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Ventilation and Perfusion Distribution during Altered PEEP in the Left Lung in the Left Lateral Decubitus Posture with Unchanged Tidal Volume in Dogs

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Abstract

Previous studies in anesthetized humans positioned in the left lateral decubitus (LLD) posture have shown that unilateral positive end-expiratory pressure (PEEP) to the dependent lung produce a more even ventilation distribution and improves gas exchange. Unilateral PEEP to the dependent lung may offer special advantages during LLD surgery by reducing the alveolar-to-arterial oxygen pressure difference {(A-a)PO_2 or venous admixture} in patients with thoracic trauma or unilateral lung injury. We measured the effects of unilateral PEEP on regional distribution of blood flow ($\dot{Q}$) and ventilation ($\dot{V}_A$) using fluorescent microspheres in pentobarbital anesthetized and air ventilation dogs in left lateral decubitus posture with synchronous lung inflation. Tidal volume to left and right lung is maintained constant to permit the effect on gas exchange to be examined. The addition of unilateral PEEP to the left lung increased its FRC with no change in left-right blood flow distribution or venous admixture. The overall lung $\dot{V}_A/\dot{Q}$ distribution remained relatively constant with increasing unilateral PEEP. Bilateral PEEP disproportionately increased FRC in the right lung but again produced no significant changes in venous admixture or $\dot{V}_A/\dot{Q}$ distribution. We conclude that the reduced dependent lung blood flow observed without PEEP occurs secondary to a reduction in lung volume. When tidal volume is maintained, unilateral PEEP increases dependent lung volume with little effect of perfusion distribution maintaining gas exchange.

Key Words: **gas exchange, lung mechanics, fluorescent microspheres, regional pulmonary blood flow distribution**

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Introduction

During surgery in the left lateral dependent (LLD) posture the dependent left lung is particularly prone to poor ventilation and impaired gas exchange presumably because its relatively small size makes it susceptible to compression by the mediastinal and abdominal contents (13, 17, 19, 23). During surgery, applying PEEP increases lung volume to a point well up the pressure-volume relationship close to total lung capacity, reduces airway closure, and improves gas exchange (3, 16). However, PEEP is accompanied by deleterious effects of lung barotrauma and reduced cardiac output (11).

Pulmonary perfusion is decreased to non-dependent lung and increased to dependent lung in the lateral decubitus posture (18). Recent studies (10, 14, 18) using new high resolution techniques show that there is a considerable degree of perfusion heterogeneity within isogravitational regions and reveals a gravity-independent central-to-peripheral flow gradient. These findings suggested that factors other gravity may play an important role in controlling the distribution of pulmonary blood flow. Positive end-expiratory pressure (PEEP) redistributes blood flow further from the top lung to the dependent lung regions as shown in supine dogs with 5 (10) and 20 cm H_2O PEEP (11) and in lateral posture dogs with 10 cm H_2O PEEP (6). Moderate PEEP inducing blood flow redistribution in healthy lung has little clinical significance. However, the effect may have major impact during lung dysfunction.

The use of controlled ventilation to each lung (differential ventilation) with unilateral PEEP to the dependent lung in the LLD posture has been proposed as being superior to conventional ventilation with bilateral PEEP. In anesthetized humans, differential ventilation produced higher PaO_2 and a lower $(A\text{-}a)PO_2$ than a single ventilator supplying a free distribution of ventilation between lungs either without or with 9 cm H_2O PEEP (11). Differential lung ventilation decreased $(A\text{-}a)PO_2$ by 30% compared with conventional ventilation. Unilateral PEEP to the dependent lung decreased $(A\text{-}a)PO_2$ by 13% (3) in human subjects. This behavior was attributed to the increased compliance, reduced airway resistance, and a more even ventilation distribution in the dependent lung as a result of the differential ventilation with and without unilateral PEEP (15).

The aim of this study was to use injected and aerosolized fluorescent microspheres to investigate the effect of unilateral and bilateral PEEP on the redistribution of blood flow and ventilation between the left and right lungs during constant tidal volume in the left lateral decubitus posture.

Materials and Methods

Animal Preparation

This study was approved by the University of Washington Animal Care Committee. Mongrel dogs (n = 6, 20-23 kg) were anesthetized with pentobarbital sodium (30 mg/kg, iv) and anesthesia was maintained by added doses (25-50 mg/h). Detailed procedures have been described (6). The animals were mechanical ventilated with a constant volume piston pump (Harvard Apparatus, South Natick, MA, USA) with room air having inspired fractional oxygen concentration (FIO_2) of 0.21, tidal volume of 15 ml/kg and a varied ventilatory rate which was adjusted to obtain an arterial PCO_2 of 35-40 mmHg. Tidal volume and ventilation of the right and left lung were measured by spirometry. Lungs were hyperinflated every 15 min for 30 sec before measurements.

