Redistribution of Blood Flow and Lung Volume between Lungs in Lateral Decubitus Postures during Unilateral Atelectasis and PEEP

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Abstract

The effect of left lung atelectasis on the regional distribution of blood flow (Q), ventilation (V_A) and gas exchange on the right lung ventilated with 100% O_2 was studied in anesthetized dogs in the lateral decubitus posture. Q and V_A were measured in 1.7 ml lung volume pieces using injected and aerosolized fluorescent microspheres, respectively. Hypoxic pulmonary vasoconstriction (HPV) in the atelectatic lung shifted flow to the ventilated lung. The increased flow in the ventilated lung ensured adequate gas exchange, compensating for the hypoxemia due to shunt contributed by the atelectatic lung. Left lung atelectasis caused a compensatory increase in the ventilated lung FRC that was smaller in the right (RLD) than left (LLD) lateral posture, the effect of lung compression by the atelectatic lung and mediastinal contents in the RLD posture. The O_2 deficit measured by (A-a)DO_2 increased with left lung atelectasis and was exacerbated in the LLD posture by 10 cm H_2O PEEP, a result of increased shunt caused by a shift in Q from the ventilated to the atelectatic lung. The PEEP-induced O_2 deficit was eliminated with inversion to the RLD posture.

Key Words: distribution of ventilation, pulmonary gas exchange; spatial gradients, hypoxic pulmonary vasoconstriction, mediastinal shift, hyperoxia, fluorescent microspheres

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Introduction

Several factors determine the regional distribution of blood flow and ventilation in the lung. These include the effects of gravity (4, 20, 23, 24, 36, 44, 45), regional lung volume distribution (7, 21), hypoxic pulmonary vasoconstriction (HPV) (6, 26, 27) and intrinsic vascular structure (8). In mechanically ventilated, anesthetized dogs studied in the lateral decubitus posture, blood flow in the left lateral decubitus (LLD) posture was lower in the dependent lung than in the nondependent lung, a behavior opposite to that expected due to gravity (31). This behavior in conjunction with a lower regional PO_2 (P_RO_2) in the dependent lung that was reversed with body inversion to the right lateral decubitis (RLD) posture implicated HPV as the dominant mechanism for the low dependent blood flow in the LLD posture (12). The low P_RO_2 was attributed to a compression of the dependent left lung by the mediastinal contents and abdomen that reduced ventilation and lowered V_A/Q. The low P_RO_2 was abolished either by positioning the left lung nondependent in the RLD posture or by 10 cm H_2O positive-end expiratory pressure (PEEP).

In this study, we attempted to determine whether PEEP and posture in the lateral decubitus position affect the regional distribution of blood flow and ventilation and gas exchange after left lung atelectasis. We used intravenously injected and aerosolized fluorescent microspheres (FMS) to study the spatial distribution in blood flow and ventilation. We studied the effects of changing from LLD to RLD posture to evaluate the effects of the weight of the heart, abdomen and left atelectatic lung on the ventilated right lung. We used 100% O_2 ventilation to remove any HPV in the right ventilated lung. Any changes in blood flow of the ventilated lung with PEEP or a change in posture were attributed to lung volume-induced or gravity (height)-dependent changes in pulmonary vascular resistance (PVR). The results might provide a better understanding of the mechanisms responsible for gas exchange impairment in the lateral position and might be applicable to the optimal use of PEEP and body position in the ventilation of patients with unilateral lung disease or of patients after acute unilateral pneumonectomy.

Materials and Methods

Animal Preparation

This study was approved by the University of Washington Animal Care Committee. Six mongrel dogs weighing 20-23 kg of mixed gender were anesthetized with pentobarbital sodium (30 mg/kg, i.v.) and the lungs were mechanical ventilated *via* an intratracheal tube (tidal volume, 15 ml/kg). Respiration rate was adjusted to maintain arterial PCO_2 at 35-40 Torr. Tidal volume and minute ventilation of right and left lungs, respectively, were measured by spirometry. Lungs were hyperventilated (30-40 cm H_2O) every 15 min, lungs were hyperinflated for 30 seconds before experimental measurements to minimize atelectasis.

