Different Responses of Pulmonary and Extrapulmonary Acute Respiratory Distress Syndromes to Prone Position: Results of a Pilot Study

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Abstract

Objective: The pathophysiology of early pulmonary acute respiratory distress syndrome ($ARDS_p$) is different compared to that of extrapulmonary ARDS ($ARDS_{exp}$). We aimed to compare the hemodynamic and respiratory responses to prone position between $ARDS_p$ and $ARDS_{exp}$ in the present study. **Design:** Prospective controlled clinical study. **Setting:** General intensive care unit of university hospital. **Methods:** Eleven intensive care unit patients with ARDS (6 $ARDS_p$, 5 $ARDS_{exp}$) were included in the study. Hemodynamic and respiratory parameters were recorded at supine position (Supine) and also at 50 min ($Prone_{50min}$) and 130 min ($Prone_{130\ min}$) after establishment of prone position. **Interventions:** Invasive hemodynamic monitoring via pulmonary and radial artery catheters, and prone positioning. **Measurements and Main Results:** In both groups, arterial oxygen partial pressure increased and the alveolar-arterial oxygen tension difference decreased at $Prone_{50min}$ and $Prone_{130\ min}$ compared with Supine ($p < 0.05$). Respiratory index decreased at $Prone_{130\ min}$ ($p < 0.05$) in the $ARDS_p$ group, and at both $Prone_{50min}$ ($p < 0.05$) and $Prone_{130\ min}$ ($p < 0.05$) in the $ARDS_{exp}$ group compared with Supine. Oxygen saturation of the hemoglobin and oxygen content of mixed venous blood increased at $Prone_{50min}$ ($p < 0.05$) and $Prone_{130\ min}$ ($p < 0.05$) only in the $ARDS_{exp}$ group compared with Supine. These parameters did not reach statistical significance in the $ARDS_p$ group. In the $ARDS_p$ group, oxygen content of arterial blood increased only at $Prone_{130min}$ compared with Supine ($p < 0.05$). Intrapulmonary shunt decreased at $Prone_{50min}$ (< 0.05) and pulmonary vascular resistance increased at $Prone_{50min}$ and at $Prone_{130\ min}$ in the $ARDS_p$ group compared with Supine ($p < 0.05$). **Conclusions:** We found different hemodynamic and respiratory responses to prone position in the early stages of both $ARDS_p$ and $ARDS_{exp}$. These responses may differ according to the type of the insult.

Keywords: acute respiratory distress syndrome, prone position, oxygenation, intrapulmonary shunt fraction, respiratory mechanics, etiology

INTRODUCTION

The acute respiratory distress syndrome (ARDS) is thought to be a uniform expression of a diffuse and overwhelming inflammatory reaction of the pulmonary parenchyma to a variety of serious underlying diseases. In 1994, the American-European Consensus Conference [1] defined two pathogenetic pathways leading to ARDS: a direct (pulmonary ARDS) ($ARDS_p$) and an indirect (extrapulmonary ARDS) ($ARDS_{exp}$) insult.

The alveolar-capillary barrier is formed by vascular endothelium and alveolar epithelium. Primarily injured structures were the alveolar epithelium and the vascular endothelial cells in the experimental primary [2,3] and secondary [4,5] pulmonary injury models, respectively. Primary pulmonary insult causes an activation of alveolar macrophages and the inflammatory network, leading to intrapulmonary inflammation. Epithelial damage causes alveolar filling by edema, fibrin, collagen and neutrophilic aggregates (pulmonary consolidation). The pathologic alteration due to a secondary pulmonary insult is primarily represented by microvessel congestion and interstitial edema [6].

Gattinoni et al. [7] reported that the estimated recruitment at the 15 cm H_2O of positive end expiratory pressure (PEEP) level is higher in $ARDS_{exp}$ than in $ARDS_p$. Evidences indicated that the pathophysiology of early ARDS differs according to the type of the insult [8-10]. Lim et al. [11] also reported that pulmonary and extrapulmonary ARDS in their early stages respond diffently to the prone position. The exact mechanisms of different responses to the prone position in ARDS of different origin remain unclear. In this study, we aimed to compare the hemodynamic and respiratory responses of $ARDS_p$ and $ARDS_{exp}$ to prone position.

