, which are now nondependent. At the same time, the hydrostatic pressure gradient favors a better distribution of blood to the anterior areas of the lung, now dependent. The net effect of both combined is a better match between lung ventilation and lung perfusion, thus reducing both the shunt and dead space. Such matching improvement is expected to reduce resistance to blood flow in the lung, which is a major afterloading factor for the right ventricle (RV) and is functionally affected during the course of ARDS.^{4,5}

In January 1998, we started a prospective study focused on patients with severe ARDS who were treated by PP to improve oxygenation. All of these patients were monitored daily by transesophageal echocardiography, our usual strategy in ARDS monitoring.⁶ We have now recorded a complete data set, including respiratory and echocardiographic measurements, in 42 patients. This gives us the unique opportunity to report the short-term effect of PP on RV function in patients with severe ARDS. Both PP and bedside transesophageal echocardiography have been accepted as a routine strategy in ARDS patients by the Ethics Committee of the "Société de Réanimation de Langue Française."

MATERIALS AND METHODS

Within the ARDS population treated between January 1998 and December 2006, we selected those patients meeting the following inclusion criteria: (1) patients with "severe" ARDS, leading to a $\text{PaO}_2/\text{fraction of inspired oxygen (FIO}_2\text{)}$ ratio of < 100 mm Hg after 48 h of respiratory support with our "low-stretch" respiratory strategy; and (2) treatment by PP during the first week of respiratory support.

Mechanical Ventilation and PP

Our low-stretch strategy has been extensively described elsewhere.⁷ Briefly, we use a controlled mode with a limited airway pressure (plateau pressure, < 30 cm H_2O), a low respiratory rate, and a positive end-expiratory pressure (PEEP) determined by the criteria of Suter et al.⁸ Tidal volume, as the consequence of these choices, differed considerably from patient to patient (from 4 to 10 mL/kg measured body weight; average, 8 mL/kg). Patients were sedated with a continuous IV infusion of midazolam and sufentanil, and were paralyzed by cisatracurium besylate, which is our usual strategy during the first 48 h of respiratory support in ARDS patients.

With this low-stretch strategy, PP was systematically implemented after 48 h of respiratory support in patients with severe

ARDS.⁷ We used the method described by Chatte et al.⁹ During PP, we never use thoracopelvic support, and the anterior walls of the thorax and the abdomen lie directly on the plane of the bed. Each PP session lasts 18 h per day and is repeated over 3 to 4 days, thus restoring supine ventilation at the end of the first week of respiratory support. In these selected cases, sedation and curarization were pursued throughout PP. In hypercapnic ARDS patients, we also systematically used a heated humidifier, instead of a heat and moisture exchanger.¹⁰

Echocardiographic Examination

During the first days of respiratory support, bedside echocardiographic evaluations of left and RV function by a transesophageal approach are performed daily in all ARDS patients who are receiving mechanical ventilation in our unit.⁶ All echocardiographic studies were recorded on videotape, permitting computer-assisted measurements, and all recordings are kept in our videotape bank. In the present study, we compared echocardiographic measurements that were performed with patients in the supine position, just before the first PP session, which lasted 18 h, and was repeated just after; thus, also with the patient in supine position too.

We used a wide-angle, phased-array digital sector scanner (Corvision, model SSA-350A; Toshiba; Otawarashi, Japan; or Sequoia C 256; Siemens Medical Solutions; Malvern, PA), equipped with a multiplane transesophageal transducer. Using the signal from the respirator, airway pressure was displayed on the screen of the echo-Doppler device, accurately timing cardiac events during the respiratory cycle and permitting the selection of an end-expiratory beat for measurements.

During an echocardiographic study, we first examined a long-axis, four-chamber view of the cardiac chambers. From this view, left ventricular (LV) and RV areas were measured at end-diastole (ED) and at end-systole (ES). From these measurements, we calculated the RV ED area (RVEDA)/LV ED area (LVEDA) ratio. RV dilatation was defined by an RVEDA/LVEDA ratio of > 0.6 . LV ED and LV ES long axes were measured as the distance from the apex to the midpoint of the mitral valve ring, and LV volumes were calculated using the single-plane, area-length formula. Ejection fraction was calculated as $(\text{LVEDV} - \text{LVESV})/\text{LVEDV}$. During echocardiographic study by this approach, we also noted the absence or the presence of tricuspid regurgitation (TR) using color Doppler, and the severity of TR was graded from digital planimetry of the area of color-coded regurgitant flow. An area < 2 cm² was considered as mild TR (+), and an area between 2 and 4 cm² as moderate TR.¹¹

A short-axis cross-sectional view of the LV at the mid-papillary muscle level was obtained secondarily by a transgastric approach. From this view, septal motion at ES/early diastole was carefully examined to detect any systolic septal dyskinesia, and this abnormality was quantified by measuring the eccentricity index of the LV chamber at ES.¹² Acute cor pulmonale was defined by the combination of RV enlargement with septal dyskinesia.¹³ Finally, the measurement of aortic diameter and continuous Doppler recording of aortic flow by a specific approach were used to quantify cardiac output.¹⁴

Statistical Analysis

Statistical calculations were performed using a statistical software package (Statgraphics Plus package, version 5; Manugistics; Rockville, MD). The data are expressed as the mean $\pm$ SD. Paired comparison of quantitative variables were performed using a Wilcoxon signed rank test, whereas a χ^2 test was used to compare qualitative variables. A p value of < 0.05 was considered to be statistically significant.