Systemic arterial blood pressure (Psa), heart rate (HR), pulmonary artery pressure (Ppa) and airway pressure (Paw) were continuously measured. A pulmonary artery catheter was placed in the jugular vein to measure body temperature and cardiac output. Arterial and mixed venous blood gases and hemoglobin were measured.

A double-lumen endotracheal tube (broncho-Cath, left; Mallinckrodt Medical, Inc., St. Louis, MO, USA) was inserted *via* a subcricoid tracheostomy. Both lungs were air-ventilated synchronously with a dual-piston ventilator (Harvard Instruments, South Natick, MA, USA). Tidal volumes were set at 6 ml/kg and 9 ml/kg for the left and right lung, respectively after determining the distribution during ventilation with a single endotracheal tube. These settings were based on left and right lung tidal volumes that were measured in turn by in line pneumotachographs (Korr Medical Inc, Salt Lak City, UT, USA). The tidal volume was maintained constant throughout the study. Inspired and end-tidal PCO_2 and PO_2 were measured by mass spectrometry from each lung. The respiratory rate was adjusted to maintain $PaCO_2$ between 35 and 40 mm Hg. Left and right lung tidal volumes were measured in the LLD posture without PEEP and maintained constant for the different PEEP conditions. Cardiac output (CO) measurements (*via* the thermodilution technique) and blood temperature were measured with a cardiac output computer (Baxter Edwards Sat2, Irvine, CA, USA). CO was maintained constant by saline infusion.

Study Protocol

In the LLD posture, after obtaining right and left lung tidal volumes at FRC, the dependent left lung received 0, 5, or 10 cm H_2O PEEP and both lungs 10 cm H_2O PEEP, in random order. After 20 min, tidal volumes, arterial and mixed blood gases, mean expired CO_2, hemodynamic variables, pulmonary capillary wedge pressure (Pcwp) were measured. FRC of left and right lung were measured simultaneously by using helium dilution method. The respiration rate did not adjust once the data collection started.

Measurement of Regional $\dot{V}_A$ and $\dot{Q}$ Distributions

Regional ventilation and perfusion were measured by aerosolized 1-μm fluorescent microspheres and intravenous injection of 15-μm fluorescent microspheres over 5 min, as previously described (6). Following the final measurements, heparin (10,000 U, i.v.) and papaverine (60 mg, i.v.) were administered, the animals were exsanguinated, the lungs were excised and perfused and air-dried at TLC.

After the dried lungs were encased in foam, they were sliced into cubes (1.2 cm sides), and the pieces were weighed. Each lung piece was assigned an X (left-to-right), Y (dorsal-to-ventral), Z (caudal-to-cranial) coordinate position. Fluorescent intensity of each piece was measured spectrophotometrically (25).

Data Processing

Detailed procedures have been described (24). Briefly, without PEEP the dimension of the lung cubes dried at TLC was adjusted to those at FRC (6). Adjustments were also made for the vertical gradient of transpulmonary pressure (Ptp).

For 5 cm H_2O PEEP to the dependent lung, cube dimensions were based on measured FRC. No adjustment was made to the dependent lung pieces with 10 cm H_2O PEEP. The nondependent right lung pieces with PEEP to the left lung were adjusted to dimensions similar to those without PEEP.

Volume Normalization of Blood Flow and Ventilation

For the plots of the spatial distribution of *in vivo* regional blood flow, fluorescent intensity representing blood flow ($\dot{Q}$) and ventilation ($\dot{V}_A$) to each piece was converted into units of ml/min per unit of *in vivo* regional lung volume (6). Anatomic dead space was estimated using Fowler's method (8).

Gas Exchange Parameters $\dot{V}_A/\dot{Q}$ and PO_2

End-capillary PO_2 was calculated from the $\dot{V}_A/\dot{Q}$ measurement made on each lung piece. We calculated regional PO_2 (P_RO_2), PCO_2 and (A-a)PO_2 of each lung piece using the $\dot{V}_A$ and $\dot{Q}$ fluorescent intensities, body temperature, Hb concentration and mixed venous blood gases (2). (A-a)PO_2 was also calculated using the alveolar gas equation (12) with a respiratory quotient of 0.8.

Statistics

Data are presented as mean ± SD. The slopes of linear relationships were compared with zero with a single Student's two-tailed *t*-test. The influence of PEEP on flow gradients, and blood gases per condition was analyzed with a two-tailed Student's paired *t*-test. Differences between conditions were also analyzed using ANOVA repeat measurement. A *P*-value < 0.05 was considered statistically significant.

Results

Physiological Measures

Cardiac output. Psa, Ppa, heart rate, body temperature, hemoglobin, respiratory rate, and tidal volume to right and left lung, respectively, were unchanged throughout the study (Table 1).

