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Improvement in oxygenation by prone position and nitric oxide in patients with acute respiratory distress syndrome

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Abstract *Objective*: Inhaled nitric oxide (NO) and prone position improve arterial oxygenation in patients with the acute respiratory distress syndrome. This study was undertaken to assess the combined effects of NO and prone position in these patients.
Design: Prospective clinical study.
Setting: General intensive care service in a community teaching hospital.
Patients: 14 mechanically ventilated adult patients with the acute respiratory distress syndrome (mean lung injury score 3.23 ± 0.27).
Measurements and results: We measured hemodynamic and oxygenation parameters in the supine position and 2 h later in the prone position, before and during inhalation of 10 ppm NO. A positive response in oxygenation was defined as a ≥ 20 % increment in the arterial oxygen tension/fractional inspired oxygen ratio (PaO_2/FIO_2). In the prone position PaO_2/FIO_2 increased significantly (from 110 ± 55 to 161 ± 89 mmHg, $p < 0.01$) and venous admixture decreased (from 38 ± 12 to 30 ± 7 %, $p < 0.01$) compared to the supine position. Ten of the 14 patients were responders in the prone position. In the supine position, inhalation of NO improved oxygenation to a lesser extent, increasing PaO_2/FIO_2 to 134 ± 64 mmHg ($p < 0.01$) and decreasing venous admixture to 35 ± 12 %, ($p < 0.01$). Five of the 14 patients responded to NO inhalation supine and 8 of 14 responded prone ($p = 0.22$). The combination of NO therapy and prone positioning was additive in increasing PaO_2/FIO_2 (197 ± 92 mmHg) and decreasing venous admixture (27 ± 8 %) ($p < 0.01$). This combination also showed a positive oxygenation response on compared to the supine value without NO in 13 of the 14 patients (93 %). NO-induced changes in PaO_2/FIO_2 were correlated to changes in pulmonary vascular resistance only in the prone position.
Conclusions: In patients with the acute respiratory distress syndrome, the combination of NO and prone position is a valuable adjunct to mechanical ventilation.

Key words Prone position · Nitric oxide · Acute respiratory distress syndrome · Oxygenation

Introduction

The acute respiratory distress syndrome (ARDS) is characterized by non-cardiogenic pulmonary edema which causes severe ventilation-perfusion heterogeneity and elevated intrapulmonary shunt. Treating the resultant hypoxia without causing morbidity is one of the most challenging facets of the care of patients with ARDS. For many years, positive end-expiratory pressure (PEEP) has been the only widely accepted treat-

Table 1 Demographic and clinical characteristics of patients (*LIS* lung injury score, *PEEP* positive end-expiratory pressure, *ARDS* acute respiratory distress syndrome, *RR* respiratory rate, V_E minute ventilation)

Patient/age (years)	Diagnosis	LIS	Onset of ARDS (days)	RR (min^{-1})	V_E (l/min)	PEEP (cmH_2O)	Outcome
1/71	Sepsis	3.00	13	23	9.9	7	Died
2/66	Sepsis	3.25	11	24	12.7	12	Survived
3/77	Bacterial pneumonia	3.25	6	25	11.0	10	Died
4/23	Sepsis	3.50	4	20	14.2	12	Survived
5/82	Bacterial pneumonia	3.00	4	15	8.5	10	Survived
6/60	Bacterial pneumonia	3.50	2	25	10.0	12	Died
7/24	Hypothermia	3.75	1	25	9.1	8	Survived
8/63	Bacterial pneumonia	2.75	30	22	12.0	2	Survived
9/19	Near drowning	3.25	5	16	7.7	8	Died
10/65	Bacterial pneumonia	3.25	5	19	10.8	12	Survived
11/72	Bacterial pneumonia	3.25	1	20	10.4	12	Died
12/67	Vasculitis	3.50	2	24	10.8	12	Survived
13/72	Multiple injuries	3.25	2	25	10.7	13	Survived
14/36	Bacterial pneumonia	2.75	5	25	10.8	10	Died
Mean		3.23	6.5	22	10.6	10	
SD		± 0.27	± 7.3	± 3	± 1.6	± 3	

ment to ameliorate hypoxemia in ARDS. It has been demonstrated that nitric oxide (NO) [1–7] and prone position [8–17] may improve oxygenation when they are used separately. NO inhalation improves gas exchange by inducing vasodilation in ventilated areas and diverting blood flow away from shunt areas [18]. Prone position is associated with an improvement in ventilation-perfusion matching caused either by an increase in ventilation of posterior lung regions and/or by redirection of perfusion away from shunt regions [19].