RESULTS

Between January 1998 and December 2006, 144 patients meeting the ARDS criteria were treated by controlled mechanical ventilation in our eight-bed medical ICU. Transesophageal echocardiographic evaluation, which was performed during the first 48 h of respiratory support, revealed acute cor pulmonale, which was defined as RV dilatation associated with septal dyskinesia, in 32 patients. The crude incidence of this complication was thus 22%. The respective incidence of this complication in the whole group was significantly related to the range of PaCO_2 and the range of plateau pressure, as illustrated in Fig 1. Among these 144 patients, 42 (29%) exhibited severe ARDS, which was defined as a $\text{PaO}_2/\text{FIO}_2$ ratio of < 100 mm Hg after 48 h of respiratory support, and were treated by PP. These 42 patients (22 men, 20 women; mean age, 51 ± 15 years) constituted the study population.

The average simplified acute physiology II score at hospital admission was 48 ± 13 . Acute respiratory failure resulted from extensive bacterial pneumonia (21 cases), aspiration (14 cases), extrapulmonary sepsis (2 cases), pneumocystis pneumonia (2 cases), chicken pox pneumonia (1 case), cryptococcus pneu-

monia (1 case), and near-drowning (1 case). All patients underwent three to four PP sessions during the first week of respiratory support, and 34 patients were weaned from mechanical ventilation after an mean duration of 25 ± 15 days (range, 7 to 75 days), and were discharged from the hospital. Eight patients ultimately died, after a mean duration of mechanical ventilation of 23 ± 20 days (range, 7 to 70 days). The final hospital mortality rate in the study population was thus 19%.

Among the 42 patients exhibiting severe ARDS, 21 also had acute cor pulmonale documented by echocardiography (group 1). The incidence of this complication was thus 50%, which is significantly higher than its incidence among all 144 ARDS patients who were treated during the study period. On echocardiographic examination, the remaining 21 patients (group 2) had an enlarged RV without septal dyskinesia (7 cases), or a normal RV (14 cases).

Group 1 patients had a significantly lower respiratory system compliance compared to group 2 patients (22 ± 7 vs 28 ± 7 mL/cm H_2O , respectively; $p = 0.008$). As a result, the tidal volume used was significantly lower (6.6 ± 1.4 vs 7.9 ± 1.4 mL/kg, respectively; $p = 0.005$) and was associated with a higher respiratory rate (18 ± 5 vs 16 ± 2 breaths/min, respectively; $p = 0.016$). There was no significant difference concerning average $\text{PaO}_2/\text{FIO}_2$ ratio (74 ± 18 vs 81 ± 12 mm Hg, respectively; $p = 0.14$) or mean PaCO_2 (54 ± 18 vs 51 ± 7 mm Hg, respectively; $p = 0.15$). The same PEEP level (6 ± 1 cm H_2O) was used in both groups). Main respiratory changes produced by PP are presented in Table 1. In both groups, despite an unchanged tidal volume, PP applied for 18 h produced a significant decrease in plateau pressure. In the same manner, despite an unchanged tidal volume, PP applied for 18 h produced a significant decrease in PaCO_2 in both groups (Table 1).

The main hemodynamic and echocardiographic changes produced by PP are presented in Table 2. PP, when applied for 18 h, produced a significant improvement in RV function in group 1 patients, with a significant decrease in RVEDA/LVEDA ratio and a significant decrease in systolic eccentricity (Table 2). An illustrative example is shown in Fig 2. The incidence of TR was also significantly reduced by PP in group 1 (Table 2).

