Respiratory and haemodynamic effects of the prone position at two different levels of PEEP in a canine acute lung injury model

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ABSTRACT: This study was designed to examine whether the oxygenation response in the prone position differs in magnitude depending on the level of positive end-expiratory pressure (PEEP) applied in the supine position, and whether cardiac output (CO) increases in the prone position.

In seven supine dogs, acute lung injury was established by saline lavage (arterial oxygen tension (P_{a,O_2})/inspiratory oxygen fraction (F_{I,O_2}) 17.8 ± 9.6 kPa (134 ± 72 mmHg)), and inflection point (P_{flex}) of the respiratory system was measured (6.6 ± 1.4 cmH₂O). $P_{a,O_2}/F_{I,O_2}$ and CO of the supine and prone positions were obtained under the application of low PEEP and then under optimal PEEP (2 cmH₂O below and above P_{flex} , respectively).

The net increase in $P_{a,O_2}/F_{I,O_2}$ by prone positioning was greater at low PEEP (27.3 ± 12.0 kPa (205 ± 90 mmHg)) than at optimal PEEP (4.41 ± 3.0 kPa (33 ± 98 mmHg)) ($p=0.006$). CO decreased significantly with optimal PEEP in the supine position (2.4 ± 0.5 versus 3.1 ± 0.4 L·min⁻¹ at baseline, $p<0.001$), and increased to 3.4 ± 0.6 and 3.6 ± 0.7 L·min⁻¹ in the prone position at 5 min and 30 min, respectively (both $p=0.018$). When the dogs were turned supine at optimal PEEP, CO again decreased (2.4 ± 0.5 L·min⁻¹, $p<0.001$).

In conclusion, the prone position augmented the effect of relatively low positive end-expiratory pressure on oxygenation, and attenuated the haemodynamic impairment of relatively high positive end-expiratory pressure in a canine acute lung injury model. *Eur Respir J 1999; 13: 163–168.*

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Positive end-expiratory pressure (PEEP) has been the most important tool for improving oxygenation in the patients with acute respiratory distress syndrome (ARDS). Although pulmonary oedema of ARDS is diffuse throughout the lung, the requirement for PEEP differs regionally owing to the tissue pressure superimposed along the ventrodorsal axis of the lung [1–3]. In this regard, PEEP slightly above the inflection point (P_{flex}) on the pressure–volume curve is proposed as an optimal level for the recruitment of the collapsed alveoli in ARDS [4, 5].

Positioning patients with severe respiratory failure in the prone position has shown beneficial effects on oxygenation in approximately two-thirds of cases [6–13] and also on cardiac output (CO) in a few cases [6, 14]. The factors involved in the oxygenation response to the prone position are largely unknown, but it was recently shown to be determined by the baseline and the change of supine chest wall compliance in the prone position [15]. There is growing evidence that the compromised ventilation of the dependent lung in the supine position is improved in the prone position [13, 16, 17], while the regional distribution of pulmonary blood flow is little changed or even preferentially distributed to the nondependent lung region [18, 19]. Improved regional ventilation of the dependent lung is believed to be due to the decreased pleural pressure gradient in the prone position, which is translated into a

lower requirement of opening pressure for the dependent alveoli [16, 20–22]. Based on these backgrounds, it was postulated that the prone position may exert a differing effect on oxygenation depending on the level of PEEP applied in the supine position. If PEEP in the supine position is high enough to overcome P_{flex} , or the critical opening pressure (COP) of the dependent alveoli, there will be little gain in oxygenation by prone positioning. If PEEP in the supine position is, on the other hand, just beneath COP, the improvement will be greater because COP can now be overcome as the regional pleural pressure becomes lowered in the prone position.

As to the haemodynamic effect of the prone position, the majority of studies reported no overall change in haemodynamic parameters [12, 13, 15]. There are, however, some anecdotal cases showing increased CO in the prone position compared with the supine position [6, 14]. Regarding this possible benefit of the prone position, it was suggested that the prone position can divert positive pressure surrounding the heart (juxtacardiac pleural pressure) toward the recruited dorsal lung [23]. The diversion of juxtacardiac positive pressure toward the dorsal lung will lessen the lifting of the cardiac fossa incurred by PEEP. This study also evaluated whether the prone position can improve CO impaired by PEEP in the supine position, and which haemodynamic variables are influenced by position change.