Lung volumes. Compared to 0 cm H_2O PEEP, FRC of the left lung was increased by 55 and 110% with 5 and 10 cm H_2O (unilateral) PEEP to the left lung, respectively, and by 83% with 10 cm H_2O (bilateral) PEEP to both lungs (Fig. 1). FRC of the right lung was unaffected with unilateral PEEP, but more than doubled with 10 cm H_2O bilateral PEEP. A PEEP of approximately 5 cm H_2O applied to the dependent lung returned the dependent lung FRC to its original value in the supine position (Fig. 1).

In the left lung, Paw was increased with 5 and 10 cm H_2O unilateral PEEP to the left lung (17 and 20 cm H_2O) and 10 cm H_2O bilateral PEEP (20 cm H_2O) from the value measured without PEEP (11 cm H_2O). By contrast in the right lung, only bilateral PEEP (23 cm H_2O) increased Paw above that under zero PEEP conditions (11 cm H_2O). Compared with 10 cm H_2O unilateral PEEP, Pcwp was increased ~ 4 cm H_2O with 10 cm H_2O bilateral PEEP.

Gas exchange. Compared to 0 cm H_2O PEEP, PaO_2, $PaCO_2$ or venous admixture did not change with unilateral PEEP to the left lung or with 10 cm H_2O bilateral PEEP. Values of (A-a)PO_2 measured using the alveolar gas equation were somewhat higher but not significantly different from values calculated using the fluorescent microsphere data.

Microsphere Data

Analysis of regional perfusion and ventilation were carried out on between 1058-1337 lung pieces (93.3 ± 2.6%) per animal. Lung pieces (82 ± 40) with > 25% pulmonary airways and with fluorescent

Table 1. Cardiopulmonary variables

PEEP (cm H_2O)	0 both	5 dependent	10 dependent	10 both
T (°C)	37.3±0.4	37.5±0.4	37.2±0.4	37.3±0.5
Psa (mm Hg)	114±14	102±12	107±9	103±19
HR (beats · min^{-1})	110±18	111±12	115±16	116±15
Ppa (cm H_2O)	24±7	24±8	26±6	29±4
Ppcw (cm H_2O)	7±4	9±6	9±6	13±4*
$\dot{Q}_T$ (l · min^{-1})	2.8±0.3	2.7±0.2	2.6±0.3	2.7±0.4
R_T, cm H_2 · L^{-1} · min^{-1}	6.2±1.4	5.7±1.3	6.4±1.5	5.9±2.6
R_L, cm H_2O · L^{-1} · min^{-1}	5.3±3.9	15.1±9.7	18.4±7.3	11.8±6.4‡
R_R, cm H_2O · L^{-1} · min^{-1}	0.4±5.6	9.3±7.4	10.0±7.5	12.2±5.2
RR (breaths · min^{-1}),	8±2	17±2	18±2	18±2
V_T (ml), left	19±31	119±33	120±32	119±33
right	17±39	214±39	215±39	215±37
MV (l · min^{-1}), left	2.1±0.7	2.0±0.7	2.1±0.8	2.1±0.8
right	3.7±0.4	3.6±0.4	3.7±0.4	3.6±0.4
V_D/V_T (%) left	40±5	45±3	48±4	45±6
V_D/V_T (%) right	29±6	31±4	29±4	36±6
Paw (cm H_2O), left	11±2	17±3*	20±2*†	20±2*
right	11±2	10±2	11±1	23±3*†‡
PaO_2 (mm Hg)	98±18	99±12	107±26	93±19
$PaCO_2$ (mm Hg)	31±3	31±3	31±3	34±3
(A-a)PO_2 (mm Hg)	17.7±17.4	12.1±12.4	12.6±14.5	18.7±19.8
Venous Admixture (%)	14.0±7.5	11.0±5.4	12.3±5.4	15.6±8.2
pH	7.38±0.03	7.39±0.62	7.36±0.03	7.34±0.02
$P\overline{v}O_2$ (mm Hg)	44±6	43±6	45±6	43±4
$P\overline{v}CO_2$ (mm Hg)	36±4	36±5	37±3	39±3
FRC (ml) left	183±48	283±74*	386±65*†	335±66*†‡
right	402±80	392±95	354±79	879±104*†‡
Hb (g · dl^{-1})	13±2	13±1	13±1	13±1