Recently, two studies [20, 21] investigating the combined effects of NO and prone position in ARDS patients have reported conflicting results. Jolliet et al. [20] studied the combined effects of NO, prone position, and almitrine bismesylate and found that NO and prone position used separately have no effect on arterial oxygen tension (PaO_2) or on venous admixture (Q_s/Q_t), whereas the combination of the two increased PaO_2 but did not change Q_s/Q_t. Papazian et al. [21] found comparable improvements in oxygenation with NO and prone position (57 and 64%, respectively), noting the additive effects on oxygenation when the two were combined in ARDS patients.

The objective of the present study was to assess the combined effects of NO and prone position in ARDS patients with a variety of predisposing diseases and to test the hypothesis that in ARDS the response to inhaled NO can be modified by turning the patients to the prone position.

Material and methods

Patients

We prospectively studied 14 consecutive patients, aged between 19 and 77 years (mean ± SD 57 ± 21) who were admitted to the general intensive care service of the Hospital of Sabadell. All of them had ARDS, diagnosed according to the criteria of the expanded definition of the syndrome [22]. Inclusion criteria were a $PaO_2 < 200$ mmHg for at least 12 h despite PEEP and a fractional inspired oxygen (FiO_2) of 1.0. The lung injury score [23] was 3.23 ± 0.27 (range 2.75–3.75). Patients with previous chronic obstructive pulmonary disease, chest wall abnormalities (flail chest or pneumothorax), evidence of left heart failure, and cranial trauma were excluded. Patients were sedated with intravenous midazolam in combination with morphine. Muscle relaxant agents were allowed for patient care. Demographic data of the patients, PEEP level at the time of the study, previous number of days on mechanical ventilation, and outcome are listed in Table 1. The protocol was approved and conducted according to the principles established in Helsinki and in accordance with the requirements of the Clinical Research Committee of the Hospital of Sabadell. Informed consent was obtained from patients' closest relatives prior to the study.

Materials

Patients were orally intubated with a cuffed endotracheal tube with an internal diameter (i.d.) ranging from 8 to 9 mm and were ventilated in the volume assist/control mode with a constant (square wave) inspiratory flow. Mean FiO_2 was 0.85 (range 0.65–1). The level of PEEP that was previously set was kept constant throughout the study protocol. Patients were ventilated using a Siemens 900 C Servo–Ventilator (Siemens, Sweden) or an Evita 2 or 4 (Draëger, Germany) ventilator. Standard monitoring included heart rate, electrocardiogram, and continuous non-invasive assessment of oxygen saturation by pulse oximetry (HPM1020 A, Palo Alto, Calif., USA). All patients had indwelling radial or femoral artery catheters for blood gas estimation and blood pressure moni-

toring. Eleven of the 14 patients had a 7.5 Fr pulmonary artery thermodilution catheter (93A831H Baxter, Irvine, Calif., USA) in place to measure pulmonary artery pressure, pulmonary capillary wedge pressure, and thermodilution cardiac output (HPM1012 A, Palo Alto, Calif., USA), and to sample mixed venous blood. All pressures were measured by pressure gauge transducers (HPM1006 A, Palo Alto, Calif., USA), which were zeroed and calibrated in reference to atmospheric pressure at the level of the mid-ventral-dorsal thoracic diameter. Cardiac output was determined by the average of three consecutive measurements. The iced indicator was injected at the beginning of the expiratory phase of the respiratory cycle. Immediately after cardiac output measurement, arterial and mixed venous blood samples were simultaneously withdrawn for blood gas determinations (ABL 500, Radiometer Copenhagen, Denmark), and hemoglobin concentration, hemoglobin saturation, and methemoglobin determination (Hemoximeter Osm3, Radiometer Copenhagen, Denmark).

