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Chae-Man Lim
Eun Kyung Kim
Jin Seoung Lee
Tae Sun Shim
Sang Do Lee
Younsuck Koh
Woo Sung Kim
Dong Soon Kim
Won Dong Kim

Comparison of the response to the prone position between pulmonary and extrapulmonary acute respiratory distress syndrome

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C.-M. Lim (✉) · E. K. Kim · J. S. Lee · T. S. Shim · S. D. Lee · Y. Koh · W. S. Kim · D. S. Kim · W. D. Kim
Division of Pulmonary and Critical Care Medicine, Asan Medical Centre,
College of Medicine, University of Ulsan,
Seoul 138-600, Korea
E-mail: cmlim@www.amc.seoul.kr
Phone: +82-2-22243135
Fax: +82-2-22246968

J. S. Lee · S. D. Lee
Department of Radiology,
Asan Medical Centre, College of Medicine,
University of Ulsan, Seoul 138-600, Korea

Abstract *Objectives:* To determine whether the response to the prone position differs between acute respiratory distress syndrome (ARDS) resulting from a pulmonary cause ($ARDS_p$) and that from an extrapulmonary cause ($ARDS_{exp}$).
Design and setting: Prospective observational study in a medical ICU of a university-affiliated hospital.
Subjects: A consecutive series of 31 patients with $ARDS_p$ and 16 with $ARDS_{exp}$ within 3days of onset of ARDS.
Intervention: Prone position for at least 2 h.
Measurements and results: In $ARDS_p$, compared with the supine position (121 ± 49 mmHg), PaO_2/FIO_2 was not increased after 0.5 h but was increased after 2 h in the prone position (158 ± 60 mmHg). In $ARDS_{exp}$, compared with the supine position (106 ± 53 mmHg), PaO_2/FIO_2 was increased after 0.5 h (155 ± 91 mmHg), but was not further changed after 2 h. Marked oxygenation response (increase in $PaO_2/FIO_2 > 40\,\%$ from baseline) after 0.5 h was 23 % in $ARDS_p$ and 63 % in $ARDS_{exp}$, and that after 2 h was 29 % and 63 %, respectively. Static respiratory compliance decreased in the prone position in $ARDS_{exp}$ (30 ± 11 ml/cmH_2O at baseline, 27 ± 11 after 0.5 h and 25 ± 9 after 2 h) but not in $ARDS_p$. Consolidation score as determined on the first chest radiography taken in the prone position decreased to a greater degree in $ARDS_{exp}$ (–2.4 ± 4.1) than in $ARDS_p$ (0.3 ± 4.1).
Conclusion: Pulmonary ARDS and extrapulmonary ARDS in their early stages respond differently to the prone position with regard to the time course of oxygenation, respiratory mechanical behaviour, and radiographic change. These findings suggest that the early pathophysiology of ARDS differs according to the type of primary insult to the lung.

Key words Acute respiratory distress syndrome · Aetiology · Prone position · Oxygenation · Respiratory mechanics · Chest radiography

Introduction

In the field of mechanical ventilation acute respiratory distress syndrome (ARDS) has been regarded as a single clinical entity irrespective of its cause. Recently, however, Gattinoni and colleagues [1] have demonstrated that the mechanical response (elastance) to an incremental level of positive end-expiratory pressure (PEEP) differs between ARDS caused by a direct insult or pulmonary ARDS ($ARDS_p$), and ARDS caused by an indirect insult or extrapulmonary ARDS ($ARDS_{exp}$).

Although various causes of ARDS result in a uniform pathology in the late stage [2, 3, 4, 5], evidence indicates that the pathophysiology of early ARDS may differ according to the type of the primary insult [4, 6, 7, 8]. Interstitial/alveolar oedema and compressive atelectasis are the prominent features in an extrapulmonary insult, whereas epithelial damage and exudative inflammation of lung units (alveoli plus bronchioles) are more prominent in a pulmonary insult [4, 6, 7]. Therefore the response of the lung with ARDS to mechanical ventilation may differ between patients especially in the early stages of ARDS. Compressive atelectasis of $ARDS_{exp}$ would presumably yield more readily to ventilatory measures that increase transpulmonary pressure such as PEEP than parenchymal consolidation of $ARDS_p$.

The prone position may allow the lungs to fit more uniformly into the thorax such that pleural pressure becomes less positive in the dependent regions than in the supine position, which is believed to be an important mechanism of alveolar recruitment in that position [9, 10, 11, 12, 13]. A lowering of pleural pressure at a given ventilator setting means an increase in the effective transpulmonary pressure available for alveolar opening (= alveolar pressure-pleural pressure) [14, 15, 16]. In this sense, the prone position shares a common mechanism of action with PEEP that increases transpulmonary pressure by increasing alveolar pressure. We therefore postulated that $ARDS_p$ and $ARDS_{exp}$ show different respiratory responses to prone positioning, as in the response to PEEP. In this study changes in oxygenation, static respiratory system compliance, and radiographic pattern during the prone position were compared between $ARDS_p$ and $ARDS_{exp}$ patients enrolled in the early stages of disease.