Values are means ± SD (n = 6). BT, body temperature; Psa, mean systemic arterial pressure; HR, heart rate; Ppa, mean pulmonary artery pressure; Ppcw, pulmonary capillary wedge pressure; $\dot{Q}_T$, cardiac output; RR, respiratory rate; V_T, tidal volume; R: vascular resistance; MV, minute ventilation; Paw, peak airway pressure; PaO_2 , arterial O_2 tension; $PaCO_2$, arterial carbon dioxide tension; (A-a)PO_2 , venous admixture (%); alveolar and arterial O_2 tension difference; pH, arterial blood pH; $P\overline{v}O_2$, mixed venous oxygen tension; $P\overline{v}CO_2$, mixed venous carbon dioxide tension; FRC, functional residual capacity; Hb = arterial hemoglobin. *$P < 0.05$, compared with no PEEP. $^{†}P < 0.05$, compared with 5 cm H_2O unilateral PEEP. $^{‡}P < 0.05$, compared with 10 cm H_2O unilateral PEEP.

microsphere intensity (11 ± 7) beyond the range of ±4SD of the mean values were discarded. For the analysis of $\dot{V}_A/\dot{Q}$ and regional P_RO_2, we rejected data (19 ± 7 lung pieces or 1.6%) outside the range of mean ±3SD of ln ($\dot{V}_A/\dot{Q}$) to eliminate lung pieces predominantly with dead space (large $\dot{V}_A/\dot{Q}$) and shunt (low $\dot{V}_A/\dot{Q}$).

Distribution of $\dot{Q}$ and $\dot{V}_A$ between Lungs

Tidal volume of the dependent left lung (119 ml), which was about 55% tidal volume of the nondependent right lung. Since the left lung was under a constant ventilation, this relative low tidal volume indicated that the ventilation of the left lung was much lower than that of the right lung. Ventilation to the left lung was disproportionately lower than the right based on lung size. On average, the left lung weighed ~25% less than the right lung.

The total blood flow measured by fluorescent microspheres was distributed 41% to the dependent left lung and 59% to the nondependent lung with 0 cm H_2O PEEP (Table 2). Unilateral dependent lung PEEP (5 or 10 cm H_2O) did not change blood flow to the left lung or the blood flow distribution between lungs. This behavior in conjunction with the constant tidal volume indicated that unilateral PEEP per se had no beneficial effect on gas exchange to the left lung.

Table 2. Relative percentages of fluorescent microsphere signals from left and right lungs representing relative cardiac output ($\dot{Q}$) and minute ventilations to left and right lungs, respectively during differential ventilation with unilateral (LL) dependent PEEP and bilateral (WL) PEEP in left LLD

		LLD			
	PEEP, cm H_2O	0	5LL	10LL	10WL
$\dot{Q}$ (%)	Left lung	41±3	40±5	36±5	$52{\pm}5^{*\dagger\ddagger}$
$\dot{Q}$ (%)	Right lung	59±3	60±5	64±5	48±5
$\dot{V}_A$ (%)	Left lung	29±10	26±9	$22{\pm}6^{*\dagger}$	$33{\pm}10^{\dagger\ddagger}$
$\dot{V}_A$ (%)	Right lung	71±10	74±9	78±6	67±10

Values are mean ± SD (n = 6). LLD: left lateral decubitus posture. 5LL: LL PEEP of 5 cm H_2O, 10LL: LL PEEP = 10 cm H_2O. 10WL: whole lung bilateral PEEP of 10 cm H_2O. *$P < 0.05$, compared with no PEEP. $^{\dagger}P < 0.05$, compared with 5 cm H_2O unilateral PEEP. $^{\ddagger}P < 0.05$, compared with 10 cm H_2O unilateral PEEP.

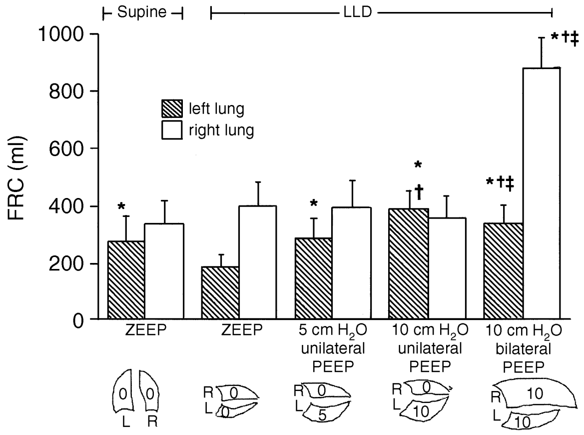

Fig. 1. Left and right lung volume changes during ZEEP compared to unilateral and bilateral PEEP in LLD posture. Values of FRC are mean ± SD (n = 6). ZEEP represented 0 cm H_2O. LLD with ZEEP is the reference condition. *$P < 0.05$ comparison of same lung with LLD ZEEP. †$P < 0.05$, significantly different from 5 cm H_2O unilateral dependent PEEP in the same lung. ‡$P < 0.05$, significantly different from 10 cm H_2O unilateral dependent PEEP.

By contrast, 10 cm H_2O bilateral PEEP increased the fraction of cardiac output to the left lung by 11-16% compared to 0 cm H_2O PEEP or 5 and 10 cm H_2O unilateral PEEP.