NO administration

NO was continuously administered into the proximal end of the inspiratory limb of the ventilator. NO was supplied from a tank with an NO concentration of 800 ppm in pure nitrogen (Vadinal A, Air Liquide, Spain). The precision flowmeter of the tank was connected to the inspiratory limb via a non-compliant tube (Polyethylene extension tube, i.d. 1.5 mm, Vygon, France). We measured continuously mean NO and nitrogen dioxide concentrations at the level of the main carina using a fast-response chemiluminescent analyzer (NOX4000, Seres, France). For this purpose, we advanced a sterile non-compliant tube (Polyethylene extension tube, i.d. 1.5 mm, Vygon, France) into the trachea 2 cm beyond the tip of the endotracheal tube and continuously aspirated tracheal air at a rate of 150 ml/min. The effect of NO instillation (at a flow rate of 130 ± 20 ml/min and respiratory rate of 22 ± 3 min^{-1}) on FIO_2 and tidal volume is negligible [24].

Prone position

Patients were turned from supine to prone position by a team of five nurses and a physician as previously described [15]. Briefly, in the prone position the entire body was in contact with the bed. Patients were first turned to the lateral decubitus position and then prone. As a part of the turning routine, pressure to the neck and face was alleviated using soft pillows and the eyes were protected. Protective pads were placed at the shoulders, iliac crests, and knees. Shoulders and elbows were placed in physiologic positions and the arms were positioned alongside the body during the study protocol.

Measurements and calculations

We measured arterial and mixed venous blood gases, mean systemic and pulmonary artery pressures, central venous pressure, capillary wedge pressure and cardiac output at each step of the protocol. We calculated the following parameters using standard formulas: PaO_2/FIO_2, Q_s/Q_t and oxygen delivery. Static airway pressure and airflow were measured with the pneumotachographs built into the ventilators. The plateau pressure was measured as the airway opening pressure after a 4-s occlusion at end-inspiration which was taken to represent the elastic recoil pressure of the respiratory system (Pel,rs). Static compliance of the respiratory system was obtained in supine and prone positions by dividing the tidal volume by the difference between Pel,rs and the total PEEP (external PEEP + auto-PEEP).

Protocol

The study protocol consisted of recording the hemodynamic and gas exchange parameters in the supine and prone positions consecutively before NO inhalation and during NO inhalation (NO 10 ppm). Pulmonary secretions were carefully suctioned when the patients were supine and after they were turned to the prone position before all measurements and calculations were performed. In 7 patients (patients 8 to 14 in Table 1), the effect of time was controlled by recording physiologic data 20 min after discontinuing NO in the supine as well as in the prone position. A concentration of 10 ppm was chosen as it has been recommended as the appropriate dose in septic patients with acute respiratory failure [6,25]. A $\geq 20\,\%$ increment in PaO_2/FIO_2 was considered a positive response to a treatment intervention: change in position without NO inhalation or the effect of NO inhalation in each position.

Duration of prone position before NO inhalation was 2 h. Measurements were sequentially obtained in steady–state conditions after a minimum of 10 min without any variations in hemodynamic, gas exchange, and ventilatory parameters. This usually occurred after 20 min at each step. Patients did not undergo changes in the ventilator settings, extra volume infusions, or changes in doses of vasoactive drugs between comparisons.

Statistical analysis

All values are presented as mean ± SD. Comparisons of repeated measurements were assessed by using two within-factors repeated measures analysis of variance. Responders versus non-responders were compared by using a contingency table using Fisher's exact test. Associations among variables were analyzed using Pearson's correlation coefficient with two-tailed significance. Significance was taken as $p < 0.05$.

Results

The demographic and clinical parameters of the study population are shown in Table 1. All patients completed the study protocol. Clinically relevant complications were not detected while turning patients from supine to prone position or during the period the patients remained prone. After the study protocol was complete, the decision to return the patient to the supine position was left to the attending physician.

Effects of position

In the supine position without NO inhalation, PaO_2/FIO_2 and Q_s/Q_t were 110 ± 55 mmHg and $38 \pm 12\,\%$, respectively. Turning patients prone (without NO inhalation) increased PaO_2/FIO_2 to 161 ± 89 mmHg ($p < 0.01$) and decreased Q_s/Q_t to $30 \pm 9\,\%$ ($p < 0.01$) and the hemoglobin oxygen saturation increased from 93 ± 6 to $96 \pm 4\,\%$ ($p < 0.01$). This was not associated with any changes in arterial carbon dioxide tension ($PaCO_2$), mean systemic arterial and pulmonary pressures, central venous pressure, pulmonary capillary wedge pressure, cardiac output, oxygen delivery, and