Materials and methods

Animal preparation

Seven male mongrel dogs (20.0 ± 3.9 kg) were used for this study. The following protocol was approved by the Animal Use Committee of the Asan Institute for Life Sciences and the dogs were handled in accordance with the National Institutes of Health guidelines. After induction of anaesthesia with ketamine $5 \text{ mg} \cdot \text{kg}^{-1}$ *i.m.* in the thigh muscle and thiopental sodium $5 \text{ mg} \cdot \text{kg}^{-1}$ *i.v.* bolus *via* the cephalic vein, the dogs were intubated orotracheally with a cuffed endotracheal tube of 8 mm internal diameter. The dogs were ventilated with a Servo 900C (Siemens-Elma, Solna, Sweden) at tidal volume (V_T) $15 \text{ mL} \cdot \text{kg}^{-1}$, respiratory frequency $20 \text{ beats} \cdot \text{min}^{-1}$, inspiratory:expiratory (I:E) = 1:3, pause time 10%, PEEP 0 cmH_2O and inspiratory oxygen fraction (F_{I,O_2}) 1.0. External electrodes were placed at appropriate sites for cardiac frequency (f_c) and electrocardiac monitoring. The femoral artery was cannulated for arterial blood gas analysis using Blood gas system 288 (Ciba-Corning, Medfield, MA, USA) and for mean arterial pressure (MAP) monitoring with Escort II (Medical Data Electronics, Arleta, CA, USA). Through either the femoral vein or the external jugular vein, a 7.5 Fr Swan-Ganz catheter (Edwards Critical Care Division, Baxter, Irvine, CA, USA) was placed at the main pulmonary artery under the guidance of pressure profile for recording mean pulmonary artery pressure (MPAP), and pulmonary artery occlusion pressure (PAOP). The midaxillary plane was the reference for pressure measurement in both positions. CO, stroke volume (SV), right ventricular ejection fraction (RVEF) and right ventricular end-diastolic volume (RVEDV) were measured with a thermodilution technique using Explorer® (Edwards Critical Care Division). Thermodilution injection was performed at end-expiration using 5 mL cold saline aliquots, repeated four times with a 1-min interval and averaged to derive CO, SV, RVEF, and RVEDV. Anaesthesia was maintained throughout the study with thiopental sodium $3 \text{ mg} \cdot \text{kg}^{-1} \cdot \text{h}^{-1}$ *i.v.* *via* the cephalic vein, and pancuronium bromide $0.05 \text{ mg} \cdot \text{kg}^{-1}$ was given *i.v.* every 30 min to prevent spontaneous respiration. Volume expansion was avoided during the study, except for the intravenous anaesthesia.

Control data and saline lavage

At the completion of all vascular procedures, 30–45 min was allowed for stabilization of blood pressure and pulse rate. After the dog was stabilized, respiratory variables (arterial blood gas analysis (ABGA), total respiratory system compliance (C_{rs})) were measured in the supine position and at 30 min after being turned to the prone position. Haemodynamic variables (MAP, f_c , CO, MPAP, PAOP, SV, RVEF, RVEDV) were measured in the supine position, and at 5 and 30 min of the prone position. Pulmonary vascular resistance (PVR) was calculated by the equation:

$$\text{PVR} (\text{dyne} \times \text{s} \times \text{cm}^{-5}) = 80 \times (\text{MPAP} - \text{PAOP}) / \text{CO}.$$

After these control measurements, acute lung injury was induced in the dog by saline lavage as described below to the point of $P_{a,O_2}/F_{I,O_2}$ ratio $<26.6 \text{ kPa}$ ($<200 \text{ mmHg}$).