MATERIALS AND METHODS

This study protocol was approved by the ethics committee of Dokuz Eylul University School of Medicine. An informed consent was obtained from the next of kin of the patients before inclusion in the study. Eleven intensive care unit patients within the first three days of ARDS who met the ARDS criteria were included in the study. ARDS

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was defined according to the criteria established by the American-European Consensus Conference on ARDS [1], i.e., acute onset, arterial oxygen partial pressure/fraction of inspired oxygen (P_{aO2}/F_{iO2})<200 mm Hg (regardless of PEEP level), bilateral infiltrates seen on frontal chest radiograph, and pulmonary capillary wedge pressure (PCWP) below 18 mm Hg.

Six of eleven patients were assigned to the $ARDS_p$ and the others to the $ARDS_{exp}$ groups by three independent physicians. Every patient had an arterial cannula and a Swan-Ganz pulmonary-artery catheter inserted for clinical monitoring. The Acute Physiology and Chronic Health Evaluation II (APACHE II) scores were recorded on the day of the study.

The patients were excluded in cases of hemodynamic instability, severe ascites, unstable bone fracture, injury of medulla spinalis and vertebral column or air leak in leakage test.

All patients were orotracheally intubated (Saviour cuffed-endotracheal tube of 7-8.5 mm internal (ID); Zhanjiang Star Enterprise Corporation, Guangdong, China) and were mechanically ventilated using a Servo 300 ventilator (Siemens-Elema AB, Solna, Sweden). The basic ventilatory setting was in accordance with our institutional protocol for ARDS: pressure control mode at I/E ratio 1/1 including pause 20%, tidal volume 6-8 ml kg^{-1}, and PEEP 10 cm H_2O. PEEP was planned to adjust by 2-3 cm H_2O in the prone position as long as systolic blood pressure remained above 90 mm Hg and hourly urine output was not less than 0.5 ml kg^{-1} h^{-1}. The ventilatory settings remained unchanged during the study period except F_{iO2}. F_{iO2} was set to 1 for three periods of 20 min to produce 100% oxyhemoglobin saturation in the pulmonary capillary blood for intrapulmonary shunt calculation [12].

Midazolam 50 µg kg^{-1} h^{-1} (La Roche Ltd, Basel, Switzerland), fentanyl 2 µg kg^{-1} h^{-1} (Abbott Laboratories, Abbott Park, Illinois, USA) and vecuronium 0.1 mg kg^{-1} h^{-1} (N.V. Organon, Oss, Holland) were given to all patients during the study period.

Patients were turned to prone position as described previously [11,13]. All patients were kept in the prone position at least 3 h and returned to supine position when P_{aO2}/F_{iO2} became greater than 200 mm Hg or had risen above 100 mm Hg from the baseline supine position value at original F_{iO2}.

Study protocol

Patients were ventilated with 100% oxygen for 20 min in supine position (Supine) and arterial and mixed venous blood were obtained for blood gas analysis. After the recording of the hemodynamic and respiratory parameters,

cardiac output (CO) was recorded as the means of the three determinations by thermodilution technique, using 10 ml iced 5% dextrose in water. F_{iO2} was then set to the original value and the patients were turned to prone position 30 min later. After ventilation in prone position with original F_{iO2} for 30 min, F_{iO2} was set to 1 for 20 min and the same procedure was performed ($Prone_{50min}$). The patients were then ventilated with their original F_{iO2} level for 1 hour and the same procedure was performed again at the end of the last 1 hour ($Prone_{130min}$). Figure 1 shows the schematic presentation of the study protocol.

Heart rate (HR), mean arterial pressure (MAP), mean pulmonary artery pressure (MPAP) and PCWP were monitored (Athena type 9060 monitor, S&W Medico Technique A/F, Albertslund, Denmark). CO was determined using the Abbott Critical Care Systems Oximetrix 3 SO_2/CO Computer (Abbott Laboratories, North Chicago, IL, USA). Cardiac index (CI), systemic vascular resistance (SVR), pulmonary vascular resistance (PVR), oxygen content of mixed venous blood (C_{O2}) and arterial blood (C_{aO2}), oxygen delivery (D_{O2}) and oxygen consumption (V_{O2}), and body surface area (BSA) were calculated by the aid of the computer. Blood gas analyses were performed on Nova-Biomedical Stat Profile M Blood Gases Analyzer (Nova Biomedical Corporation, Waltham, USA). Pulmonary static compliance was determined using Servo 300 ventilator and Servo Screen 390 monitor (Siemens-Elema AB, Solna, Sweden). Peak ($P_{aw\ peak}$) and mean ($P_{aw\ mean}$) airway pressures and expiratory minute ventilation (Ve) were also monitored.