Table 2 Comparison of physiologic measurements in supine and prone positions before NO inhalation (NO off) and during NO inhalation (NO 10 ppm). Values are mean ± SD (*MAP* mean arterial pressure, *CVP* central venous pressure, *mPAP* mean pulmonary artery pressure, *PCWP* pulmonary capillary wedge pressure, *PVR* pulmonary vascular resistance, *HR* heart rate, *CO* cardiac output, DO_2 oxygen delivery, SaO_2 hemoglobin oxygen saturation, Q_s/Q_t intrapulmonary shunt, *Crs* respiratory system compliance)

	Supine		Prone	
	NO off	NO 10 ppm	NO off	NO 10 ppm
MAP (mm Hg)	75 ± 9	75 ± 10	77 ± 11	78 ± 6
CVP (mm Hg)	8 ± 3	8 ± 3	9 ± 3	8 ± 4
MPAP (mm Hg)	29.1 ± 6.7	27.1 ± 6.5*	31 ± 8	27 ± 6*
PCWP (mm Hg)	11 ± 4	11 ± 4	12 ± 4	11 ± 3
PVR (dyn.s/cm^5)	275 ± 127	245 ± 111*	301 ± 172	255 ± 118*
HR (min^{-1})	96 ± 21	93 ± 22	99 ± 21	96 ± 19
CO (l/min)	6.1 ± 2.8	6.0 ± 2.4	5.8 ± 2.4	5.7 ± 2.0
DO_2 (ml/min)	756 ± 382	760 ± 335	768 ± 377	761 ± 332
PaO_2/FiO_2 (mm Hg)	110 ± 55	134 ± 64*	161 ± 89**	197 ± 92* ***
$PaCO_2$ (mm Hg)	50 ± 8	47 ± 8*	49 ± 8	47 ± 9*
SaO_2 (%)	93 ± 6	95 ± 5*	96 ± 4**	98 ± 2* ***
Q_s/Q_t (%)	38 ± 12	35 ± 12*	30 ± 9**	27 ± 8* ***
Crs (ml/cmH_2O)	28.4 ± 11.9	–	31.9 ± 13.6	–

* $p < 0.01$ compared with NO off in the same position (effect of NO)
** $p < 0.01$ compared with Supine NO off (effect of prone position)
*** $p < 0.01$ compared with Supine NO on (combined effects of NO and prone position)

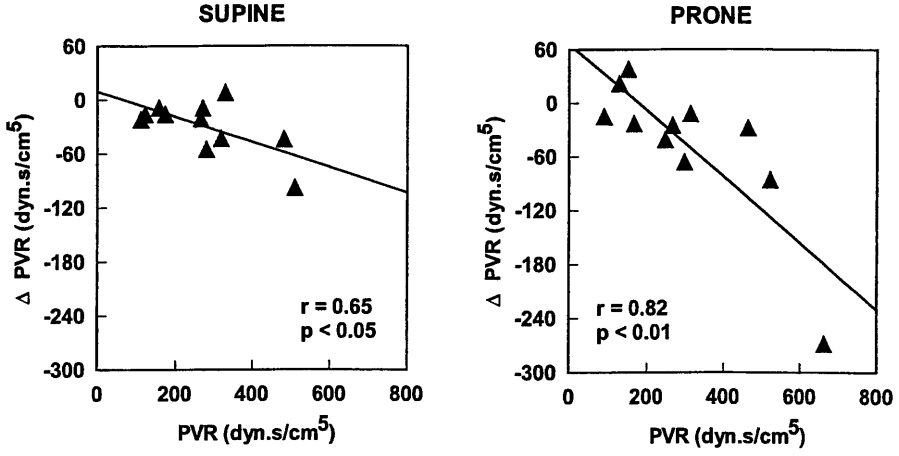

Fig. 1 Effect of inhaling 10 ppm NO on the pulmonary circulation in supine and prone positions. A significant correlation was found between basal pulmonary vascular resistance (*PVR*) and the NO-induced decrease in PVR (ΔPVR)

static compliance. The effects of position on the measured and calculated physiologic parameters are given in Table 2. A positive prone position response with respect to the supine value was observed in 10 of the 14 patients (71%). Four patients did not respond in the prone position. The incidence of pneumonia was no different between responders and non-responders.