Catheters were inserted in one carotid and femoral artery and in both femoral veins. Mean systemic blood pressure (Psa), heart rate (HR), pulmonary artery pressure (Ppa), pulmonary capillary wedge pressure (Ppcw) and airway pressure (Paw) were continuously recorded. A catheter was placed in the pulmonary artery *via* the jugular vein to measure body temperature and cardiac output. Arterial and mixed venous blood gases were measured.

A double-lumen endotracheal tube (broncho-Cath, left; Mallinckrodt Medical, Inc.) was inserted *via* a subcricoid tracheostomy. The isolation of the left lung from the right lung was confirmed by ventilating one lung and checking for leaks in the other lung. Both lungs were ventilated synchronously with a dual-piston ventilator. Inspired and end-tidal PCO_2 and PO_2 were measured with a mass spectrometer. The right lung was ventilated with 100% O_2 throughout the study. The left lung was made atelectatic by ventilating it with 100% O_2 for ~ 5 min, occluding the left limb of the double lumen tube and allowing 30 min for complete O_2 absorption. Before left lung atelectasis, tidal volume to the right lung was measured and subsequently used after left lung atelectasis. Intravenous normal saline (100-200 ml/h) was administered to maintain constant cardiac output after left lung atelectasis and with 10 cm H_2O PEEP. $NaHCO_3$ was given as needed to reduce metabolic acidosis with left lung atelectasis.

Study Protocol

Control studies. We studied the effect of body position and PEEP on regional blood flow and end-capillary PO_2. The dog was positioned in the left (LLD) or right (RLD) lateral decubitus posture and PEEP was administered to both lungs in randomized order. Both lungs were ventilated with 100% O_2. After 20 min, tidal volume to the right and left lungs was measured. Cardiac output, Ppa, Psa and Pcwp were measured at end expiration. Arterial and mixed venous blood and exhaled gas were sampled for pH, PCO_2, and PO_2 analysis and the analysis of multiple inert gas elimination. One of four different colored 15 μm microspheres was injected i.v. over 5 min. Functional residual capacity (FRC) of both right and left lung was measured by helium dilution.

Left lung atelectasis. We studied the redistribu-

tion of regional blood flow and gas exchange in the LLD and RLD postures after left lung atelectasis with and without PEEP to the right lung. After choosing the body posture, the right lung received 0 or 10 cm H_2O PEEP in random order. After inducing left lung atelectasis, the right lung was ventilated with 100% O_2. After 20 min blood gases, hemodynamic measurements, FRC and arterial, mixed venous and exhaled gas samples were obtained. Then aerosolized 1 μm microspheres to the right lung and intravenous 15 μm microspheres were delivered.

Regional Distribution of V_A and Q Using FMS

Terminally, heparin (10,000 U, i.v.) and papaverine (60 mg, i.v.) were administered. The animal was exsanguinated, the lungs isolated, perfused with a dextran solution, and dried at total lung capacity (30 cm H_2O Paw). The dried lungs were encased in foam in a box. The lung was cut into cubes (1.2 cm sides). Each lung piece was weighed; pieces less than 8 mg were discarded. Each lung piece was assigned an X (right-to-left), Y (dorsal-to-ventral) and Z (caudal-to-cranial) rectangular coordinate position. Each lung piece was soaked with 2-ethoxyethyl acetate to extract the FMS. Fluorescent intensity was measured spectrophotometrically (40).

Data Analysis

Adjusting cube dimensions from TLC to FRC before left lung atelectasis. Detailed data adjustments have been described by Chang (11). Briefly, the spatial dimensions of lung cubes dried at TLC were adjusted to the *in vivo* FRC condition using lung lengths measured in previous studies. A further adjustment was applied for the vertical gradient of transpulmonary pressure (Ptp). The vertical Ptp gradient was 0.5 cm H_2O/cm (1). No adjustment was made to the dried lung cube length at 10 cm H_2O PEEP.