Materials and methods

Subjects

Subjects were recruited between December 1996 and December 1998 in the medical intensive care unit of the Asan Medical Centre, Seoul, Korea. The study was approved by the institutional ethics committee for clinical studies. The prone position protocol, ventilatory strategy and measured variables were not altered throughout the study period. All subjects were enrolled consecutively in the study within 3days of onset of ARDS.

Over this period 67 ARDS patients were diagnosed as defined by the American-European Consensus Conference [17]. Fourteen were judged unsuitable for the prone position trial due to haemodynamic instability (systolic blood pressure less than 90 mmHg or supraventricular tachyarrythmia) ($n = 5$), a time lapse of more than 3days since onset of ARDS ($n = 5$), recent abdominal surgery ($n = 2$), severe ascites ($n = 1$), or an unhealed rib fracture ($n = 1$). Two other patients were excluded because of premature termination of the study due to hypotension in the prone position. Of the remaining 51 patients 47 were grouped as $ARDS_p$ ($n = 31$: witnessed aspiration, 7; diffuse bilateral pneumonia, 24) or $ARDS_{exp}$ ($n = 16$: sepsis syndrome) [17]. Grouping of the subjects into $ARDS_p$ and $ARDS_{exp}$ was straightforward except for cases with simultaneous positive cultures of airway secretions and blood. Patients in this category were classified as $ARDS_p$ if signs of pneumonia preceded the development of ARDS without additional positive cultures from a third focus ($n = 2$). They were classified as $ARDS_{exp}$ if other concomitant cultures (bile, urine, closed pus, etc.) were also positive ($n = 4$). Four of the 51 patients were not classifiable by the above criteria, and thus not included in analysis of data. Clinical characteristics and ventilatory settings of $ARDS_p$ and $ARDS_{exp}$ are shown in Table 1. Bacteriological profiles of the two groups are summarised in Table 2.

Table 1 Clinical characteristics of the subjects (*APACHE III* Acute Physiology and Chronic Health Evaluation III, *MOSF* multiple organ systems failure, C_{st} static respiratory system compliance, *MAP* mean arterial pressure, *PR* pulse rate, *MV* mechanical ventilation, *PP* prone position, *COD* cause of death)

	$ARDS_p$ ($n = 31$)	$ARDS_{exp}$ ($n = 16$)
Age (years)	63 ± 14	61 ± 18
Sex (M/F)	23/8	7/9
APACHE III	67 ± 24	55 ± 16
Number of MOSF	1.4 ± 0.6	1.3 ± 0.6
Lung injury score	2.9 ± 0.5	3.1 ± 0.8
FIO_2	0.78 ± 0.25	0.70 ± 0.21
PaO_2/FIO_2	121 ± 49	106 ± 53
PEEP (cmH_2O)	9 ± 4	8 ± 3
C_{st} (ml/cmH_2O)	26 ± 10	30 ± 11
MAP (mmHg)	90 ± 14	89 ± 16
PR (per min)	119 ± 25	126 ± 20
Total MV time (days)	15 ± 17	11 ± 10
Total PP time (hours)	56 ± 45	43 ± 37
Survivors (%)	13 (42 %)	12 (75 %)*
COD (respiratory/non-respiratory)	8/10	2/2

* $p = 0.065$

Mechanical ventilation

Patients were ventilated using a Servo 900C or Servo 300 (Siemens-Elema, Solna, Sweden). The basic ventilatory setting was in accord with our institutional protocol for ARDS: volume control mode at I:E ratio 1:1 including pause 20 %, tidal volume 6–8 ml/kg, PEEP 10 cmH_2O. PEEP was adjusted by 2–3 cmH_2O (upper limit 15 cmH_2O) in the supine position as long as systolic blood pressure remained above 90 mmHg and hourly urine output was not less than 30 ml. The ventilatory setting, including that for FIO_2, was not changed from at least 30 min prior to until 2 h after the position change. Patients were paralysed during data acquisition by an administration of vecuronium or atracurium along with appropriate sedatives, which were also begun at least 30 min before the position change. As soon as patients recovered from the primary cause of respiratory failure, mechanical ventilation was tapered to pressure support mode. After clinical and respiratory status were well maintained with 0.5 FIO_2 and PEEP of 4 cmH_2O or less, patients were weaned from the ventilator, and supplemental oxygen was supplied via a T-piece. Patients were observed in the ICU for at least 48 h after weaning and for another 48 h after the endotracheal tube was removed. Patients were counted as survivors if discharged to the general ward with stable haemodynamics and respiratory status.