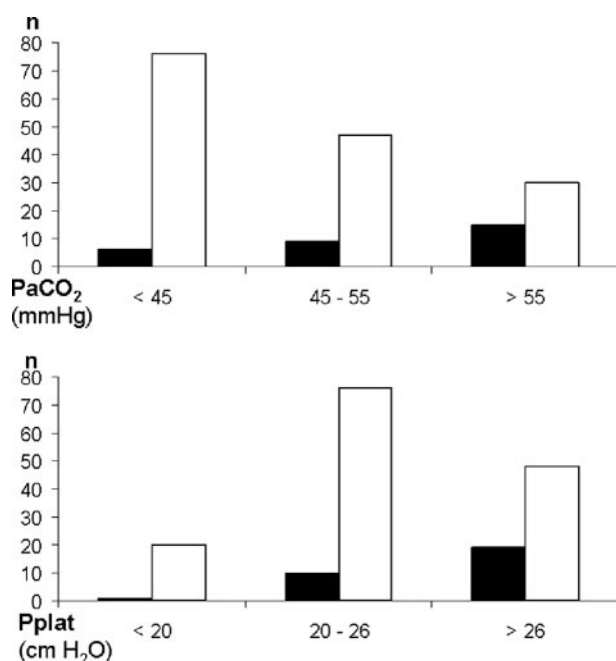


FIGURE 1. The number of patients exhibiting acute cor pulmonale (black column) and the number of patients free of this complication (white column) are plotted against three ranges of PaCO_2 (top) and against three ranges of plateau pressure (Pplat) [bottom]. The progressive increase in the incidence of acute cor pulmonale with PaCO_2 range (ie, 9%, 19%, and 50%) and the progressive increase in the incidence of acute cor pulmonale with Pplat range (ie, 5%, 13%, and 40%) were both statistically significant.

DISCUSSION

When measured during a period of no flow, tracheal pressure in a mechanically ventilated patient reflects alveolar pressure. Thus, introducing an end-inspiratory pause, which produces a plateau,

Table 1—Comparison Between Respiratory Data Recorded in Supine Position Before and After 18 h of PP*

Variables	Before PP	After 18 h PP	p Value
Group 1 (n = 21)			
Tidal volume, mL/kg	6.6 ± 1.4	6.6 ± 1.4	
RR, breath/min	18 ± 5	18 ± 5	
Plateau pressure, cm H ₂ O	27 ± 3	25 ± 3	0.000
PEEP, cm H ₂ O	5.8 ± 1.1	5.8 ± 1.1	
PaO ₂ /FIO ₂ ratio, mm Hg	74 ± 18	115 ± 40	0.000
PaCO ₂ , mm Hg	54 ± 8	50 ± 9	0.005
Group 2 (n = 21)			
Tidal volume, mL/kg	7.8 ± 1.5	7.8 ± 1.5	
RR, breath/min	16 ± 2	16 ± 2	
Plateau pressure, cm H ₂ O	26 ± 2	23 ± 3	0.000
PEEP, cm H ₂ O	5.7 ± 1.2	5.7 ± 1.2	
PaO ₂ /FIO ₂ ratio, mm Hg	81 ± 12	131 ± 33	0.000
PaCO ₂ , mm Hg	51 ± 7	47 ± 9	0.004

*Values are given as the mean ± SD, unless otherwise indicated. RR = respiratory rate.

permits the measurement of alveolar pressure at end-inspiration. Because airway pressure transmission to the pleural space in an ARDS patient is minor,¹⁵ alveolar pressure constitutes the major determinant of transpulmonary pressure (*ie*, the alveolar distending pressure). This distending pressure is exerted on the intraalveolar vessels (*ie*, capillaries) and is a major component of pulmonary vascular resistance. The relation between airway pressure and pulmonary vascular resistance was described experimentally a long time ago by

Whittenberger et al,¹⁶ and, when the lung is inflated by a positive pressure above its functional residual capacity (*ie*, end-expiratory lung volume), pulmonary vascular resistance is increased exponentially.¹⁶ As evidenced by the “U” shape of the Whittenberger curve, there is a level where at which a minor increase in airway pressure may produce a marked increase in pulmonary vascular resistance and induce excessive afterload in the RV.¹⁶

At a time where airway pressure was not limited during mechanical ventilation, ARDS patients

Table 2—Comparison Between Hemodynamic Data Recorded in the Supine Position Before and After 18 h of PP

Variables	Before PP	After 18 h of PP	p Value
Group 1 (n = 21)			
SAP, mm Hg	115 ± 12	117 ± 14	NS
HR, beats/min	107 ± 15	100 ± 13	0.019
CI, L/min/m ²	2.9 ± 0.8	3.4 ± 0.8	0.013
RVEDA/LVEDA ratio	0.91 ± 0.22†	0.61 ± 0.21	0.000
Eccentricity	1.5 ± 0.2†	1.1 ± 0.1	0.000
TR, No.			0.000
+	13	5	
++	7	2	
LVEDV, mL/m ²	45 ± 13†	64 ± 21	0.000
LVEF, %	58 ± 11	60 ± 9	NS
Group 2 (n = 21)			
SAP, mm Hg	118 ± 13	112 ± 19	NS
HR, beats/min	106 ± 16	94 ± 22	0.002
CI, L/min/m ²	3.5 ± 1.1	3.5 ± 1.3	NS
RVEDA/LVEDA ratio	0.60 ± 0.15	0.54 ± 0.11	NS
Eccentricity	1.1 ± 0.1	1 ± 0.1	NS
TR, No.			NS
+	3	2	
++	1	0	
LVEDV, mL/m ²	60 ± 15	60 ± 15	NS
LVEF, %	55 ± 13	59 ± 11	NS

*Values are given as the mean ± SD, unless otherwise indicated. + = mild TR; ++ = moderate TR; SAP = systolic arterial pressure; HR = heart rate; CI = cardiac index; eccentricity = end-systolic eccentricity index in the short axis; LVEDV = LV ED volume; NS = not significant; LVEF = LV ejection fraction.