Adjusting cube dimensions from TLC to FRC after left lung atelectasis. The pieces of the right and left lung were analyzed separately. We assumed that the atelectatic left lung was isotropically expanded and that the atelectatic lung volume consisted of the volume of the wet tissue mass and blood. Tissue volume averaged ~7% TLC. Blood volume was the product of blood flow and vascular transit time. We used a transit time of 5 seconds measured previously in the dog (11). Blood flow to the atelectatic lung was the product of cardiac output and the fraction of FMS intensity. Blood volume of the atelectatic left lung averaged 42.7 ± 24.3 ml or 6.7 ± 3.7%TLC in the LLD posture and it varied with body inversion to the RLD posture (30.1 ± 14.3 ml or 4.9 ± 2.3%TLC) and PEEP in the right lung. The adjusted lung cube length after left lung atelectasis averaged ~0.5 that at TLC.

The dimensions of the right lung with the left lung atelectatic were calculated as follows. First, an adjustment from TLC to FRC was based on a uniform contraction. FRC (gas volume) of the right lung was obtained by helium dilution (Table 1). With left lung atelectasis, the right lung at FRC expanded by 25.5 ± 27.3%, producing a regional volume of 67.4 ± 22.5%TLC and a cube dimension of 88 ± 4% the value at TLC. No adjustment was made for the vertical Ptp gradient, which was reduced with lung inflation above FRC (2).

Volume normalization of blood flow and ventilation. Fluorescent intensity of each lung piece representing Q and V_A was converted to units of ml/min (11). Q and V_A were further converted to units of ml/min per unit regional lung volume at FRC by dividing by piece volume ΔVi. ΔVi of each lung piece at Xi was related to its dry weight ΔWi, mean lung density (ρ), and the deformed cube length (ΔXi):

$$\Delta Vi = 4.7\ \Delta Wi\ (\Delta Xi/\Delta Xu)^3/\rho \qquad (1)$$

The term $(\Delta Xi/\Delta Xu)^3$ adjusts the mean density for the vertical Ptp gradient (11). The wet weight for each piece is 4.7 ΔWi. The mean lung density at FRC was the total lung wet weight divided by the total lung volume at FRC (air volume at FRC + volume of tissue mass). Tissue density was 1g/ml for the atelectatic left lung. Dry lung weight for left and right lung averaged 8.9 ± 1.1 and 11.6 ± 1.4 g, respectively. The measured FRC (gas volume) values are summarized in Table 1. With both lung inflated, mean lung density averaged 0.14 ± 0.02 (SD, n = 6) and 0.08 ± 0.01 g/ml at FRC and 10 cm H_2O PEEP, respectively. Mean lung density of the right lung after left lung atelectasis averaged 0.11 ± 0.03 and 0.06 ± 0.01 g/ml at FRC and 10 cm H_2O PEEP, respectively.

The anatomic deadspace was estimated using Fowler's method (17). Pieces were excluded if the fluorescent intensity was outside the range of mean ± 4SD. For the multiple linear regression analysis of V_A/Q and end-capillary P_RO_2, we excluded pieces outside the range of mean ± 3SD of ln (V_A/Q).

Gas exchange parameters: V_A/Q and PO_2. V_A- and Q- weighted V_A/Q distribution and gas exchange estimates derived from FMS data were compared with those from MIGET. We calculated end-capillary O_2 (P_RO_2) and CO_2 content of each lung piece using the V_A and Q fluorescent intensities, body temperature, Hb concentration and mixed venous blood gases (14) in conjunction with mass balance equations for O_2, CO_2 and N_2. Arterial PO_2, PCO_2, alveolar-arterial O_2 difference and end-capillary PO_2 were calculated by summation of piece data.