Effects of nitric oxide

Inhalation of 10 ppm NO reduced mean pulmonary artery pressure (PAP) and pulmonary vascular resistance (PVR) in both supine and prone positions (Table 2). A significant correlation between basal mean PAP and an NO-induced decrease in mean PAP was found only in the prone position ($r = 0.75$, $p < 0.01$). Basal PVR and the NO-induced decrease in PVR correlated in both supine and prone positions, but the relationship was closer in the prone (supine, $r = 0.65$, $p < 0.05$; prone, $r = 0.82$, $p < 0.01$) (Fig. 1). Inhalation of NO increased PaO_2/FIO_2 and oxygen saturation and decreased Q_s/Q_t and $PaCO_2$ significantly in both positions ($p < 0.01$, Table 2). Basal PVR and the NO-induced increase in PaO_2/FIO_2 were not correlated to the NO-induced decrease in PVR in the supine position (with and without outlying data points) but were correlated in the prone position ($r = 0.73$, $p < 0.01$) (Fig. 2). With NO inhalation in each position, no significant differences were observed in mean systemic arterial pressure, central venous pressure, pulmonary capillary wedge pressure, cardiac output, or oxygen delivery. A positive NO response was observed in 5 of the 14 patients (36%) in the supine position compared with 8 of the 14 patients (57%) in the

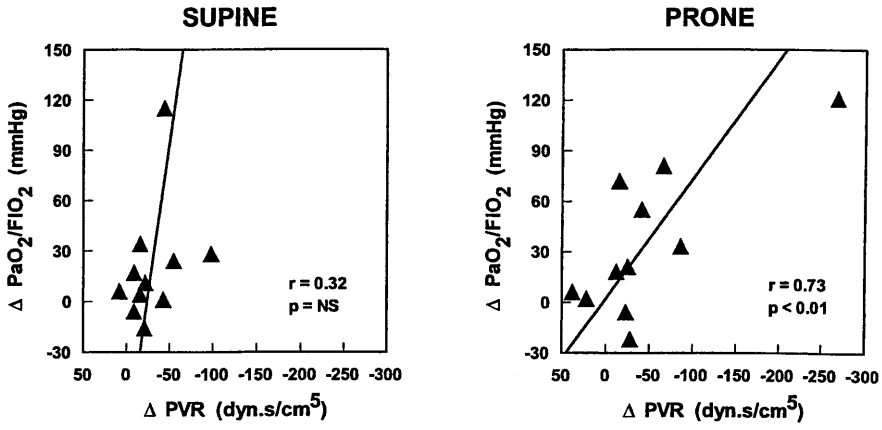

Fig. 2 Effect of inhaling 10 ppm NO on the pulmonary circulation and on oxygenation index PaO_2/FIO_2 in supine and prone positions. NO-induced increase in PaO_2/FIO_2 ($\Delta PaO_2/FIO_2$) was correlated to NO-induced decrease in PVR (ΔPVR) only in the prone position ($r = 0.73$, $p < 0.01$)

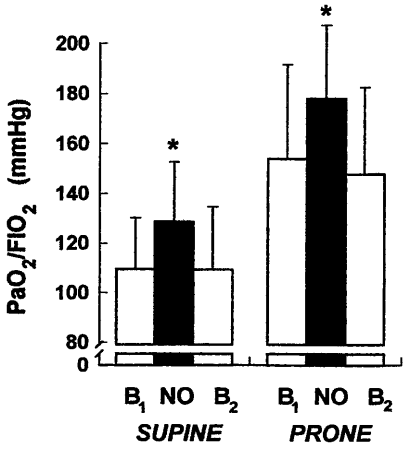

Fig. 3 Average PaO_2/FIO_2 values obtained in 7 patients before and after treatment with 10 ppm NO in supine and prone positions. Baselines before B_1 and after B_2 treatment with NO in both positions were not significantly different. *Significant ($p < 0.01$) change from both baselines

prone position ($p = 0.22$). Five patients did not respond to NO inhalation in either position. The incidence of pneumonia was no different between responders and non-responders. Gas exchange was assessed before and after discontinuation of NO in both supine and prone positions in 7 patients to control for a time effect. As shown in Fig. 3, time exerted no effect on oxygenation and $PaCO_2$ (data not shown). Methemoglobin levels remained below 2% and nitrogen dioxide concentration in the carina did not exceed 2 ppm throughout the study.

Combined effects of position and NO

Simultaneous treatment with prone position and NO was additive in increasing oxygenation and decreasing Q_s/Q_t (Table 2). The combination of prone position and NO increased PaO_2/FIO_2 by 79% and decreased Q_s/Q_t by 41% ($p < 0.001$) (Fig. 4). The combination of prone position and NO inhalation showed a positive response on PaO_2/FIO_2 (≥ 20% increment) compared to the supine value without NO in 13 of the 14 patients (93%).