Regional distribution of $\dot{Q}$. The redistribution of volume normalized regional blood flow was shown in Fig. 2. Vertical height up the lung was plotted against regional blood flow. Figure 2A, 2B, 2C and 2D show blood flow in the left lateral position with PEEP = 0 cm H_2O, left lung PEEP = 5 cm H_2O, left lung PEEP = 10 cm H_2O, and bilateral PEEP = 10 cm H_2O, respectively. The blood flow was normalized by lung piece volume. Thus, although total blood flow to the left lung did not change appreciably in panels A, B & C, the higher $\dot{Q}$ values in panel A reflected in the lower volume per piece at zero end-expiratory pressure (ZEEP). Increased lung volume due to PEEP resulted in a decrease in volume-normalized blood flow to each piece.

Regional distribution of $\dot{V}_A/\dot{Q}$. The regional distribution of $\dot{V}_A/\dot{Q}$ was shown in Fig. 3. The influence of increased lung volume has identical effects on perfusion per unit lung volume and ventilation per unit lung volume. Figure 3A, 3B, 3C and 3D show blood flow in the left lateral position with PEEP = 0 cm H_2O, left lung PEEP = 5 cm H_2O, left lung PEEP = 10 cm H_2O, and bilateral PEEP = 10 cm H_2O, respectively. The relative $\dot{V}_A/\dot{Q}$ heterogeneity changes very little amongst the four situations consistent with the lack of change in venous admixture.

Discussion

In this study, we measured the effect of unilateral and bilateral PEEP on the regional distribution of blood flow and ventilation with constant tidal volume to both lungs in the LLD posture. The major findings of this study were as follows. First, with constant (35-65%, left-right lung) tidal volume in the LLD posture, neither unilateral PEEP (5 and 10 cm H_2O) to the dependent lung nor bilateral PEEP improved gas exchange, as indicated by venous admixture. Therefore, a PEEP-induced increase in alveolar ventilation was most likely responsible for the improved gas exchange observed previously with conventional mechanical ventilation (15). Second, unilateral PEEP to the dependent left lung had no effect on blood flow. Third, the PEEP-induced increase in FRC to the dependent left lung with unilateral PEEP and bilateral PEEP produced no change in venous admixture.

Methodological Issues

We studied dogs since the pattern of lobar bronchial branching from the trachea allowed differential ventilation to the left and right lungs with a double-

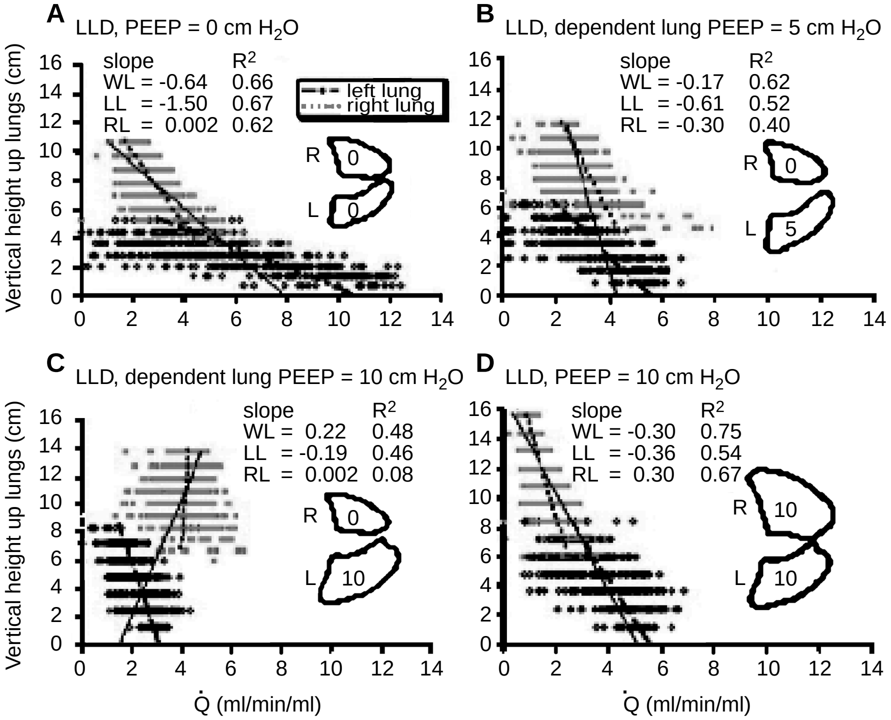

Fig. 2. Blood flow per unit regional lung volume (ml blood/min/ml lung volume) *vs.* lung height (H) for a representative dog in the LLD posture (A) without PEEP, (B) with 5 cm H_2O unilateral dependent PEEP, (C) with 10 cm H_2O unilateral dependent PEEP and (D) with bilateral 10 cm H_2O PEEP (D). Left lung (open points). Right lung (solid points). The lines represent best-fit values from multiple linear regression analysis at center of mass for the whole lung (WL), left lung (LL) and right lung (RL). Slope is dQ/dH, the inverse of the plotted axes.