Oxygen content of pulmonary capillary blood ($C_{c'O2}$), alveolar oxygen partial pressure (P_{AO2}), respiratory index (RI), oxygen extraction ratio (O_2ER) and venous admixture (Qs/Qt) were calculated as follows (12,14,15):

- Oxygen content (ml dl^{-1})=(0.003 ml O_2 dl^{-1} blood mm Hg^{-1} x P_{O2}) + (S_{O2} x Hb x1.31 ml^{-1} dl^{-1} blood)
- Qs/Qt (%)=$C_{c'O2}$- C_{aO2}/ $C_{c'O2}$- C_{O2} where P_{O2} is partial pressure of oxygen (mm Hg), S_{O2} is oxygen saturation of hemoglobin (%), Hb is hemoglobin concentration (g dl^{-1}), and assuming $S_{c'O2}$ is equal to 1 and pulmonary capillary oxygen partial pressure ($P_{c'O2}$) is equal to P_{AO2}.

If the patients are ventilated with 100% oxygen, $P_{c'O2}$ can be calculated as follows:

- $P_{c'O2}$= P_{AO2}=F_{iO2}x[(P_B+ $P_{aw\ mean}$)- P_{H2O}]-P_{aCO2} where F_{iO2} is equal to 1, P_B is barometric pressure (=760 mm Hg at sea level), and P_{H2O} is water vapor pressure (=47 mm Hg at sea level). Our institute is at sea level.

- RI= $P_{(A-a)O2}$/P_{aO2}
- $P_{(A-a)O2}$=P_{AO2}- P_{aO2}
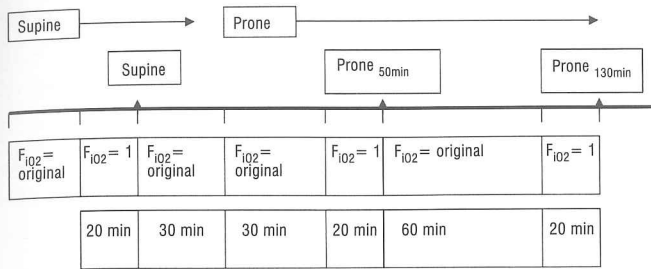- O_2ER= C_{aO2}- C_{O2}/ C_{aO2}

Figure 1: The schematic presentation of the study protocol.

Statistics

All values were expressed as mean ± SD. Significance within the group was determined using Freidman's test. When a significance was obtained, individual comparisons between the measurement times were made using Wilcoxon signed ranks test. Comparison between the groups was made using Mann-Whitney U test. Values of $p \leq 0.05$ were taken to be statistically significant.

RESULTS

All patients tolerated prone position well and completed the study. No clinically important complications or events were seen during the study period. The usual treatments were continuously administered without modifications.

Four of the six patients in the $ARDS_p$ group and two of the five patients in the $ARDS_{exp}$ group died.

There were no differences between groups regarding age, sex, BSA, APACHE II score, days of onset of ARDS and P_{aO2}/F_{iO2}. Tables 1 and 2 show the clinical characteristics and diagnoses of the patients and sources of infections.

There were no differences between the groups at all measurement times except PCWP at Supine. PCWP was significantly higher in the $ARDS_{exp}$ group than in the $ARDS_p$ group (p=0.03).

P_{aO2} increased significantly at $Prone_{50 min}$ and $Prone_{130min}$ compared with Supine in both the ARD-
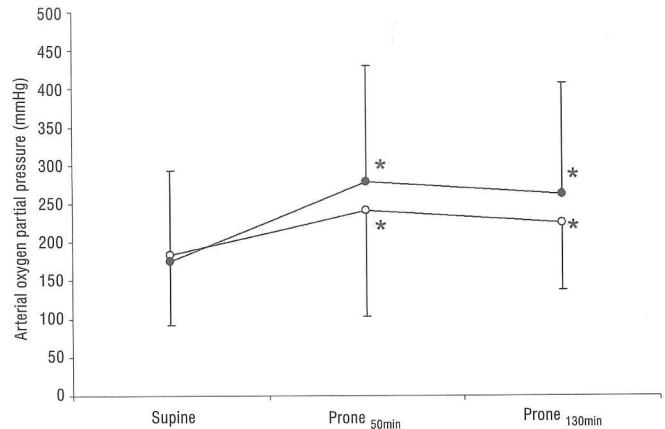

Figure 2: Changes in oxygenation in the $ARDS_p$ and $ARDS_{exp}$ groups.