Table 2 Underlying diseases and results of the microbiological studies of the subjects (*CVA* cerebrovascular accident, *CTD* connective tissue disease, *MRSA* methicillin-resistant *Staphylococcus aureus*)

	$ARDS_p$ ($n = 31$)	$ARDS_{exp}$ ($n = 16$)
Underlying disease	Primary pneumonia (8) Malignancy (8) CVA (5) Hepatic disease (3) Diabetes mellitus (2) Miscellaneous (5) Miscellaneous (4)	Primary septicaemia (2) Malignancy (3) CVA (2) Intrahepatic stone (1) Septic arthritis (2) CTD (2)
Culture result	*Airway secretion*[a]	*Blood*
Gram positive	MRSA (12) Others (2)	MRSA (5) Others (2)
Gram negative	*Klebsiella pneumoniae* (5) *Acinetobacter baumanii* (5) *Pseudomonas aeroginosa* (4) Others (2)	*Escherichia coli* (4) *Acinetobacter baumanii* (1) *Pseudomonas aeroginosa* (1) Others (2)
Miscellaneous	*Mycobacterium tuberculosis* (2) Cytomegalovirus (2) Others (2)	*Corynebacterium* (1)

[a] Excess number is due to isolation of multiple pathogens from one specimen

Prone position

After stabilisation in the supine position, patients were manually turned to the prone position by two physicians and two nurses. Patients' faces were turned laterally and supported by an air-filled ring. The arms were laid parallel to the trunk and the pubic area was lifted in men to avoid pressure on the genitalia. The abdomen was allowed to contact the bed without support. While in the prone position the longitudinal axis of the patients' trunk was rotated within 15 ° every 2 h to prevent pressure sore at the shoulder, elbow or iliac crest. All patients were remained in the prone position at least 2 h and returned to the supine position when PaO_2/FIO_2 became greater than 200 mmHg and had risen more than 100 mmHg from the baseline value in the supine position. In some patients who were tracheostomised before the study Safety-Flex (Mallincrodt Medical, Athlone, Ireland) was used to replace the airway. This metal ring-reinforced endotracheal tube ensured a flexible and stable airway during the position change.

Data acquisition

Arterial blood was taken at the radial artery of the non-dominant arm and was analysed for gas partial pressures using standard electrodes, Blood Gas System 288 (Ciba-Corning, Medfield, Mass., USA). Airway pressures were read directly from the digital display on the ventilator. Gas exchange (PaO_2/FIO_2), static respiratory system compliance [C_{st} = inspired tidal volume/(inspiratory pause pressure-total PEEP)] and haemodynamics (mean blood pressure, pulse rate) were determined in the supine position (baseline), after 0.5 h (early response), after 2 h (delayed response) and at the time of the first chest roentgenography in the prone position. Frequencies of a moderate (20–39 % increase in PaO_2/FIO_2 above the baseline) and a marked response (40 % or more increase in PaO_2/FIO_2 above the baseline) were determined at the early and delayed time points.

Changes in chest radiographic patterns in the prone position were analysed by a radiologist (J.S.L.) who was blinded to the ARDS classification of the subjects. The lung was divided into three zones of equal craniocaudal height (a total of six zones in one patient), and was evaluated regarding the presence and extent of consolidation (a homogeneous increase in density that obscures the vascular margins and airway walls), ground-glass opacity (a hazy homogeneous density with preserved vascular margins), and reticular density (linear densities that interlace as a mesh). The extent of the radiographic densities was scored using a three-point scale: score 0 (none), score 1 (less than 50 % of the zone), and score 2 (51 %–100 % of the zone). Scores of the three radiographic patterns in the baseline (supine) radiograph and their individual changes on the first prone radiograph (taken at 10.1 ± 2.3 h in $ARDS_p$, 9.4 ± 2.5 h in $ARDS_{exp}$; $p = 0.172$) were compared between $ARDS_p$ and $ARDS_{exp}$.

Other clinical data included Acute Physiology and Chronic Health Evaluation (APACHE) III score [18], the number of organ failures according to the APACHE II criteria [19] and the lung injury score [20]. Amongst the non-survivors, a cause of death was determined as respiratory or non-respiratory. Respiratory causes of death included (a) intractable hypoxia at 100 % oxygen with or without inhaled nitric oxide (b) severe respiratory acidosis (pH < 7.2 with $PaCO_2 > 60$ mmHg) not intended as permissive hypercapnia and (c) pneumothorax. None of these was preceded by hypotension or metabolic acidosis.