Table 1. Hemodynamic and blood gas data

	LLD				RLD				
	Non-atelectasis		Atelectasis		Non-atelectasis		Atelectasis		
PEEP, cm H_2O	0	10	0	10	0	10	0	10	Significant Difference
Psa, cm H_2O	94±5	91±7	83±6	79±6	88±7	91±9	91±6	94±6	
Ppa, cm H_2O	17±2	24±1	22±4	28±4	16±2	23±2	20±2	28±2	PEEP***(P+:26±2, P-:19±2) Atel*(A+:25±3, A-:20±2)
Ppcw, cm H_2O	5±0.8	11±1.5	10±2.6	13±1.9	7±0.8	12±1.5	8±2.3	11±2	PEEP**(P+:12±1, P-:8±1)
Paw.cm H_2o	10±1	21±1	10±1	25±6	10±1	20±1	11±2	21±2	PEEP***(P+:22±2, P-:10±1)
V_T,right (ml)	252±13	205±11	226±13	221±8	188±9	220±9	213±6	213±5	
RR (min^{-1}}	14±1	18±3	16±1	16±2	24±5	29±7	23±3	28±6	
Q_T, l-min^{-1}	3.3±0.2	3.2±0.2	3.2±0.3	2.9±0.1	3.4±0.2	3±0.1	3.1±0.1	3±0.1	PEEP*(P+:3.05±0.11, P-:3.26±0.13)
Q_L, %	45±3	58±3	18±4	25±6	31±2	22±3	10±3	12±3	Post***(LLD:37±3, RLD:19±2) PEEP*(P+:29±3, P-:26±2) Atel***(A+:16±3, A-:39±2)
PVR_T	3.5±1.0	3.8±1.6	4.7±0.8	6.0±0.9	2.8±1.0	3.7±0.8	3.7±1.8	5.8±1.5	PEEP** (P+:4.8±1.6, P-:3.6±1.4) Atel** (A+: 5.0±1.5, A-: 3.5±1.3)
PVR_L	6.4±2.2	6.2±2.9	18.7±8.5	22.6±9.7	8.2±4.1	15.6±6.2	30.0±10.1	45.4±27.9	Post* (LLD: 13.5±9.6, RLD:24.7±20.2) Aetl** (A+:29.1±18.2, A-:9.1±5.4)
PVR_R	6.3±2.3	9.7±3.5	5.5±1.5	8.0±0.5	4.0±1.5	4.5±1.5	4.3±2.1	6.5±1.2	Post** (LLD: 7.3±2.7, RLD: 4.9±1.8) PEEP** (p+:7.2±2.7, p-:5.0±2.0)
Pao_2, Torr	559±24	506±35	367±63	230±73	493±60	594±10	401±42	373±61	Atel**(A+:442±21, A-:387±31) Post* (LLD:415±42, RLD:465±32)
$Paco_2$, Torr	40±0.7	36±0.3	39±1.3	40±0.9	37±0.3	37±1	40±1.8	39±1.6	Atel*(A+:39±0.9, A-:37±0.4)
pH	7.32±0.01	7.33±0.01	7.30±0.02	7.29±0.01	7.34±0.01	7.33±0.01	7.29±0.02	7.30±0.01	Atel*(A+:7.3±0.01, A-:7.33±0.01)
Pvo_2, Torr	68±6	65±5	57±4	46±4	67±5	63±3	59±3	55±3	PEEP*(P+:57±3, P-:63±4) Atel**(A+:54±3, A-:67±5)
(A-a)DO_2, Torr	157±27	214±41	351±69	486±81	226±64	124±17	315±51	344±66	Atel**(A+:374±62, A-:180±33) Post*(LLD:302±50, RLD:252±40)
FRC_R (ml)	463±90	894±168	513±229	963±335	281±93	542±51	365±101	751±221	Post***(LLD:709±72, RLD:492±45) PEEP***(P+:787±59, P-:406±45)
FRC_L (ml)	143±45	306±72			286±130	547±160			Post**(LLD:230±21, RLD:394±52) PEEP**(P+:430±51, P-:214±36)