†p < 0.05 (subgroup 1 vs subgroup 2).



FIGURE 2. An illustrative example of echocardiographic changes observed before PP (top) and after 18 h of PP (bottom). The RV at ED (underlined by a broken contour) was observed in the long axis, whereas the LV at ES was observed in the short axis. The arrow shows septal dyskinesia. LA = left atrium; RA = right atrium.

commonly exhibited pulmonary artery hypertension,⁴ and severe RV dysfunction was frequent.⁵ Because nothing was done at this time, when pulmonary hypertension was observed, this disorder progressively worsened,¹⁷ and enlargement of the RV produced compression of the LV, which finally resulted in refractory circulatory failure.¹⁸ Considering the close relation between distal airways and intraalveolar vessels, tidal hyperinflation, which is now accepted as a major factor inducing lung injury, was obviously responsible for pulmonary artery hypertension at this time in this clinical setting where the presence of microthrombi has also been repeatedly reported.

Airway pressure limitation has markedly reduced the incidence of acute cor pulmonale in ARDS patients.¹⁹ Yet, even though it is less frequent and is sometimes considered to be a dreaded complication of the past,²⁰ acute cor pulmonale has not totally disappeared. In the present report, the incidence of this complication was 22% in a series of 144 consecutive ARDS patients. In the same manner, tidal hyperinflation, even if less frequent, may also persist with the strategy of tidal volume reduction, as recently evidenced by Terragni et al.²¹ Moreover, tidal volume reduction has induced hypercapnia,²² and,

even if “permissive,” hypercapnia also increases pulmonary artery pressure.^{23,24} In one study,¹⁹ we observed that hypercapnia was the only factor significantly associated with acute cor pulmonale in ARDS patients when airway pressure was limited. Nevertheless, even if plateau pressure was kept below 30 cm H₂O, it remains a potential afterloading factor for the RV, particularly in the crucial range of > 26 to 28 cm H₂O.²⁵ It is noteworthy that the same level was also crucial for Terragni et al²¹ in determining tidal hyperinflation. In this setting, a slight (2 to 3 cm H₂O) decrease in plateau pressure may reduce both alveolar stress and RV outflow impedance. But, this decrease should be obtained without any increase in hypercapnia, which would tend to neutralize its beneficial effect on the RV.²³

PP appears to be the only way to achieve this beneficial effect. Mechanical improvement by PP in ARDS patients has been well documented. Servillo et al²⁶ have reported that PP improves the compliance of the respiratory system, so airway pressure can be slightly reduced for a constant tidal volume. Pelosi et al,²⁷ who used thoracopelvic supports, did not confirm this mechanical improvement in patients during PP but observed it as soon as the patient resumed the supine position.

More recently, we have demonstrated a significant mechanical improvement when PP was implemented without thoracopelvic supports,²⁸ and our results were confirmed by another report.²⁹ This mechanical improvement not only concerned respiratory system compliance, but also airway resistance, with a shortened time constant, which suggested a more homogeneous distribution of tidal volume.^{28,29} The net result can be considered as “functional recruitment” and was accompanied by a significant improvement in alveolar ventilation.^{28,29} It may coincide with the “anatomic” recruitment demonstrated by CT scan studies.³⁰ This concept is also in accord with a recent report by Albert and Hubmayr,³¹ who demonstrated by CT scan studies that PP eliminated the compressive force of the heart on the dorsal lung regions. These authors³¹ suggested that this change would lower the inspiratory pressure required to obtain maximal airspace recruitment. This recruitment is expected to improve functional residual capacity and, thus, to reduce pulmonary vascular resistance. This short-term beneficial effect of PP was clearly illustrated by the present study. Changes produced by PP on the RV are characteristic of those resulting from a sudden reduction in pressure overload.

In conclusion, despite airway pressure limitation, patients with severe ARDS with a $\text{PaO}_2/\text{FIO}_2$ ratio < 100 mm Hg after 48 h of respiratory support still exhibit an abnormally high incidence of acute cor pulmonale. In this specific setting, PP, which permits an additional limitation in airway pressure, associated with a slight reduction in hypercapnia, might represent the best therapeutic strategy for treating this dreaded complication.

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