Warmed saline at 38°C ($30 \text{ mL} \cdot \text{kg}^{-1}$) was administered into the dog's lung *via* the endotracheal tube, half of the amount given in each lateral decubitus position for even distribution between the lungs. With the saline residing in the lung the mechanical tidal breaths were resumed for 1 min at the same ventilatory settings as in the control, except for occasional lowering of V_T to prevent peak airway pressure from exceeding $40 \text{ cmH}_2\text{O}$. Saline was then drained out by gravity using a large-bore 120 cm-long syphon connected to the endotracheal tube with the dog lifted slightly at the lower thorax. Saline was removed earlier if the dog showed severe bradycardia ($<40 \text{ beats} \cdot \text{min}^{-1}$). A second drainage was attempted in 2 min if the retrieved amount of saline was less than half ($15 \text{ mL} \cdot \text{kg}^{-1}$) of the administered amount. Half to two-thirds of the administered saline was usually recovered. The dogs remained supine during the whole lavage period, and underwent two or three lavages ($60\text{--}90 \text{ mL}$ of normal saline $\cdot \text{kg}^{-1}$ in total). When the $P_{a,O_2}/F_{I,O_2}$ ratio met the criteria for acute lung injury, 30 min was allowed for the blood pressure and pulse rate to stabilize. At the end of the stabilization period, the $P_{a,O_2}/F_{I,O_2}$ ratio was again confirmed to be $<26.6 \text{ kPa}$ ($<200 \text{ mmHg}$) and then P_{flex} was measured using the constant flow method, as described previously [24]. Briefly, the V_T of the ventilator (Servo 900C) was first decreased to 30 mL by increasing the respiratory frequency, and inspiratory pause pressure was measured by an in-spiratory hold of 3 s with PEEP at 0 cmH_2O . After the inspiratory pause pressure of V_T 30 mL was obtained, V_T was returned to the dog's normal V_T for the following five breaths to regain the volume history. The same manoeuvre was repeated at increasing V_T by 20 mL until the dog's normal V_T ($15 \text{ mL} \cdot \text{kg}^{-1}$) was reached. A total of 13–21 pause pressures were obtained in the dogs, and plotted against the inspired volumes (fig. 1). The pressure at the intersection of the starting compliance and the inflational compliance was defined as the P_{flex} .

Prone position at low-PEEP versus optimal PEEP

Two arbitrary levels of PEEP were applied to each dog: PEEP of 2 cmH_2O below the P_{flex} (low PEEP), and 2

Fig. 1. – Pressure–volume curve obtained in a dog after the establishment of acute lung injury by saline lavage. Inspiratory pressures were measured using the constant flow method with the ventilator *in situ* at increasing tidal volumes, and the inflection point (C) was determined at the intersection of the starting compliance (A) and the inflational compliance (B) (the steepest portion).

cmH₂O above the P_{flex} (optimal PEEP). After the respiratory and haemodynamic measurements at zero end-expiratory pressure (ZEEP; first ZEEP), low PEEP was applied for 30 min in the supine position, and then the dog was positioned prone for another 30 min at the same PEEP. Respiratory variables were measured at the end of the supine position (supine), and at 30 min of the prone position (prone 30 min). Haemodynamic variables were obtained at the end of the supine position and at 5 min (prone 5 min) and 30 min of the prone position. After the low PEEP trial, PEEP was turned off for 15 min and another set of physiological data were measured (second ZEEP). Optimal PEEP was then applied to the dog and the respiratory and haemodynamic data were collected at the same time points as in low PEEP. At the end of the prone position under optimal PEEP, the dog was turned to the supine position again with the same optimal PEEP and the haemodynamic variables were measured at 5 min (resupine) to see if the haemodynamic effect of the prone position persists or disappears.

Computed tomography scan in one of the dogs

In a representative animal (the last dog in which the lung lavage and intervention were reliably accomplished), computed tomography (CT) of the lower thorax was performed with Somatom Plus (Siemens, Erlangen, Germany) to see how the dependent lung aeration was affected in the prone position under low PEEP *versus* optimal PEEP. Scans were performed in 1 mm collimation thickness, 20 mm interval at 275 mA, 137 kV using a high-frequency reconstruction algorithm with window width=1,500, window centre=-650.