Values are means ± SD for 6 dogs. Psa, means systemic arterial pressure; Ppa, mean pulmonary artery pressure; Ppcw, pulmonary capillary wedge pressure; Paw, peak airway pressure; VT:tidal volume; RR: respiratory rate; Q_T, total cardiac output; Q_L, left lung blood flow; PVR: pulmonary vascular resistance; V_T, whole lung; R, right lung; L, left lung; PaO_2, arterial PaO_2; $PaCO_2$, arterial $PaCO_2$; PvO_2, mixed venous PO_2; (A-a)DO_2, alveolar and arterial oxygen tension difference; FRC, functional residual capacity. atel, atelectasis; post, position; A+: with atelectasis; A-: no atelectasis; P+: with PEEP; P-: no PEEP. *$P < 0.05$, **$P < 0.01$, ***$P < 0.001$. PVR units: cm H_2O/l/min

Table 2. Coefficient of correlation between V_A and Q in the right lung during left lung atelectasis

	LLD		RLD	
PEEP	0	10	0	10
Animal 1	0.70	0.64	0.29	0.57
Animal 2	0.79	0.80	0.77	0.90
Animal 3	0.68	0.52	0.71	0.50
Animal 4	0.50	0.44	0.59	0.67
Animal 5	0.62	0.90	0.67	0.60
Animal 6	0.47	0.74	0.33	0.47
Mean ± SD	0.63±0.12	0.67±0.17	0.56±0.20	0.62±0.16

Statistical Analysis

Volume-normalized Q and V_A were used for all analysis. Values were presented as mean ± SD. A paired t test was used to test for a significant difference between two treatments in the same animals. ANOVA repeat measures were used to evaluate differences among more than two groups. Correlation was determined using Pearsons correlation.

Results

The hemodynamic and blood gas data are shown in Table 1. Body temperature, Psa and Hb were constant throughout the study. Cardiac output did not change with body position or left lung atelectasis, but decreased slightly with PEEP.

Overall Gas Exchange

For the control lung with 100% O_2 ventilation, PaO_2 was greater (559 Torr *vs.* 493 Torr) in the LLD than the RLD posture without PEEP but less (506 *vs.* 594 Torr) with PEEP. With 10 cm H_2O PEEP, (A-a) DO_2 in the control lung was greater (214 *vs.* 124 Torr) in the LLD than the RLD posture, and increased (486 *vs.* 344 Torr) with left lung atelectasis. Left lung atelectasis decreased PaO_2, pH and $P\bar{v}O_2$ and increased $PaCO_2$ and (A-a)DO_2 in both postures. With 10 cm H_2O PEEP, the atelectasis-induced reduction in PaO_2 was greater (373 *vs.* 230 Torr) in the RLD than in the LLD posture.

With 100% O_2 ventilation, $P\bar{v}O_2$ averaged 63-68 mm Hg in both LLD and RLD posture and decreased with PEEP and left lung atelectasis. With left lung atelectasis, $P\bar{v}O_2$ was similar in LLD and RLD postures (57 mm Hg), but decreased with PEEP in the LLD posture (46 mm Hg). Except for the LLD posture with PEEP, ventilation with 100% O_2 with left lung atelectasis always increased $P\bar{v}O_2$ above the normal value measured with air ventilation of both lungs (47 mm Hg). With air ventilation, $P\bar{v}O_2$ did not change with body posture or PEEP. The relatively high PaO_2 and $P\bar{v}O_2$ measured with left lung atelectasis and 100% O_2 ventilation to the right lung eliminated any HPV in the right lung. Changes in Q observed in the right lung with PEEP and posture was attributed to factors other than HPV.