Statistical analysis

All data are expressed as mean ± SD unless otherwise stated. The two groups were compared by the *t* test. Categorical data were analysed by the χ^2 test. Significance of within-subject variables was tested by analysis of variance with post hoc analysis using the Student-Newman-Keuls method. Values of $p \leq 0.05$ were taken to be statistically significant.

Results

Oxygenation response to the prone position

PaO_2/FIO_2 in the supine position did not differ between $ARDS_p$ and $ARDS_{exp}$ (Fig. 1). In $ARDS_p$, compared with the supine position, PaO_2/FIO_2 was not increased after 0.5 h, and increased only after 2 h in the prone po-

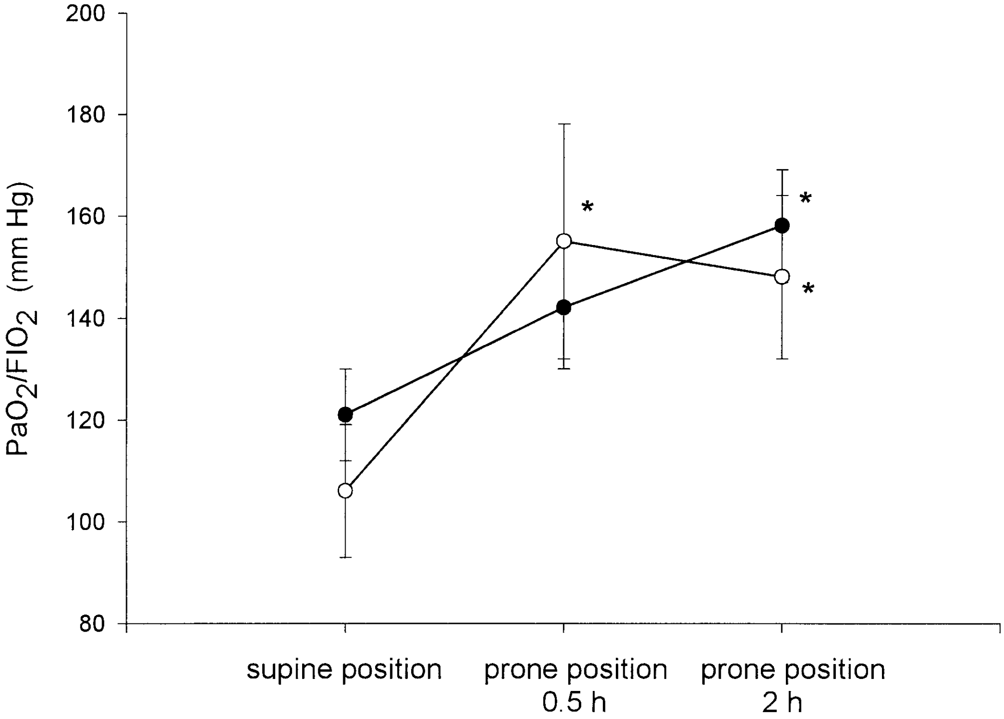

Fig. 1 Change in oxygenation (mean ± SEM) occurring over 2 h after being turned to the prone position in $ARDS_p$ *(closed circles)* and $ARDS_{exp}$ *(open circles)*. $*p < 0.05$ vs. supine position

sition ($p < 0.001$). In $ARDS_{exp}$, compared with the supine position, PaO_2/FIO_2 was significantly increased after 0.5 h in the prone position ($p = 0.001$) without further change after 2 h.

The increase in PaO_2/FIO_2 after 0.5 h in the prone position was 21.8 ± 43.7 % in $ARDS_p$, and 45 ± 42 % in $ARDS_{exp}$ ($p = 0.024$), while that after 2 h in the prone position was 37.2 ± 43.6 % and 46.6 ± 34.1 %, respectively ($p = 0.201$).

The cumulative frequency of a marked response in PaO_2/FIO_2 after 0.5 h in the prone position was 23 % (7/31) in $ARDS_p$ and 63 % (10/16) in $ARDS_{exp}$ ($p = 0.021$), and that after 2 h in the prone position was 29 % (9/31) and 63 % (10/16), respectively ($p = 0.057$). The cumulative frequency of a moderate response in PaO_2/FIO_2 after 0.5 h (10/31 in $ARDS_p$, 10/16 in $ARDS_{exp}$) or after 2 h in the prone position (18/31, 11/16, respectively) were similar between the groups (both $p > 0.05$).

Change in static respiratory system compliance in the prone position

C_{st} in the supine position did not differ between $ARDS_p$ and $ARDS_{exp}$ (Fig. 2). C_{st} in the prone position did not change in $ARDS_p$ ($p = 0.526$, analysis of variance) but decreased in $ARDS_{exp}$ ($p = 0.023$, analysis of variance).