Statistical analysis

Results are expressed as mean $\pm$ standard deviation (SD). Friedman's nonparametric analysis of variance was performed for comparison between different conditions. For individual comparison with the supine position or low PEEP, the paired t-test (for normal distribution) or Wilcoxon signed-rank sum test (if normality failed) was used. A p-value <0.05 was considered statistically significant.

Results

Respiratory effect of the prone position at low PEEP versus optimal PEEP

After acute lung injury was established, the $P_{a,O_2}/F_{I,O_2}$ ratio was 17.8 ± 9.6 kPa (134 ± 72 mmHg), and C_{rs} 18.5 ± 2.4 mL·cmH₂O⁻¹ (table 1). The inflection point of the dogs was measured as 6.6 ± 1.4 cmH₂O (range: 4.5–8.5 cmH₂O) and an example is shown in figure 1. The absolute value of the $P_{a,O_2}/F_{I,O_2}$ ratio was higher at optimal PEEP than at low PEEP both in the supine and prone positions. The net increase in the $P_{a,O_2}/F_{I,O_2}$ ratio induced by position change, however, was far greater at low PEEP compared with that at optimal PEEP (fig. 2). The net increase in the $P_{a,O_2}/F_{I,O_2}$ ratio by position change at optimal PEEP was not different from that in the control. In the CT scan at low PEEP (fig. 3a), the new dependent ventral lung remained aerated in the prone position and atelectasis of the dorsal lung in the supine position practically disappeared. The dorsal lung region at optimal PEEP (fig. 3b), on the other hand, was already aerated in the supine position, and changed little in the prone position.

Haemodynamic effect of prone position

In the control, MAP, MPAP, PVR, CO and SV were not changed between supine, prone 5 min and prone 30 min (table 2). Compared with supine, $\dot{V}_C$ was higher and PAOP was lower at prone 5 min.

At low PEEP, all haemodynamic variables except $\dot{V}_C$ were not changed from ZEEP in supine. Compared with supine, CO tended to be higher at prone 5 min and prone 30 min, but did not reach statistical significance.

At optimal PEEP, MAP, CO and SV decreased from the values at ZEEP in supine. Compared with supine, MAP, CO and SV all increased at prone 5 min and prone 30 min. MPAP was higher at prone 5 min and prone 30 min, PAOP was lower at prone 5 min, and PVR was lower at prone 30 min. $\dot{V}_C$ was not changed significantly with position change. At resupine, MAP, CO, and SV all decreased from the values at prone 30 min, while PAOP was elevated again (table 2).

Table 1. – Respiratory variables in the supine position *versus* prone position in the control and in acute lung injury (ALI) at low positive end-expiratory pressure (PEEP) or optimal PEEP

		pH	P_{A-a,O_2}	$P_{a,O_2}/F_{I,O_2}$	$\Delta P_{a,O_2}/F_{I,O_2}$	P_{pause}	C_{rs}
Control	Supine	7.43 $\pm$ 0.07	220 $\pm$ 76	445 $\pm$ 74		11.3 $\pm$ 4.8	36.3 $\pm$ 13.2
	Prone 30 min	7.44 $\pm$ 0.07	186 $\pm$ 57	480 $\pm$ 57	33 $\pm$ 98	11.4 $\pm$ 4.1	35.2 $\pm$ 13.0
ALI							
First ZEEP	Supine	7.29 $\pm$ 0.09*	523 $\pm$ 73*	134 $\pm$ 72*		19.5 $\pm$ 2.3*	18.5 $\pm$ 2.4*
Low PEEP	Supine	7.35 $\pm$ 0.08	463 $\pm$ 111	195 $\pm$ 112		20.1 $\pm$ 3.2	22.4 $\pm$ 2.9
	Prone 30 min	7.38 $\pm$ 0.08	261 $\pm$ 31 [†]	400 $\pm$ 33 [†]	205 $\pm$ 90 [§]	18.4 $\pm$ 3.8	25.7 $\pm$ 4.1
Second ZEEP	Supine	7.30 $\pm$ 0.10*	526 $\pm$ 86*	132 $\pm$ 78*		19.9 $\pm$ 3.2*	18.3 $\pm$ 2.6*
Optimal PEEP	Supine	7.38 $\pm$ 0.08	195 $\pm$ 62 [‡]	466 $\pm$ 63 [‡]		22.1 $\pm$ 2.3 [‡]	25.3 $\pm$ 5.9
	Prone 30 min	7.38 $\pm$ 0.07	162 $\pm$ 60 ^{†‡}	499 $\pm$ 63 ^{†‡}	33 $\pm$ 33	20.6 $\pm$ 2.3 ^{†‡}	28.5 $\pm$ 6.5 [†]