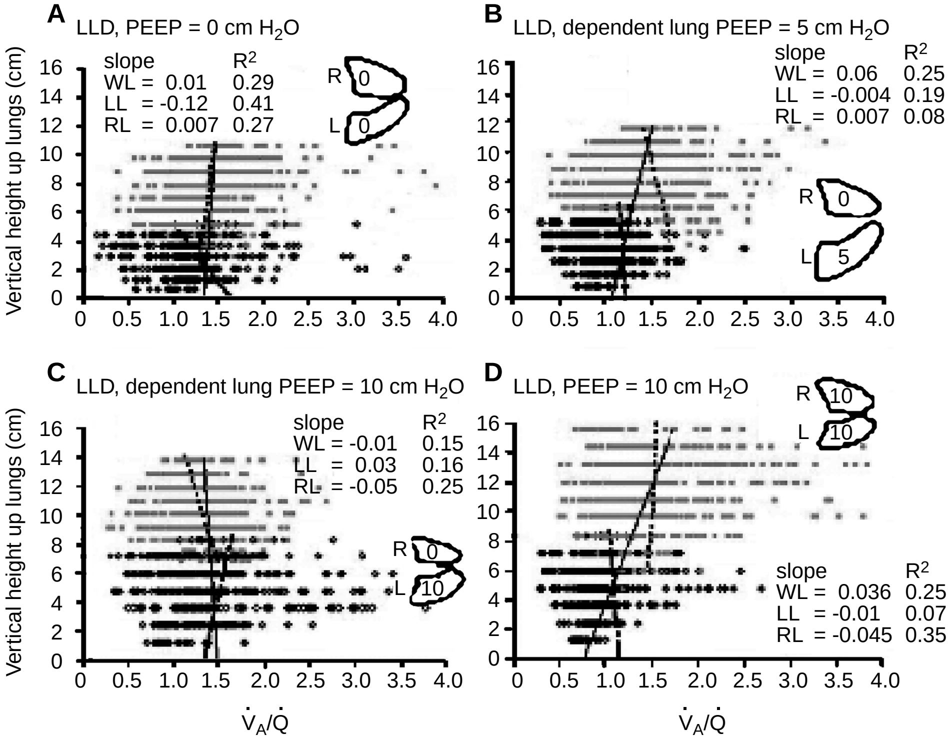

Fig. 3. $\dot{V}_A/\dot{Q}$ *vs.* lung height (H) for the same representative dog as in Fig. 2 in the LLD posture (A) without PEEP, (B) with 5 cm H_2O unilateral dependent PEEP, (C) with 10 cm H_2O unilateral dependent PEEP and (D) with bilateral 10 cm H_2O PEEP (D). R right lung (solid points), L left lung (open points). The lines represent best-fit values from multiple linear regression analysis at center of mass for the whole lung (WL), left lung (LL) and right lung (RL). Slope is $d\dot{Q}/dH$, the inverse of the plotted axes.

lumen tube. We used the fluorescent microsphere technique to measure the regional distribution of $\dot{Q}$ and $\dot{V}_A$ because of its much greater spatial resolution compared to other techniques. Three-dimensional data of the regional distribution of $\dot{Q}$. $\dot{V}_A$, $\dot{V}_A/\dot{Q}$ and regional P_RO_2 were obtained in ~2.0 ml pieces of the isolated lung dried at TLC.

Both injected and aerosolized fluorescent microspheres were delivered *in vivo* across several respiratory cycles, while the fluorescent intensity was measured *in vitro* in the dry lung pieces near total lung capacity. Several adjustments were made to estimate the regional ventilation and perfusion per *in vivo* regional lung volume (6). First, anisotropic reduction of the cubic lengths in the 3 dimensions from TLC to FRC was made using previous measurements (9, 20). Second, we imposed a distortion to the vertical dimension (X) of each lung piece to account for the vertical Ptp gradient (1). No adjustment was made for the Ptp gradients in the other two axes (Y and Z) in the absence of reported data. The adjustment for the vertical Ptp gradient was only needed for the bilateral ventilation without PEEP and for unilateral ventilation with 5 cm H_2O PEEP.

$\dot{Q}$ and $\dot{V}_A$ were normalized by dividing estimated *in vivo* regional volume, to conform to spatial measurements using imaging techniques. This adjustment required the use of lung density of the inflated lung at FRC. Blood volume was excluded from the estimate of lung density because the dried lung pieces were blood-free.