S_p (p=0.04, p=0.02, respectively) and $ARDS_{exp}$ groups (p=0.04, p=0.04, respectively) (Figure 2).

$P_{(A-a)O2}$ decreased significantly at $Prone_{50min}$ and $Prone_{130min}$ compared with Supine in both the $ARDS_p$ (p=0.04, p=0.02, respectively) and $ARDS_{exp}$ groups (p=0.04, p=0.04, respectively). RI decreased significantly at $Prone_{130min}$ in the $ARDS_p$ group (p=0.02) and at $Prone_{50min}$ (p=0.04) and $Prone_{130min}$ (p=0.04) in the $ARDS_{exp}$ group, all compared with Supine (Figure 3). Oxygen saturation of the hemoglobin of mixed venous blood (S_{O2}) (Figure 4) and C_{O2} increased significantly at $Prone_{50 min}$ (p=0.04, p=0.04, respectively) and $Prone_{130min}$ (p=0.04, p=0.04, respectively) in the $ARDS_{exp}$ group compared with Supine. In the $ARDS_p$ group, the increase in C_{aO2} at $Prone_{130min}$ (p=0.02) and the decrease in Qs/Qt at $Prone_{50min}$ (p=0.02) (Figure 5) were significant compared with Supine. The increase in PVR was significant at $Prone_{50min}$ (p=0.02) and $Prone_{130min}$ (p=0.04) in the $ARDS_p$ group compared with Supine (Figure 6). The results of the study are summarized in Tables 3 and 4.

DISCUSSION

The present study provides some evidences that the prone position improves arterial oxygenation in ARDS, especially in the pulmonary form, by producing alveolar recruitment as judged by the decrease in $P_{(A-a)O2}$, RI and Qs/Qt and the increase in P_{aO2} and PVR.

The alveolar dimensions depend on the transpulmonary pressure (= alveolar pressure – pleural pressure) [16]. The factors determining the pleural and transpulmonary pressure gradients are lung weight, and the shape and mechanical characteristics of the chest and lung. Previous studies [16-18] have indicated that (i) the pleural and transpulmonary pressure gradient becomes more homogeneous in the prone position than in the supine, so there is less difference between the non-dependent and dependent regions, (ii) the prone position may allow the lungs to fit

Table 1. Clinical characteristics of the patients

	ARDSp	ARDSexp
Age (year)	64±23.4	62±20.3
Sex (M/F)	4/2	2/3
APACHE II score	28.8±2.8	31±2.3
BSA (m-2)	1.8±0.1	1.8±0.2
PaO₂/FiO₂	126.3±39.6	118.2±25.1
Days of onset of ARDS	2.3±0.5	2.2±0.8

Values are means ± SD (except sex). [ARDS: Acute respiratory distress syndrome. ARDSp: Pulmonary ARDS. ARDSexp: Extrapulmonary ARDS. APACHE II: Acute Physiology and Chronic Health Evaluation II BSA: Body surface area. PaO₂: Arterial oxygen partial pressure (mm Hg). FiO²: Fraction of inspired oxygen (%). M: male. F: female.
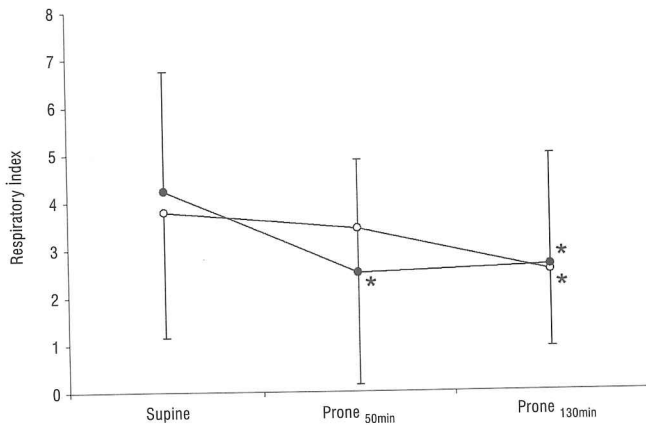
Figure 3: Changes in respiratory index in the ARDS$_p$ and ARDS$_{exp}$ groups.
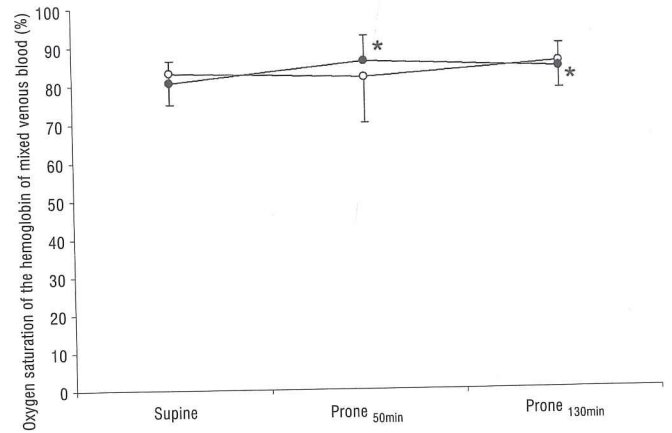