Values are expressed as mean $\pm$ SD. ZEEP: zero end-expiratory pressure; P_{A-a,O_2} (mmHg): alveolar–arterial difference of oxygen tension; $\Delta P_{a,O_2}/F_{I,O_2}$ (mmHg): difference of arterial oxygen tension (P_{a,O_2})/inspiratory oxygen fraction (F_{I,O_2}) between prone position at 30 min and supine position; P_{pause} (cmH₂O): pause pressure; C_{rs} (mL·cmH₂O⁻¹): total respiratory system compliance. *: p<0.05, ALI *versus* control at ZEEP; [†]: p<0.05, prone 30 min *versus* supine; [‡]: p<0.05, optimal PEEP *versus* low PEEP; [§]: p<0.05, low PEEP *versus* control or optimal PEEP. (0.133 kPa=1 mmHg.)

Fig. 2. – Comparison of the net increase in arterial oxygen tension (P_{a,O_2})/inspiratory oxygen fraction (F_{i,O_2}) ratio obtained by prone positioning between the control, low positive end-expiratory pressure (PEEP) and optimal PEEP. Note the increase at low PEEP is significantly greater than those at the control or optimal PEEP. *: $p < 0.05$ compared with the control or optimal PEEP.

Owing to the technical limitations of Explorer® (inability to measure RVEF at an $\dot{V}_C$ of ≥ 150 beats·min⁻¹), the ejection fraction and end-diastolic volume of the right ventricle could not be obtained in four out of the seven dogs. Therefore, the right ventricular haemodynamics were not analysed.

Fig. 3. – Computed tomography scan of a dog's lung with saline-lavage injury at end-expiration in the supine (a and c) versus prone (b and d) position at low positive end-expiratory pressure (PEEP) (a and b) and at optimal PEEP (c and d). The scans of the prone position (b and d) are presented upside down for the purpose of comparison. Note that the new dependent ventral lung at low PEEP remained aerated in the prone position, while the nondependent dorsal lung, previously collapsed in the supine position, also became aerated. The same dorsal lung region at optimal PEEP, on the other hand, was already aerated in the supine position, and changed little in the prone position.

Discussion

The purposes of this study were to investigate: 1) whether the oxygenation response to prone positioning in acute lung injury differs in magnitude according to the level of PEEP applied in the supine position; and 2) whether the prone position can restore, at least in part, the haemodynamic deterioration induced by PEEP in the supine position. The results showed that the $P_{a,O_2}/F_{i,O_2}$ ratio, only slightly increased in the supine position at PEEP 2 cmH₂O lower than the inflection point (defined as low PEEP), was markedly increased by assuming the prone position (table 1, fig. 2). In accordance with this, the end-expiratory scan of one of the dogs at low PEEP showed that the ventral lung in the prone position (now dependent) remained well ventilated, as opposed to the dorsal lung in the supine position which was previously atelectatic at the same low PEEP (fig. 3). Compared with low PEEP, application of PEEP 2 cmH₂O higher than P_{flex} (defined as optimal PEEP) restored the $P_{a,O_2}/F_{i,O_2}$ ratio to almost the control level in the supine position, and the additional change obtained by prone positioning did not differ from that in the control.