Conventional vs. Differential Mechanical Ventilation

In the lateral posture, conventional mechanical ventilation in anesthetized humans produced a mismatch between $\dot{Q}$ and $\dot{V}_A$ and impairment in gas exchange (1, 16, 21). This could be due to the result of reduced regional ventilation to the dependent lung caused by a reduced FRC due to heart (13, 19) and abdominal compression (17, 23) and a reduced lung compliance (21, 22). The increase in PO_2 to the lung caused by PEEP has been observed in our previous studies (6) due to a relative increase in ventilation to the left lung. This increase in left lung ventilation was absent in the present study, since ventilation to the left lung was kept equal to that measured without PEEP.

In our previous study in the anesthetized dog ventilated with air in the LLD posture, blood flow measured using the fluorescent microsphere technique (18) was lower in the dependent lung than in the nondependent lung, a behavior opposite to that expected due to gravity. The reduced blood flow was caused by a reduced P_RO_2 and $\dot{V}_A/\dot{Q}$, secondary to the reduced dependent lung FRC due to compression by the mediastinal content and reduced ventilation (6). The relatively low flow in the dependent lung was increased either by a change to the RLD posture or by applying 10 cm H_2O PEEP. Mechanical ventilation with 100% O_2 increased flow to the dependent lung in the LLD posture (6), consistent with hypoxic pulmonary vasoconstriction as the mechanism for the reduced flow with air ventilation.

The rationale for differential ventilation in the left lateral posture was to ensure adequate ventilation to the dependent lung by matching the greater regional perfusion in the dependent lung with an equal ventilation, thus improving gas exchange (11). Previous studies in anesthetized humans using equal ventilation to both lungs showed improved gas exchange (3, 11) The explanation given for the improved gas exchange was that differential ventilation caused more airways to open, resulting in a greater lung compliance and lower airway resistance in the dependent lung (6). However, an alternative explanation was the application of 50% of the total ventilation to the dependent left lung instead of the 35% measured with conventional ventilation (6).

The foregoing effects of differential ventilation on gas exchange differed from the present results. First, using the 35-65% left-right lung ventilation ratio measured with conventional ventilation, differential ventilation did not improve gas exchange, as measured by the venous admixture. $\dot{V}_A/\dot{Q}$ inequalities as measured by spatial gradients in $\dot{V}_A/\dot{Q}$ did not contribute to the venous admixture.

Notably absent were any significant gradients in the $\dot{V}_A/\dot{Q}$ dependent left lung with and without PEEP. This is in contrast to a previous study (6), with single tube ventilation where small but significant gradients in $\dot{V}_A/\dot{Q}$ were observed. The increased flow velocity might serve to redistribute gas more evenly in the lung periphery and result in more uniform ventilation and regional. Another potential mechanism would be decreased sequential mixing of dead space. The left lung received less re-inspired air and more alveolar ventilation. Fowler dead space measurements demonstrated that the dead space of the left lung was less than that of the right lung with double lumen tubes (Table 1). In the left lung, $\dot{V}_A$ and measured by aerosolized microspheres were distributed similarly among lobes between differential and conventional ventilation. By contrast in the right lung, $\dot{Q}$ and $\dot{V}_A/\dot{Q}$ in the caudal lobe were greater with the double lumen tube (53 and 50% total) than with the single lumen tube (38 and 35% total).

Effect of Unilateral and Bilateral PEEP with Differential Ventilation in the LLD Posture

The application of PEEP to the dependent left lung with differential ventilation improved gas exchange in humans (3, 4, 7, 11). In anesthetized humans, equal ventilation to both lung with differential ventilation produced higher PaO_2 and a lower (A-a)PO_2 than a single ventilator supplying a free distribution of ventilation between lungs either without or with 9 cm H_2O PEEP (11). Similar studies in anesthetized humans showed a 30% reduction in (A-a)PO_2 with equal ventilation to both lungs and a further 13% reduction in (A-a)PO_2 with unilateral PEEP to the dependent lung (3, 4). This behavior was attributed to the increased compliance, reduced airway resistance, and a more even ventilation distribution in the dependent lung as a result of the differential ventilation with unilateral PEEP (9).

The absence of an increase in P_RO_2 with unilateral and bilateral PEEP in the present study with constant ventilation to the dependent left lung was opposite to the PEEP-induced increase in P_RO_2 observed with conventional mechanical ventilation with a single-lumen tube (6). This indicates that PEEP did not improve gas exchange to the dependent left lung in the present study. The PEEP-induced improved gas exchange with conventional mechanical ventilation in the LLD posture was mostly likely caused by increased ventilation to the dependent left lung.