Chest radiographic change in the prone position

Radiographic patterns in the supine position did not differ between the two groups: consolidation score (7.7 ± 2.4 in $ARDS_p$, 8.0 ± 3.5 in $ARDS_{exp}$; $p = 0.713$), ground-glass opacity score (3.0 ± 3.3, 4.6 ± 3.2, respectively; $p = 0.1$) and reticular density score (7.2 ± 3.5, 6.7 ± 3.9, respectively; $p = 0.545$). The consolidation score in prone position decreased more in $ARDS_{exp}$ than in $ARDS_p$ (Fig. 3; $p = 0.047$), while the ground-glass opacity score ($p = 0.472$) and reticular density score ($p = 0.517$) changed to a similar degree (Fig. 3). PaO_2/FIO_2 at the time of chest radiography in the prone position was 157 ± 43 mmHg in $ARDS_p$ and 179 ± 35 mmHg in $ARDS_{exp}$ ($p = 0.02$). Some representative cases are presented in Fig. 4.

Haemodynamics, clinical outcome and cause of death

Mean arterial pressure did not change in the prone position in either group ($ARDS_p$: 90 ± 14 mmHg supine position, 88 ± 18 after 0.5 h prone position, 89 ± 18 after 2 h prone position; $ARDS_{exp}$: 89 ± 16, 89 ± 12 and 91 ± 9 mmHg, respectively; both $p > 0.05$). The pulse rate also did not change in either group in the prone position ($ARDS_p$: 119 ± 25, 121 ± 23 and 119 ± 19/min, respectively; $ARDS_{exp}$: 126 ± 20, 126 ± 23 and 126 ± 24/min, respectively; both $p > 0.05$). The survival rate was 42 % (13/31) in the $ARDS_p$ groups and 75 % (12/16) in

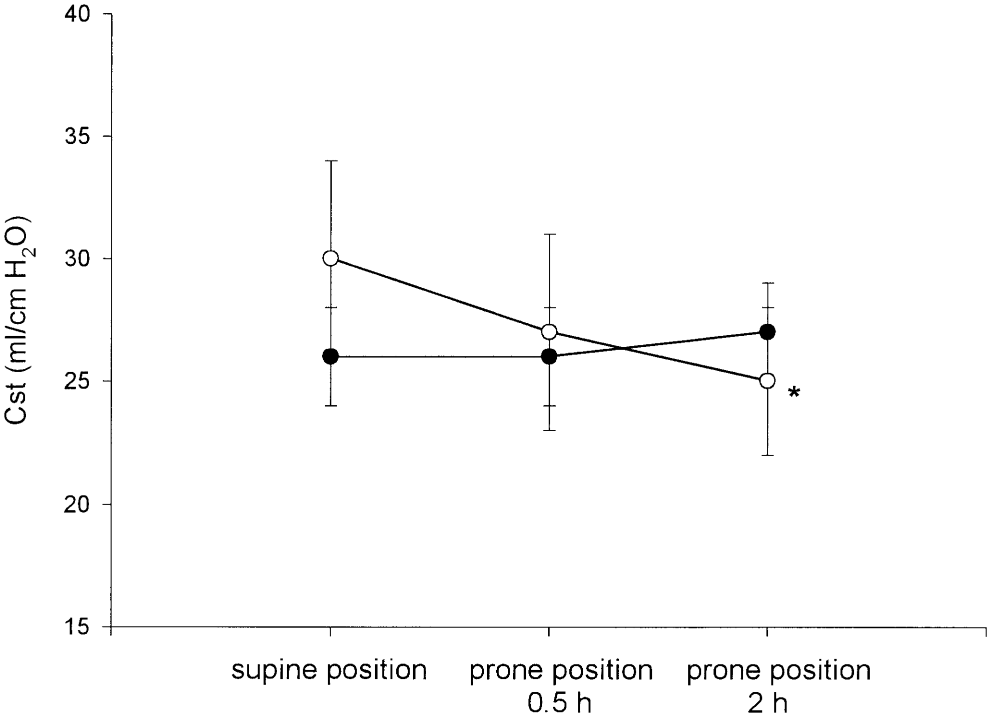

Fig. 2 Change in static respiratory system compliance (*Cst*; mean ± SEM) occurring over 2 h after being turned to the prone position in $ARDS_p$ *(closed circles)* and $ARDS_{exp}$ *(open circles)*. *$p < 0.05$ vs. supine position