The response to prone positioning may vary in individual patients [6–15]. Recently, the baseline chest wall compliance and its changes in the prone position were shown to have a role in determining the oxygenation response of the individual [15]. The mechanism of improved oxygenation, however, is not yet fully understood. The proposed mechanisms are improvement in regional ventilation of the dependent lung, increase in functional residual capacity, altered movement of the diaphragm, improved ventilation/perfusion ratio ($\dot{V}/\dot{Q}$) matching, and better drainage of dependent lung secretion [7, 10, 12–16, 25, 26]. Among these, improved regional ventilation of the dependent lung is gaining more evidence in human, as well as animal studies [12, 15–17]. More even ventilation in the prone position is believed to be effected by the change in the regional pleural pressure, one of the determinants of regional transpulmonary pressure. The vertical gradient of pleural pressure is known to change with body position and become intensified in a lung with pulmonary oedema [20–22]. In a pig ARDS model, for example, the pleural pressure of the dependent lung was 3.0 cmH₂O in the supine position, but was only 0.9 cmH₂O in the prone position [21]. Lowering of the dependent pleural pressure in the prone position favours the dependent alveoli opening at a lower airway pressure than in the supine position. The recruitment of the dependent lung along with the preserved distribution of pulmonary blood flow [25, 26] in the prone position will thus cause intrapulmonary shunt to decrease. In these results, the differential oxygenation response depending on the level of PEEP around the inflection point, *i.e.* the marked increase in $P_{a,O_2}/F_{i,O_2}$ ratio at low PEEP; and the negligible increase in $P_{a,O_2}/F_{i,O_2}$ ratio at optimal PEEP seemed consistent with the above mechanism of shunt reduction of the prone position.

The haemodynamic effect of the prone position has not been the primary interest of human or animal studies until now. DOUGLAS *et al.* [6] first noticed some patients who showed higher CO in the prone position compared with the supine position. The same phenomenon was also observed in some patients with ARDS, in whom the increased CO was not necessarily associated with the oxygenation

Table 2. – Haemodynamic variables in the supine position *versus* prone position in the control and in acute lung injury (ALI) at low positive end-expiratory pressure (PEEP) or optimal PEEP

		MAP	fC	MPAP	PAOP	PVR	CO	SV
Control	Supine	116±18	170±30	15±3	7.9±2.9	133.9±51.5	4.2±0.9	24±6
	Prone 5 min	115±15	179±34 [‡]	15±3	6.4±2.8 [‡]	154.1±61.7	4.5±1.0	25±4
	Prone 30 min	116±18	183±28	14±3	6.9±3.4	138.0±65.2	4.5±1.3	24±6
ALI								
First ZEEP Low PEEP	Supine	100±15	126±32	18±5	8.7±2.6	243.7±104.2	3.0±0.8	24±2
	Supine	104±12	141±22 [†]	19±4	8.9±2.5	296.2±128.6	3.0±0.6	22±3
	Prone 5 min	103±16	141±22 [†]	19±6	8.0±2.4	274.1±144.5	3.3±0.7	23±3
Second ZEEP Optimal PEEP	Prone 30 min	108±11	176±28 [†]	19±5	7.9±3.4	259.3±124.1	3.7±0.8	21±2
	Supine	101±17	130±26	18±4	9.0±2.9	246.0±109.4	3.1±0.4	24±3
	Supine	87±19 ^{‡§}	169±28 ^{‡§}	20±3	10.1±2.4 ^{†‡}	331.6±84.1	2.4±0.5 ^{†§}	14±2 ^{†§}
	Prone 5 min	107±18 [‡]	158±28 [†]	22±4 [‡]	9.1±2.7 [‡]	307.9±88.7	3.4±0.6 [‡]	20±2 [‡]
	Prone 30 min	108±16 [‡]	170±28 [†]	22±4 [‡]	9.0±3.1 [‡]	299.9±89.6 [‡]	3.6±0.7 [‡]	21±2 [‡]
	Resupine	92±23 [*]	173±35	20±3	10.5±2.5 [#]	341.1±106.7	2.4±0.5 [#]	14±1 [#]