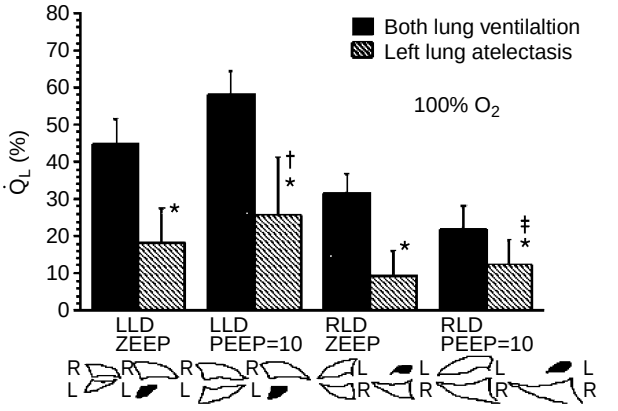

Fig. 1. Effect of position and PEEP on the left lung blood flow during bilateral ventilation and left lung atelectasis. Values are mean ± SD. $^*P < 0.05$, left atelectatic lung compared with control at the same position and PEEP condition. $^\dagger P < 0.05$, left atelectatic lung between 0 and 10 cm H_2O PEEP. $^\ddagger P < 0.05$, left atelectatic lung with 10 cm H_2O PEEP between LLD and RLD posture.

Redistribution of Blood Flow between Right and Left Lung

Effect of posture and PEEP, bilateral ventilation. Without PEEP with both lungs ventilated with 100% O_2 (control), total Q of the dependent left (right) lung was greater (45% *vs.* 31%) in the LLD (RLD) than in the RLD (LLD) posture (Fig. 1). This behavior was accentuated with 10 cm H_2O PEEP. This behavior was also found with air ventilation except for the LLD posture without PEEP where HPV reduced blood flow in the dependent lung (see Discussion).

Effect of left lung atelectasis. Left lung atelectasis produced a small but significant reduction in cardiac

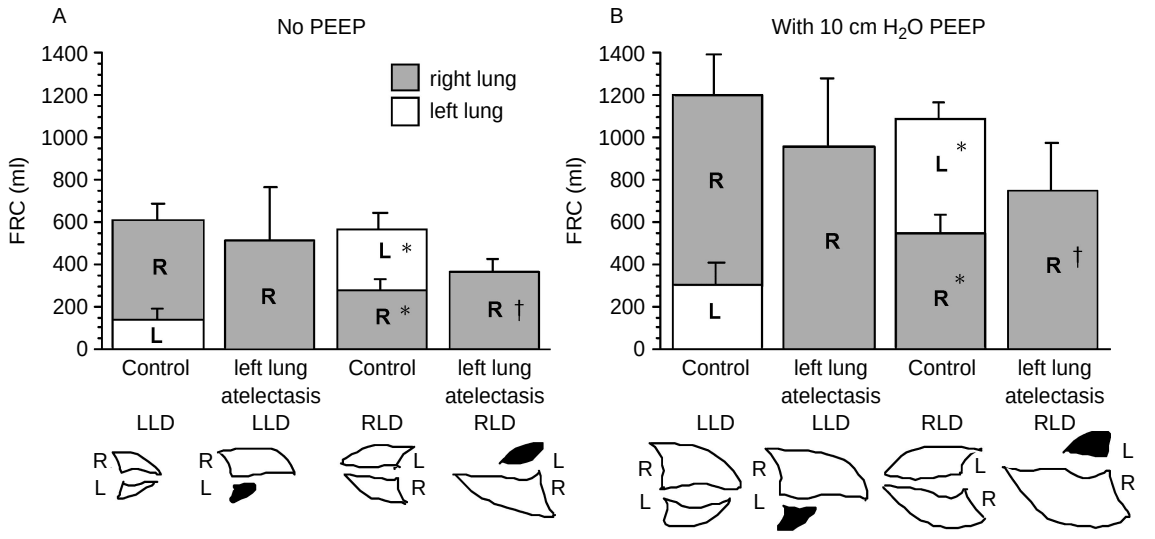

Fig. 2. Left and right lung volume changes with bilateral ventilation and after left lung atelectasis with and without PEEP in both LLD and RLD postures. Values are mean ± SD (n = 6). *$P < 0.05$ comparison of same lung between LLD and RLD during bilateral ventilation. †$P < 0.05$ comparison of right lung between LLD and RLD with left lung atelectasis.

output. The largest effect of left lung atelectasis was to reduce Q in the left lung by 60% in the LLD posture and 45% in the RLD posture, with a simultaneous increase in Q in the right lung. This behavior occurred with and without 10 cm H_2O PEEP. This reduction in flow in the left atelectatic lung was most likely due to HPV, since the $P\bar{v}O_2$ was ~55 mmHg and in the absence of ventilation blood PO_2 did not change as blood crossed the circulation (see below). The posture-induced differences in Q caused by left lung atelectasis was attributed to changes in PVR [(Ppa-Ppcw)/Q].