In the present study with 35-65% left-right lung differential ventilation, no improvement in gas exchange as indicated by constant venous admixture was observed with unilateral PEEP (5 and 10 cm H_2O) to the dependent left lung or with 10 cm H_2O bilateral PEEP. This was consistent with the constant blood flow measured in the dependent left lung with unilateral PEEP compared to zero PEEP. The absence of the effect of PEEP on the venous admixture indicated that neither small airway closure nor lung non-uniform distortion was responsible for the lower $\dot{V}_A/\dot{Q}$ observed in the dependent lung, as these two factors would be reduced by the PEEP-induced increase in FRC.

Klingstedt *et al.* (16) studied atelectasis and ventilation-perfusion distribution using multiple inert gas elimination technique (MIGET) and CT scan in the supine and lateral position of human between conventional and differential ventilation with unilateral PEEP. They found that low $\dot{V}_A/\dot{Q}$ and shunt regions were decreased and oxygenation was improved with differential ventilation with unilateral PEEP. In addition, the atelectatic region was highly correlated with the shunt measured by MIGET. They reasoned that unilateral PEEP opened closed peripheral airways, increasing compliance and ventilation of the dependent lung and reducing shunt and low $\dot{V}_A/\dot{Q}$ regions.

One difference between the human studies and ours is that cardiac output was maintained constant in our studies while it was allowed to change in the human studies. Thus in addition to the increased ventilation, a reduced blood flow to the dependent lung with differential ventilation might account for the increased $\dot{V}_A/\dot{Q}$ and reduced (A-a)PO_2 in the human studies.

Consistent with the human studies (11), the greater the unilateral PEEP to the dependent lung, the greater the increase in the volume of the dependent lung (Table 1, Fig. 2), with no change in the volume of the nondependent lung. In the human studies, the compliance of dependent lung was increased and airway resistance was decreased by unilateral dependent PEEP, causing a more uniform gas distribution. In the present study the spatial gradients in $\dot{V}_A$ observed without PEEP in the dependent left lung was reduced by unilateral or bilateral PEEP with differential ventilation, indicative of a more uniform ventilation distribution. Differential ventilation also reduced the positive dorsal-ventral gradient of $\dot{V}_A$ observed in the previous study with conventional mechanical ventilation (6).

In the present study, all measures of gas exchange efficiency from analysis of microsphere data of $\dot{Q}$ and $\dot{V}_A$ were unchanged with unilateral and bilateral PEEP, in contrast to previous studies in humans (11), in which shunt and low $\dot{V}_A/\dot{Q}$ regions were decreased by unilateral PEEP to the dependent lung. The latter was most likely caused by the PEEP-induced increased in ventilation that was constant in the present study.

Differential Ventilation with Unilateral Dependent PEEP vs. Differential Ventilation with Bilateral PEEP

The lung volume of the dependent left lung with 10 cm H_2O unilateral PEEP was greater than that of dependent lung with 10 cm H_2O bilateral PEEP while the non-dependent lung volume with bilateral PEEP doubled that with unilateral 10 cm H_2O PEEP. This behavior was similar to results found in humans studied in the LLD posture (15, 16, 22).

While unilateral PEEP had no effect on blood flow to the dependent left lung, with the same differential ventilation bilateral PEEP diverted blood flow to the dependent left lung from the nondependent lung. This increased blood flow had no effect on the venous admixture and was associated with a Pcwp-induced reduction in vascular resistance in the dependent lung. By contrast, bilateral PEEP with conventional ventilation increased $\dot{V}_A/\dot{Q}$, a reflection of increased ventilation to the dependent left lung (6).

The increase in FRC of the nondependent lung with bilateral PEEP is associated with an increased risk of barotrauma, decreased venous return and decreased cardiac output (3, 4, 11). These studies have demonstrated that equal ventilation to both lungs without and with unilateral PEEP improved gas exchange efficiency with a lower risk of barotrauma and a smaller decrease in cardiac output. However, in the present study, unilateral PEEP with ventilation to the dependent lung similar to that without PEEP did not improve gas exchange. Similarly, bilateral PEEP increased FRC but produced no change in the (A-a)PO_2 or venous admixture. This behavior was found by Dyhr and coworkers (7) who showed that 12 cm H_2O PEEP increased lung volume but not PaO_2 in patients ventilated after cardiac surgery. They speculated that a PEEP of 12 cm H_2O may not be enough to recruit atelectatic lung regions induced by anesthesia. Thus, the improved gas exchange in previous studies with differential ventilation was caused by the increased ventilation to the dependent lung and not by a PEEP-induced increased lung compliance, reduced airway resistance or reduced lung distortion.

Differential ventilation with selective PEEP to the dependent lung might be beneficial to patients with chest trauma and unilateral lung injury (5), with bilateral severe lung disease, and with certain types of thoracic surgery (25). In patients with signs of hypoxemia, differential ventilation with selective PEEP can be used to improve gas exchange by augmenting ventilation to the dependent lung and to avoid impairment of cardiac output that occurs with conventional mechanical ventilation.

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