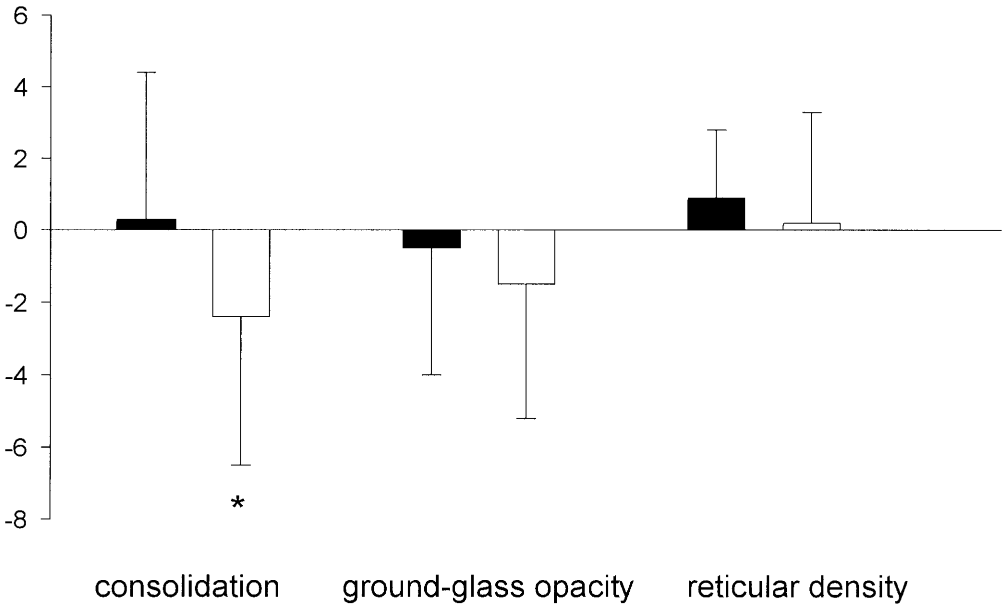

Fig. 3 Change in the radiographic densities as determined on the first chest radiography in the prone position in $ARDS_p$ *(closed bars)* and $ARDS_{exp}$ *(open bars)*. *$p < 0.05$ vs. $ARDS_p$

the $ARDS_{exp}$ group ($p = 0.065$). Mortality due to respiratory causes was similar in the two groups ($p = 0.916$).

Complications in the prone position

Facial oedema developed in almost all patients when they remained in the prone position for more than 1 day. This did not, however, warrant cessation of the prone position, and resolved spontaneously within a few hours of re-assuming the supine position. A difficulty with enteral feeding was noted in 25 % (12/47) of patients. For these patients the volume of liquid diet was reduced to less than one-half. Mild subcutaneous erosions developed at the anterior chest wall in 12 % (5/47) of patients, notably in the elderly. These did not require a