Discussion

Our results demonstrate that the combination of NO and prone position in critically ill patients with ARDS improved oxygenation in an additive fashion. This occurred without any deleterious effect on hemodynamics or in respiratory system mechanics either with NO or with prone position. Moreover, three non-responders to NO in the supine position became responders to NO prone. Considering a ≥ 20% increase in PaO_2/FIO_2 as a clinically relevant response, 93% of the patients studied responded to the combination of NO and prone position.

The treatment of ARDS is largely supportive, but in recent years both NO inhalation and prone position have gained acceptance in an attempt to improve oxygenation in critically ill patients. NO is a selective pulmonary vasodilator that dilates pulmonary vasculature in ventilated alveoli, thus diverting blood flow away from consolidated lung areas [18]. Even though inhaled NO decreased pulmonary hypertension in the majority of ARDS patients, the response of PaO_2 to NO inhalation is quite variable [26]. On the other hand, recent studies have also shown that turning critically ill, severely hypoxemic patients from the supine to the prone position is a safe and useful therapeutic intervention to increase oxygenation in approximately two thirds of subjects [10, 11, 13–17]. In a recent investigation, Jolliet et al. [20] studied the effect of the prone position, NO (20 ppm), and almitrine bismesylate in 12 patients with ARDS and pneumonia and found a significant increase in PaO_2 only when almitrine bismesylate was added to prone position and NO. On the contrary, Papazian et al. [21] reported a significant and additive effect of

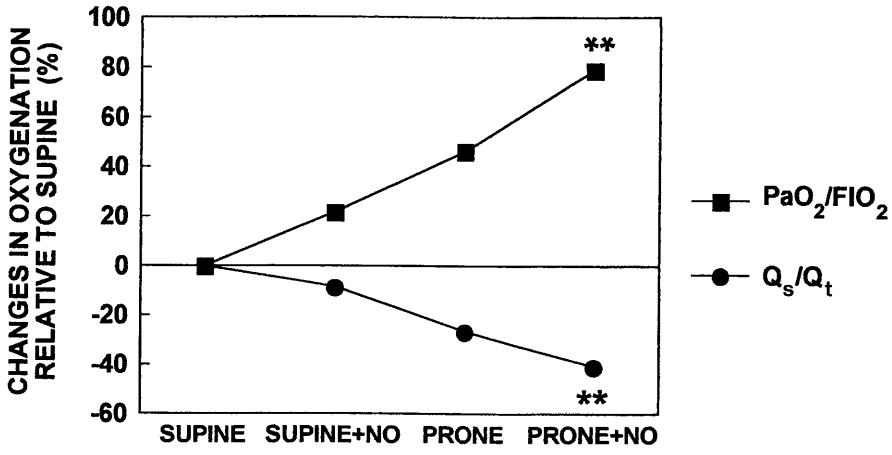

Fig. 4 Absolute increase in oxygenation PaO_2/FIO_2 and decrease in venous admixture Q_s/Q_t originated by the effect of NO and prone position relative to supine position without NO inhalation. Combined treatment with 10 ppm NO and prone position increased PaO_2/FIO_2 by 79 % and decreased Q_s/Q_t by 41 %. ** Significant ($p < 0.001$) change compared with supine

NO with prone position on both PaO_2/FIO_2 and shunt fraction in 93 % of the patients studied. In the present study and using more restrictive criteria in considering a positive response to NO (≥ 20 % increase in PaO_2/FIO_2), the response to NO and prone position, either alone or in combination, was markedly superior to that obtained by Jolliet et al. [20] and similar to that found by Papazian et al. [21]. We consider the following pathophysiologic reasons to explain our results.

Prone position improves oxygenation by several mechanisms. In animal investigations it has been found that regional lung inflation is more homogeneous in the prone position compared to supine because the pleural pressure gradient decreases in the prone position – that is, in the prone position pleural pressure increases in non-dependent regions and decreases in dependent regions [27]. Also, hydrostatic and anatomic mechanisms may influence the pattern of diaphragmatic movement in supine and prone positions. Froese and Bryan [28] showed a cephalad shift of the diaphragm largely confined to the dependent (dorsal) portions during anesthesia in humans. Neither the application of PEEP nor increasing tidal volume restored ventilation to that area, which could only be accomplished by prone positioning. Our study shows a significant improvement in gas exchange with prone position of the same magnitude reported in recent investigations [10, 11, 13–17]. We found a positive response on oxygenation in 71 % of patients in the prone position without NO compared with a 35 % response to NO inhalation in the supine position. A possible explanation for the difference in response to these two interventions is that prone position improves oxygenation by altering both ventilation and perfusion, whereas NO acts only by a vasodilating mechanism. Although physiologic and clinical rationale supports the use of the prone position in critically ill patients, one third of all reported patients are still non-responders.