In the LLD posture, PEEP caused a shift of Q from the nondependent right lung (55 to 42%, Table 2) to the dependent left lung (45 to 58%). This behavior was consistent with the PEEP-induced increase (30%) in PVR (Table 1) in the nondependent right lung in the LLD. Similarly, in the RLD posture, PEEP caused a shift of Q from the nondependent left lung (31 to 22%) to the dependent right lung (69 to 78%). This behavior was consistent with the PEEP-induced 90% increased PVR in the nondependent left lung in the RLD posture.

Effect of left lung atelectasis and body position. Left lung atelectasis increased Ppa and Ppv by 5 and 3 cm H_2O, respectively. With left lung atelectasis, Ppa increased from 21 to 28 cm H_2O with 10 cm H_2O PEEP in both postures, while Ppv and Palv increased from 9 and 5 cm H_2O without PEEP to 12 and 16 cm H_2O with 10 cm H_2O PEEP.

Lung Volumes

Bilateral ventilation (control). In the control lung ventilated with 100% O_2 with and without 10 cm H_2O PEEP, FRC of the right lung was 3-fold greater than that of the left lung in the LLD posture, but was similar to left lung FRC in the RLD posture (Fig. 2). This behavior indicated a shift in gas volume from the nondependent to the dependent lung with inversion from the LLD to the RLD posture. This effect, observed in a previous study with air ventilation (11), was most likely due to the compression of the smaller dependent left lung by the heart and abdominal weight in the LLD posture. The foregoing fractional differences in FRC between the left and right lung in the LLD and RLD posture observed without PEEP was maintained with 10 cm H_2O PEEP, in the face of a doubling of the lung volumes.

Effect of left lung atelectasis. Without PEEP, left lung atelectasis in the LLD posture caused a small (10%) increase in FRC of the right nondependent lung compensating partially for the atelectasis-induced gas loss from the left lung (Table 1, Fig. 3). In the RLD posture, the left lung atelectasis-induced increased in FRC of the right lung was increased by 30%. However, with left lung atelectasis FRC of the right lung was greater in the nondependent than in the dependent position. This behavior was most likely due to lung compression of the dependent right lung in the RLD and expansion in the LLD posture, by the weight of the atelectatic lung, heart and abdomen. Similar effects of left lung atelectasis were also observed with 10 cm H_2O PEEP.