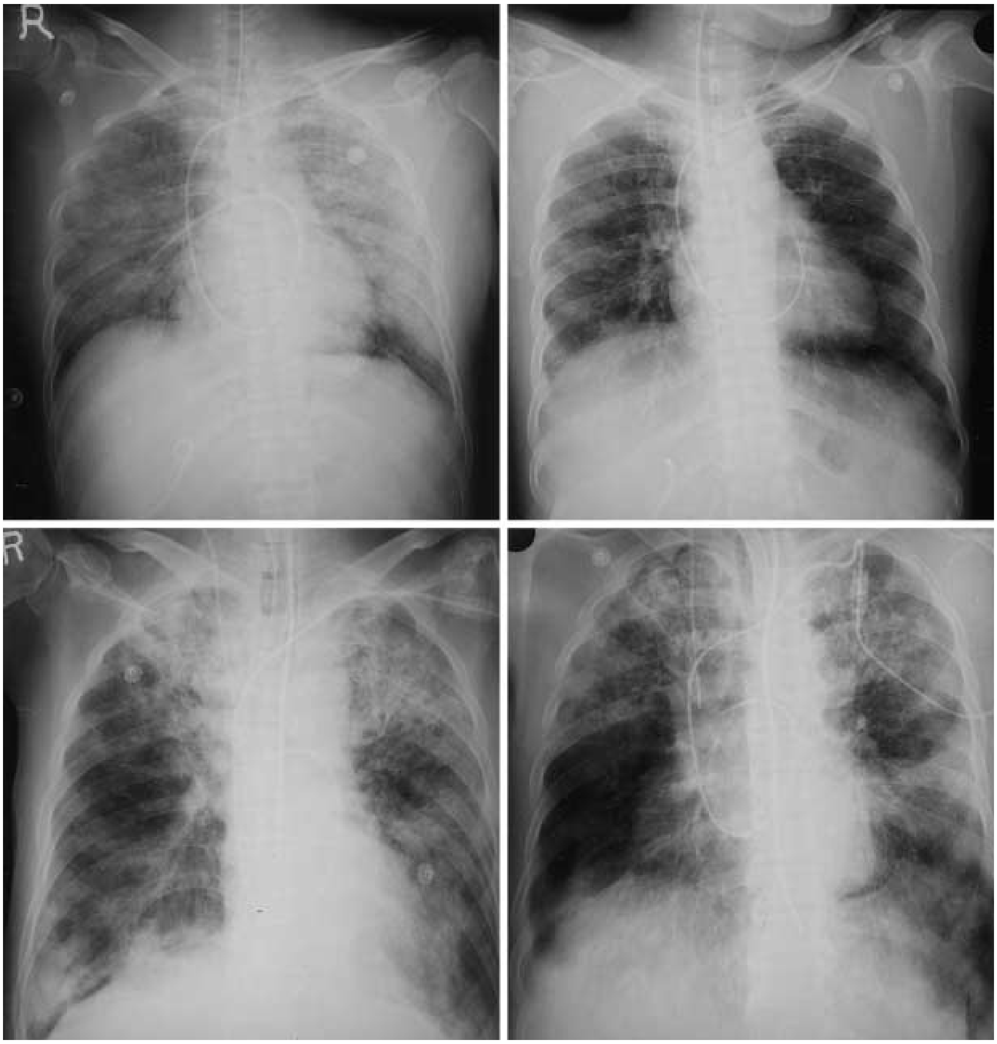

Fig. 4 Examples of chest radiography of $\mathrm{ARDS}_{\mathrm{exp}}$ (*upper panel* 49-year old woman, ARDS associated with biliary sepsis) and $\mathrm{ARDS}_{\mathrm{p}}$ (*lower panel* 79-year-old man, ARDS due to massive aspiration) at the baseline (*left of panels* supine position) and at a similar time point in the prone position *(right of panels)*

specific therapy or cessation of the prone position. The incidence of complications, including facial oedema, difficulty in feeding and subcutaneous erosion, did not differ between $\mathrm{ARDS}_{\mathrm{p}}$ and $\mathrm{ARDS}_{\mathrm{exp}}$ groups. No serious complications in the airway or the lung were noted that could be attributed to the prone position.

Discussion

In patients with early ARDS the improvement in oxygenation in the prone position was more rapid with $\mathrm{ARDS}_{\mathrm{exp}}$ than with $\mathrm{ARDS}_{\mathrm{p}}$. A marked response in oxygenation tended to be more common with $\mathrm{ARDS}_{\mathrm{exp}}$ than with $\mathrm{ARDS}_{\mathrm{p}}$. Static respiratory system compliance in the prone position decreased over the 2 h of observation in $\mathrm{ARDS}_{\mathrm{exp}}$ but did not change in $\mathrm{ARDS}_{\mathrm{p}}$. In the prone position radiographic consolidation resolved to a greater degree in $\mathrm{ARDS}_{\mathrm{exp}}$ than in $\mathrm{ARDS}_{\mathrm{p}}$.

Improvement in oxygenation differed over the time course between the various previous reports on the prone position. Oxygenation response was delayed in studies in which most of the subjects had $\mathrm{ARDS}_{\mathrm{p}}$: at least 10 of the 13 subjects could be classified as $\mathrm{ARDS}_{\mathrm{p}}$ in the study by Langer et al. [10], and 14 of the 16 subjects had $\mathrm{ARDS}_{\mathrm{p}}$ in the study by Pelosi et al. [13]. In contrast, the increase in oxygenation was significant after 0.5 h in the prone position without further increase after 2 h in the study by Pappert et al. [11], in which a majority of the subjects had $\mathrm{ARDS}_{\mathrm{exp}}$ (10 of 12 patients were associated with extrapulmonary causes, such as polytrauma, sepsis, burns, or fat embolism). The present study on two groups of ARDS ($\mathrm{ARDS}_{\mathrm{p}}$ and $\mathrm{ARDS}_{\mathrm{exp}}$) appears to replicate these discordant findings of the previous studies.

The difference in time course of oxygenation depending on the cause of ARDS suggests that the mechanism of oxygenation in the prone position may be multifactorial and/or time dependent. An attenuation of the vertical gradient of the pleural pressure or a more effective transpulmonary pressure at the dependent lung regions is obtained immediately as patients are turned to the prone position. This mechanical benefit could then result in the reversal of compressive atelectasis in ARDS_{exp}, but would not bring about an immediate change in the consolidated lung units of ARDS_{p}. The greater decrease in consolidation densities in the prone position in ARDS_{exp} than in ARDS_{p} in our result suggests this pathophysiological difference between the two syndromes. In support of our speculation, Goodman et al. [21] have shown that ARDS_{p} has more consolidation than ARDS_{exp} despite a similar total lung disease score as determined by computed tomography. ARDS_{exp} can also take advantage of improved haemodynamics in the prone position [22, 23]. The hydrostatic drainage of extravascular lung water is facilitated because a greater portion of lung is positioned above the heart in the prone position. On the other hand, in ARDS_{p} there is a greater advantage of facilitated drainage of airway secretion from the dependent lung in the prone position than in ARDS_{exp} [24]. The latter mechanism in the prone position probably affects gas exchange at a slower rate pace compared with the instantaneous changes in transpulmonary or hydrostatic pressures of the lung.