Optimization of alveolar recruitment improves NO delivery to target cells and thereby response to inhaled NO. Putensen et al. [29] demonstrated that in dogs with oleic acid induced lung injury, adequate recruitment of the lung by PEEP of 10 cmH_2O was essential to get an increase in oxygenation with inhaled NO administration, as compared with a control group without PEEP. Also, in adult patients with ARDS, Puybasset et al. [30] reported that the effect of NO on PaO_2 was potentiated by the application of 10 cmH_2O of PEEP and that response occurred only in those patients in whom PEEP induced significant alveolar recruitment. In the majority of our patients, the PEEP level was previously titrated in the supine position according to the static pressure-volume relationships of the respiratory system [31] and PEEP was kept the same in prone position. Available experimental [27, 32] and human data [17] suggest that the rise in oxygenation during prone positioning is not explained by changes in functional residual capacity. Therefore, the effect of the same PEEP in each position likely resulted in a similar effect on gas exchange. Provided that prone position re-aerates previous atelectatic lung regions by a mechanism different than PEEP, prone position should allow NO to reach previously shunted pulmonary vessels without causing overdistension, and some non-responders to NO in the supine position could still benefit from NO inhalation in the prone position with improved oxygenation.

In the supine position in normal lungs, lung perfusion distributes according to gravity. However, the vertical perfusion gradient is less important prone. Wiener et al. [33] found that regional perfusion followed a gravitational gradient before and after lung injury in dogs and was more uniformly distributed prone, with preferential perfusion of the non-dependent regions. Glenny et al. [34] examined blood flow on a much smaller scale than had previously been attempted and found that perfusion in supine animals was strongly correlated with that observed when animals were prone. This observation suggests that gravity has a minor significance in the regional distribution of pulmonary blood flow in

the prone position. These findings were confirmed in humans with ARDS. Pappert et al. [10] assessed the ventilation-perfusion (V/Q) relationships in 12 patients with ARDS using the multiple inert gas elimination technique. Improvement of oxygenation in the prone position was associated with an improvement in V/Q matching which was attributed to shifting of blood away from shunt regions. In ARDS, the greater the baseline PVR, the greater the NO-induced decrease in PVR [25, 26], although this effect is not potentiated by PEEP-induced alveolar recruitment [30]. This finding suggests that PEEP exerts a balanced effect on recruitment and on overdistension. New recruited territories will allow NO to reach new pulmonary vessels, whereas lung overdistension may cause external compression of pulmonary vessels, making them unresponsive to NO. We found that changes in PAP and in PVR induced by NO inhalation were closely correlated with basal PAP and basal PVR in the prone compared to the supine position. Interestingly, NO-induced changes in PVR were correlated with NO-induced changes in PaO_2/FIO_2 only in the prone position. These findings suggest that NO might reach new pulmonary vessels in the prone compared to the supine position.

The number of patients included in the study and the design of this protocol do not allow us to draw conclusions about the effect of the combination of NO and prone position earlier in the course of ARDS or, whether the effect was synergistic rather than additive in patients suffering from ARDS caused by different etiologies (pulmonary vs extrapulmonary) [35]. In fact, the most important difference between the Papazian et al. study [21] and our study ($>80\%$ increase in PaO_2/FIO_2 with NO and prone position) and that of Jolliet et al. [20] (38% increase in PaO_2/FIO_2 with NO and prone position) is the cause of ARDS. Further studies are needed to clarify these aspects.

In conclusion, in a population of patients with ARDS of different etiologies, we found that the combination of inhaled NO and prone position resulted in a marked increase in oxygenation without any clinical or hemodynamic adverse effects. Oxygenation improved more frequently with prone position than with NO inhalation, although some non-responders to NO responded to the prone position. The combination of NO and prone position appears to be a very useful therapy to improve oxygenation in patients with ARDS.

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