Figure 4: Changes in oxygen saturation of the hemoglobin of mixed venous blood in the ARDS$_p$ and ARDS$_{exp}$ groups.

more uniformly into the thorax such that pleural pressure becomes less positive in the lung regions near to the vertebra than in the supine position, (iii) a nongravitational gradient in perfusion has been observed in the prone position, i.e., more perfusion in the lung regions near the vertebra, and (iv) moving into the prone position may reverse the distribution of the lung weight, i.e., more weight is superimposed on the alveoli in ventral regions, while less weight is superimposed on the alveoli in the dorsal regions. These are believed to be important mechanisms of alveolar

recruitment in the prone position [18]. Briefly, the prone position improves ventilation/perfusion distrubances by generating more ventilated and more perfused lung regions. Improved arterial oxygenation and Qs/Qt values in our study may be related to this mechanism. Additionally, the significant decrease in Qs/Qt at Prone$_{50min}$ in the ARDS$_p$ group may be also explained by the notion that there is a greater advantage of facilitated drainage of airway secretions from the lung in the prone position in pulmonary ARDS than in extrapulmonary ARDS [19]. Furthermore,

Table 2. Clinical characteristics and diagnoses of the patients and sources of infections

Patient No (type of ARDS)	Age (year)	Sex	APACHE II Score	Days of onset of ARDS	PaO$_2$/FiO$_2$	Disease	Culture; identified microorganism
1 (ARDS$_p$)	72	M	31	2	165	Idiopathic megacolon, postoperative nosocomial pneumonia	ETA; Staphylococcus aureus
2 (ARDS$_p$)	56	F	26	3	87	Hypopharyngeal carcinoma, nosocomial pneumonia	ETA; Candida glabrata, Staphylococcus aureus
3 (ARDS$_p$)	78	F	32	2	83	Hip fracture, postoperative nosocomial pneumonia	ETA; Pseudomonas aeruginosa
4 (ARDS$_p$)	70	M	25	2	125	Polytrauma, postoperative nosocomial pneumonia	ETA; Escherichia coli
5 (ARDS$_p$)	87	M	30	3	180	Stomach carcinoma, postoperative nosocomial pneumonia	ETA; Staphylococcus aureus
6 (ARDS$_p$)	21	M	29	2	118	Nosocomial pneumonia	ETA; Pseudomonas aeruginosa, Acinetobacter baumanii
7 (ARDS$_{exp}$)	69	M	30	3	160	Necrotizing pancreatitis, intraabdominal sepsis	Intraabdominal fluid; Enterococcus faecalis
8 (ARDS$_{exp}$)	30	F	31	2	113	Mesenterial ischemia, intraabdominal sepsis	Intraabdominal fluid; Acinetobacter baumanii, Candida albicans
9 (ARDS$_{exp}$)	83	M	35	2	116	Incarcerated inguinal hernia, wound infection	Wound; Klebsiella pneumoniae, Enterococcus faecalis
10 (ARDS$_{exp}$)	56	F	30	1	110	Pancreas carcinoma, intraabdominal sepsis and wound infection	Wound and intraabdominal fluid; Staphylococcus aureus
11 (ARDS$_{exp}$)	72	F	29	3	92	Pancreas carcinoma, intraabdominal sepsis	Intraabdominal fluid; Staphylococcus aureus, Candida albicans