In addition to the rapidity of the oxygenation response, the initial improvement in oxygenation was more marked in ARDS_{exp} than in ARDS_{p}. In our series of patients a few cases with ARDS_{exp} showed strikingly rapid recovery from ARDS in the prone position (Fig. 4, upper panel). According to our results, the oxygenation response to the prone position can be determined as early as 30 min in ARDS_{exp}, but it must be determined somewhat later in ARDS_{p}.

The second main difference in response to the prone position between these two causes of ARDS was noted with respect to the change in respiratory mechanics. Changes in the respiratory system compliance in the prone position have rarely been reported in earlier studies [9, 10, 11]. Recently Chatte et al. [12] reported that the tidal volume of the patients on pressure-controlled inverse ratio ventilation decreased in the prone position, suggesting that respiratory system compliance is decreased in the prone position. Pelosi et al. [13] partitioned the respiratory system into lung and thoracoabdominal wall and observed decreased thoracoabdominal compliance in the prone position. Since the compliance of the respiratory system was not partitioned in this study, it is difficult to ascertain which compliance was decreased in ARDS_{exp}, and which component of the respiratory system is responsible for the difference between ARDS_{p} and ARDS_{exp}. Despite this limitation, our study revealed that the mechanical properties of the respiratory system in ARDS, when subjected to the prone position, differ depending on the primary insult. Given the common mechanism of action between the prone position and PEEP, it can be concluded that an alteration in transpulmonary pressure has different physiological and mechanical impact on the lung in ARDS_{exp} than in ARDS_{p}.

Since ventilatory strategy is now considered one of the determinants of ventilator-induced lung injury and mortality in ARDS [25, 26], future ventilatory support should address the evolving pathophysiological characteristics of individual ARDS. To our knowledge, however, pathophysiological information on ARDS has been limited largely to extrapulmonary causes and to the late proliferative stage of the disease [3, 5, 27, 28, 29, 30, 31, 32, 33]. The present study on patients with an early ARDS (within 3 days of onset) and the study by Gattinoni and colleagues [1] both suggest that a modification in ventilatory method is necessary in ARDS depending on the type of pulmonary insult. An indirect insult with predominant compressive atelectasis [6, 7] is more likely to respond to ventilatory measures that alter transpulmonary pressure such as PEEP and the prone position. On the other hand, direct parenchymal damage characterised by rigidity of the affected alveolobronchial unit [4, 34] renders the diseased lung units not easily amenable to increased transpulmonary pressure, but rather vulnerable to iatrogenic barotrauma. In view of the evolving nature of ARDS pathophysiology, a tailored mechanical ventilation would be of greater importance during the early stage of ARDS before substantial fibrosis sets in.

A few limitations of the present study need to be noted. Due to the limited number of cases with a pulmonary artery catheter, a temporal change in shunt was not evaluated in our subjects. Measurement and comparison of some other important parameters such as functional residual capacity and airway resistance would have been more informative if added to our present result. Changes in respiratory system compliance as shown in this study may not be reproducible. It may vary depending on the prevalence or severity of abdominal sepsis or use of abdominal support during the prone position [13]. Although the survival rate in ARDS_{exp} tended to be higher than that in ARDS_{p}, the impact of the prone position on survival is not yet known for ARDS. Our observation in 47 patients needs to be verified in a larger population of ARDS_{p} and ARDS_{exp}. Assigning some ARDS patients to the correct type can be difficult in the clinical situation. Furthermore, the classification criteria of ARDS varies from author to author depending on the main point of view, for example, the route of lung injury as direct or indirect [17], proximity of causation, type of cause [20], and pathogenetic role of the cause [35]. In the present study, which adopted the American-European Consensus Conference criteria [17], four patients (7.8 % of the total) were not classifiable.

In conclusion, in the early stage of disease, ARDS_p and ARDS_exp responded differently to the prone position with regard to the time course of oxygenation, respiratory mechanical behaviour and radiographic change. Our findings lend support to the hypothesis that these two categories of ARDS are different syndromes that may require different ventilatory approaches. While categorising ARDS as pulmonary or extrapulmonary may fall short in providing an exact description of the complex and evolving pathophysiology of an ARDS lung, this concept deserves attention in future clinical and basic researches on ARDS.

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