Values are expressed as mean ± SD. MAP (mmHg): mean arterial pressure; fC: (breaths·min⁻¹); cardiac frequency; MPAP (mmHg): mean pulmonary artery pressure; PAOP (mmHg): pulmonary artery occlusion pressure; PVR (dyne·s·cm⁻⁵): pulmonary vascular resistance; CO (L·min⁻¹): cardiac output; SV (mL): stroke volume. *: p<0.05, ALI *versus* control at zero end-expiratory pressure (ZEEP); †: p<0.05, PEEP *versus* ZEEP; ‡: p<0.05 prone *versus* supine; §: p<0.05 optimal PEEP *versus* low PEEP in supine; #: p<0.05 resupine *versus* prone 30 min. (0.133 kPa=1 mmHg.)

response [14]. In the present study, the decreased CO in the supine position was recovered nearly to the level of ZEEP when the dogs were positioned prone. This haemodynamic benefit of the prone position was evident soon after the position change, and was abolished immediately after the dogs were turned supine again. A similar change in CO was also demonstrated in a recent animal study by BROCCARD *et al.* [27]. In addition to decreased venous return, there are other changes that are responsible for the haemodynamic deterioration induced by PEEP [28–33]. PEEP changes the configuration of the heart and compresses the cardiac fossa which may, in effect, resemble cardiac tamponade [32, 34, 35]. In the results of the present study, the improvement in CO in the prone position was not attributable to compensatory tachycardia because there was no appreciable change in fC accompanying the increase (from supine to prone) or decrease in CO (from prone to resupine). Inadvertent fluid administration was not likely either because intravenous fluid was strictly restricted during the experiment. To the measuring capability in this study, the change in stroke volume was the only haemodynamic parameter that paralleled the change in CO. Therefore, the increased CO of these dogs in the prone position was thought to be mediated by as yet unknown mechanisms causing SV to rise. The possible mechanisms could be the diversion of the juxtacardiac pressure toward the re-aerated dorsal lung (attenuating the lifting of cardiac fossa of the supine position), or the elevation of the intra- abdominal pressure in the prone position (increasing upstream pressure for the venous return to the right heart). Decreased CO and hypotension is a frequent problem occurring in patients with ARDS on PEEP therapy. However, if CO in the prone position can be improved in certain patients with ARDS as was shown in these dogs, PEEP therapy can be conducted more safely in the prone position.

There are several limitations in this study. Firstly, saline lavage for acute lung injury cannot represent the diverse pathoetiology of human ARDS. Secondly, the inflection point (average 6.6 cmH₂O) of the dogs was relatively low. This low P_{flex} was probably related to the small number of

lavage (twice or three times only) and the constant flow method in which the compliant inspiratory limb could have compressed some of the tested volume. Thirdly, the two levels of PEEP were tested in an injured lung of the hyperacute stage (30 min from the establishment of injury) which is much earlier than the usual practice of prone positioning in patients with ARDS. Fourthly, the anatomy of the dog's thorax (relatively high anteroposterior/transverse diameter (AP/T) ratio) is very different from that of the adult human (relatively low AP/T ratio). The greater anteroposterior diameter of the dog might have undergone greater compression of the chest wall in the anteroposterior direction in the prone position, which in turn could have influenced the oxygenation and haemodynamic responses to the prone position. In view of the role of the thoraco-abdominal wall compliance in the prone position [16], the haemodynamic effect of the prone position needs to be investigated further to explain the small proportion of patients with ARDS showing higher CO in the prone position. Finally, this study lacked the measurement of tissue oxygenation indices which would be necessary for precise interpretation of the haemodynamic changes in the setting of severe hypoxaemia.

In conclusion, the prone position in a canine acute lung injury model augmented the effect of relatively low positive end-expiratory pressure on oxygenation, and also attenuated the haemodynamic impairment of relatively high positive end-expiratory pressure in the supine position. These findings imply that the ventilatory goal in acute respiratory distress syndrome can be achieved in the prone position using a positive end-expiratory pressure lower than that normally employed in the supine position, and that the haemodynamic complications of positive end-expiratory pressure in the supine position can be ameliorated in the prone position.

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