ARDS: Acute respiratory distress syndrome. ARDSp: Pulmonary ARDS. ARDS$_{exp}$: extrapulmonary ARDS. APACHE II: Acute Physiology and Chronic Health Evaluation II. P$_{aO2}$: Arterial oxygen partial pressure (mm Hg). F$_{iO2}$: Fraction of inspired oxygen (%). M: Male. F: Female. ETA: Endotracheal aspirate.
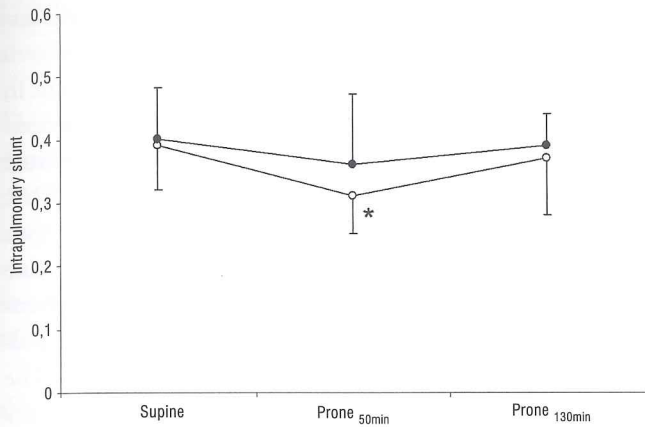
Figure 5: Changes in intrapulmonary shunt in the $ARDS_p$ and $ARDS_{exp}$ groups.
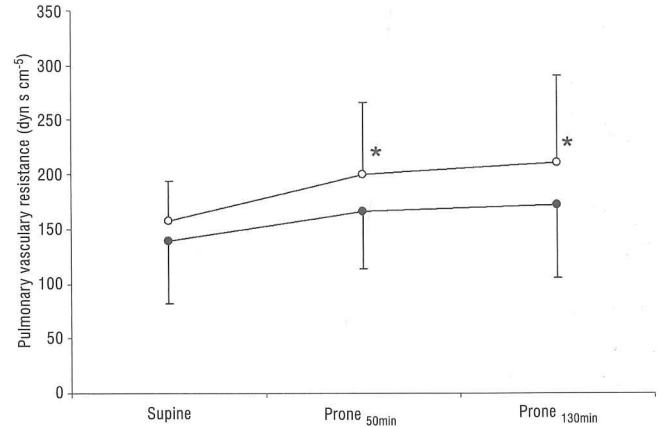

Figure 6: Changes in pulmonary vascular resistance in the $ARDS_p$ and $ARDS_{exp}$ groups.

clinical reports have indicated improved oxygenation and decreased Qs/Qt in the prone position compared with the supine [20,21]. Lim et al. [11] compared the responses to the prone position between early extrapulmonary and pulmonary ARDS groups. They found a dramatic increase in oxygenation in the extrapulmonary ARDS group after 30 min, with a smaller (nonsignificant) increase in the pulmonary group. After 2 hours in the prone position, oxygenation in the pulmonary ARDS group had contin-

ued to rise, whereas there was little further change in the extrapulmonary group (no significant difference between groups at 2 hours). Marked oxygenation response (increase in $P_{aO_2}/F_{iO_2} > 40\%$ from baseline) after 30 min was 23% in pulmonary and 63% in extrapulmonary ARDS groups. Similarly, we observed that the oxygenation response to the prone position at 50 min in the $ARDS_{exp}$ group (62%) was obvious. Lim's and the present study give some evidences that secondarily injured lungs may be more recruitable in

Table 3. Respiratory and oxygenation variables in pulmonary (ARDSp) and extrapulmonary (ARDSexp) ARDS (acute respiratory distress syndrome) groups

	$ARDS_p$ (n=6)			$ARDS_{exp}$ (n=5)		
	Supine	Prone $_{50\ min}$	Prone$_{130\ min}$	Supine	Prone $_{50\ min}$	Prone$_{130min}$
$P_{a\ CO2}$	47.1±10.5	50.5±17.1	48.9±15.8	42.5±5.8	40.5±5.7	38.7±6.9
$P_{a\ O2}$	183.7±91	241.1±136.9*	224.7±86*	175.4±119	279.4±150*	262±145*
S_{O2}	83±7.9	81.6±12	85.3±6.9	80.6±5.7	85.9±6.7*	84±6.1*
Ve	10.9±1.6	10.5±1.8	10.6±1.7	9.7±1.8	9.2±2.1	9.5±2.2
$P_{aw\ peak}$	32.8±4.4	33±4.6	33±4.6	30.6±3.5	31±3.9	30.8±3.9
$P_{aw\ mean}$	21.6±2.6	21.3±2	21.6±2.6	20.2±2.2	20.4±2	20.4±2
D_{O2}	1216±317	1035±240	1042±324	955±203	929±186	906±200
V_{O2}	221±69	205±67	179±90	216±81	190±84	198±74
$P_{(A-a)O2}$	508±93	447±136*	465±84*	521±117	419±146*	439±145*
RI	3.8±2.6	3.4±3.3	2.5±1.6*	4.2±2.5	2.5±2.4*	2.7±2.3*
O_2ER	0.2±0.1	0.2±0.1	0.2±0.1	0.2±0.0	0.2±0.0	0.2±0.1
C_{st}	28.6±9.6	29±9.3	28.1±6.9	35.4±7.6	34.2±7.8	34.4±8.8
C_{aO2}	15.1±3.1	15.2±3.1	15.3±3.2*	12.7±0.7	12.9±1.0	12.9±0.9
C_{O2}	12.4±3.1	12.1±3.0	12.7±2.7	10.0±0.9	10.7±0.9*	10.7±1.3*
F_{iO2}	1	1	1	1	1	1
PEEP	10	10	10	10	10	10

* $p<0.05$ compared with the supine position. All values are means ± SD. PaCO$_2$ = Arterial carbon dioxide partial pressure (mm Hg). PaO$_2$ = Arterial oxygen partial pressure (mmHg). SO$_2$ = Oxygen saturation of the hemoglobin of mixed venous blood (%). Ve: Expiratory minute ventilation (L). Paw peak: Peak airway pressure (cm H$_2$0). Paw mean: Mean airway pressure (cm H$_2$0). DO$_2$: Oxygen delivery (ml min^{-1}). VO$_2$: Oxygen consumption (ml.min^{-1}). P(A-a)O$_2$: Alveolar-arterial oxygen tension difference (mm Hg). RI: Respiratory index. O$_2$ER: Oxygen extraction ratio. Cst: Static compliance (L cm H$_2$O^{-1}). CaO$_2$: Oxygen content of arterial blood (ml dl^{-1}). CO$_2$: Oxygen content of mixed venous blood (ml dl^{-1}). FiO$_2$: Fraction of inspired oxygen. PEEP: Positive end-expiratory pressure (cm H$_2$O).

the prone position. This suggestion is consistent with Gattinoni's study [7], in which more estimated recruitment at 15 cm H_2O PEEP level was seen in the extrapulmonary ARDS group than in the pulmonary ARDS group.

In the present study, decrease in Qs/Qt in the $ARDS_{exp}$ group was statistically non-significant, probably due to the small number of subjects or the mis-estimation of Qs/Qt by the standard venous admixture formula. Sepsis may cause a reduction in VO_2 and is usually associated with an increase in DO_2, especially in fluid-resuscitated patients. Thus, S_{O2} is often increased under septic conditions. S_{O2} affects the result of the standard venous admixture formula. Theoretically, C_{aO2} must be between C_{O2} and $C_{\dot{c}O2}$. If systemic O_2ER is zero then $C_{O2} = C_{aO2}$ and Qs/Qt = 1. If systemic O_2ER is 1 then C_{O2} = 0 and Qs/Qt = $C_{\dot{c}O2}$ - C_{aO2} / $C_{\dot{c}O2}$. If intrapulmonary shunt fraction is 1 then $C_{aO2} = C_{O2}$ and Qs/Qt = 1. Accordingly, estimations of Qs/Qt are affected by systemic O_2ER, and thus reflect both systemic and intrapulmonary shunts. If one assumes that the systemic shunt is zero, then S_{O2} only reflects intrapulmonary shunt. Accordingly, calculated Qs/Qt by the standard venous admixture equation increases as O_2ER decreases and S_{O2} increases, and vice versa. Gowda and Klocke [22] reported that the venous admixture varies substantially with alteration of F_{iO2} in patients who have clinically important ventilation/perfusion abnormalities. They suggested that venous admixture is a poor indicator of the efficiency of pulmonary oxygen exchange, even if venous admixture is calculated from measured arterial and venous oxygen content values. Accordingly, we suggest that the increase in S_{O2} in the prone position caused overestimation of Qs/Qt in the $ARDS_{exp}$ group, so we found a statistically non-significant decrease in Qs/Qt in this group.

Decrease in the O_2ER in spite of an increase in P_{aO2} in the $ARDS_{exp}$ group can be explained by V_{O2} not being supply-dependent in this group because D_{O2} was supranormal and not critical D_{O2} [23].

The rise in PVR in the prone position was significant in the $ARDS_p$ group but not in the $ARDS_{exp}$ group. The non-significant rise in PVR in the $ARDS_{exp}$ group may be related to the small number of subjects. The significant rise in PVR in the prone position in the $ARDS_p$ group may have been caused by alveolar recruitment. In conditions with a decrease in lung compliance, the increase in alveolar pressure (alveolar recruitment) is not completely transmitted into the pulmonary capillaries, and transmural pressure increases. The increase in transmural pressure compresses the pulmonary capillaries so PVR rises [24]. West et al. [25] modelled the relationship between blood flow, pulmonary artery pressure, alveolar pressure and venous return by a Starling resistor. This is a collapsible tube ("pulmonary vessels") within a closed chamber ("pulmonary alveoli") where the pressure may be modified. When the inlet pressure (pressure in the pulmonary artery) is lower than that present in the chamber ("alveolar pressure"), the blood flow stops. On the contrary, when the inlet pressure is greater than in the chamber, the blood flow is determined by the difference between the pressure in the pulmonary artery and the alveolar pressure, or between the alveolar pressure and the venous pressure. Based on this point of view, we suggest that decreases in CI (nonsignificant) and increases in PVR (significant in the $ARDS_p$ group and insignificant in the $ARDS_{exp}$ group) may be related to alveolar recruitment (rise in the alveolar pressure in the lung with poor compliance) in the prone position. Furthermore, CI decreased non-significantly in the prone position in clinical trials [20,21,26], which is consistent with our result.

$P_{(A-a)O2}$ decreased in the prone position in our groups. This observation is consistent with the results of a previous study [27]. We suggest that decrease in $P_{(A-a)O2}$ and RI

Table 4. Hemodynamic variables in pulmonary (ARDSp) and extrapulmonary (ARDSexp) ARDS (acute respiratory distress syndrome) groups

	ARDSp (n=6)			ARDSexp (n=5)		
	Supine	Prone$_{50\,min}$	Prone$_{130\,min}$	Supine	Prone$_{50\,min}$	Prone$_{130\,min}$
HR	129.3±16.9	130±15.9	134.3±16	119±10.5	122±19	121.2±20.1
MAP	84.3±12.6	82.1±15.2	91.8±21.2	84±13.7	90.8±11.4	93.2±10.5
MPAP	29.3±3.9	30.8±3.8	31.3±4.1	29.2±3.3	29.8±5.0	30.0±4.1
PCWP	13.6±1.5	14.3±2.4	13.8±2.8	16.6±1.5	15.2±2.9	15.6±2.0
SVR	785±217	909±298	999±508	818±237	926±185	992±240
PVR	158±36	200±66*	211±80*	139±57	166±52	172±67
CI	4.4±0.5	3.8±0.9	4.0±1.0	4.2±0.9	3.9±0.6	3.7±0.7
Qs/Qt	0.4±0.1	0.3±0.1*	0.4±0.1	0.4±0.1	0.4±0.1	0.4±0.1

* $p < 0.05$ compared with the supine position. All values are means ± SD. HR: Heart rate (beats min-1). MAP: Mean arterial pressure (mm Hg). MPAP: Mean pulmonary artery pressure (mm Hg). PCWP: Pulmonary capillary wedge pressure (mm Hg). SVR: Systemic vascular resistance (dyn s cm-5). PVR: Pulmonary vascular resistance (dyn s cm-5). CI: Cardiac index (L min-1 m-2). Qs/Qt: Intrapulmonary shunt.

may be the other parameters that show the occurrence of alveolar recruitment in the prone position.

Static compliance did not change in the prone position. This observation is consistent with the results of previous studies [20,21,27]. Also, Pelosi et al. [28] observed that the prone position does not affect respiratory system compliance, lung volumes or intraabdominal pressure. Our observation of no changes in $P_{peak\ aw}$, $P_{mean\ aw}$ and Ve in the prone position in a fixed pressure control level can be suggested as indicating that prone position does not affect the lung volume.

The early pathophysiology of ARDS differs according to the type of primary insult to the lung. This hypothesis has been supported by the different responses of pulmonary and extrapulmonary ARDS to PEEP [7] and prone position [11]. The exact mechanisms underlying the different responses to recruitment maneuvers of pulmonary and extrapulmonary ARDS are still unclear. The present study is a limited study with its small number of subjects and provides only some evidences about the occurrence of the alveolar recruitment in the prone position. The question "Are pulmonary and extrapulmonary ARDS different syndromes?" remains to be clarified because the mechanisms underlying the different responses to the alveolar recruitment maneuvers are not clear. We think that there is need for studies with a large number of patients that will compare $ARDS_p$ and $ARDS_{exp}$ to identify the exact mechanisms of improved oxygenation in the prone position and the reliability of the standard venous admixture formula as a parameter in such cases.

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