Microspheres Data

For each animal, 1110-1562 lung pieces were

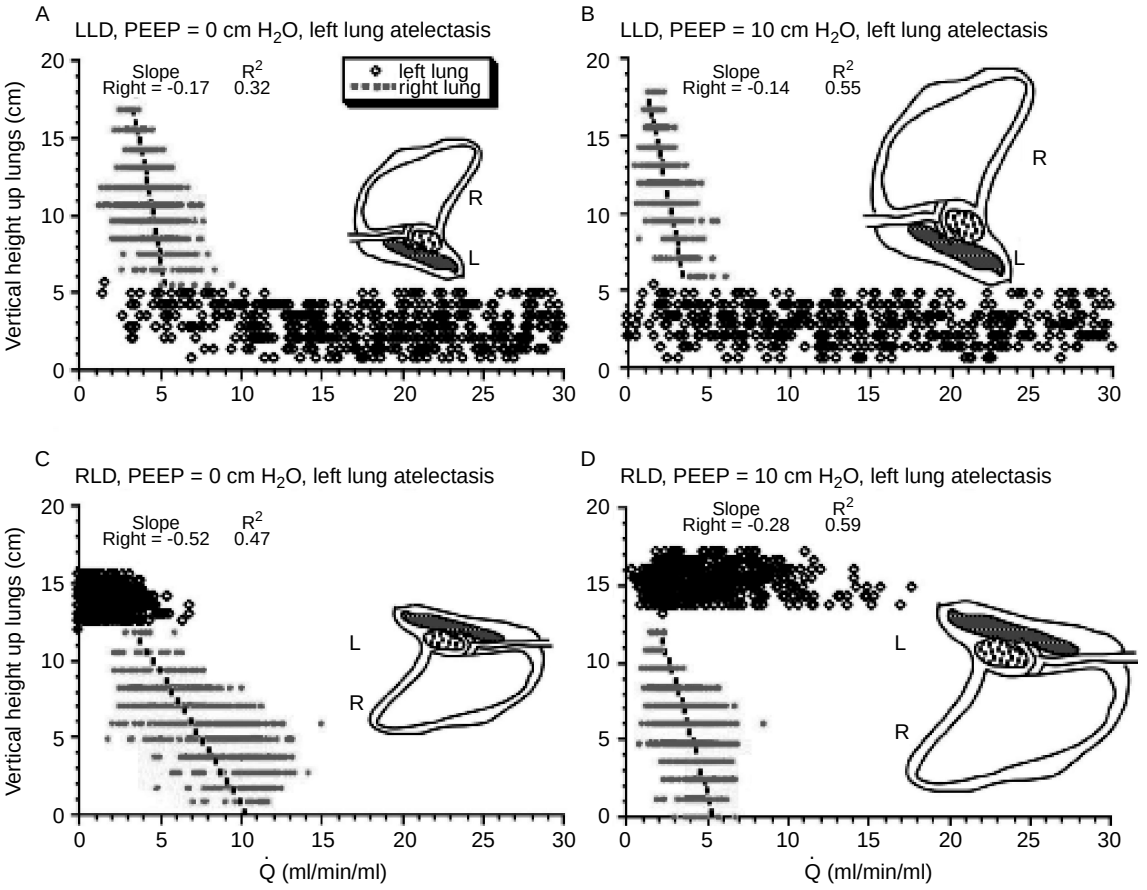

Fig. 3. Blood flow per unit regional lung volume (ml/min/ml) *vs.* lung height with left lung atelectasis for a representative dog, in the LLD (posture) without PEEP (A), LLD with 10 cm H_2O PEEP (B), RLD without PEEP (C) and RLD with 10 cm H_2O PEEP (D). R represents right lung (open points), L the left lung (solid points) and N, the number of lung pieces. The lines represent best-fit values from multiple linear regression analysis at the center of mass.

processed for regional blood flow and ventilation. An average of 126 ± 46 lung pieces (9 ±3%) with > 25% pulmonary airways and 15 ± 13 lung pieces (1 ± 1%) with fluorescent intensity outside the range of the mean ± 4SD were discarded. Regional blood flow and ventilation analysis was done on 90 ± 3% of the total lung pieces (523 ± 74 pieces in the left lung and 674 ± 127 pieces in the right lung). For the analysis of V_A/Q and P_RO_2 in the control lung and the right lung with left lung atelectasis, we discarded pieces outside the range of mean ± 3SD of ln (V_A/Q). This procedure eliminated right lung pieces (1 ± 0.3%) with deadspace (infinite or very large V_A/Q) and with shunt (very low V_A/Q).

Regional Distribution of Q in the Right Lung with Left Lung Atelectasis

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 (Fig. 1). 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. 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.

Left lung atelectasis eliminated the vertical, dorsal-ventral and caudal-cranial gradients in Q observed in the right lung without PEEP in the LLD posture (Fig. 3). This was associated with a small (10%) increase in the right lung volume (Table 1, Fig. 2) and a 50% increase in right lung blood flow (Table 1) caused by the atelectasis-induced decrease in left lung blood flow. The atelectasis-induced elimination of the Q gradients was caused by the increase in Q going to the non-dependent, ventral and cranial parts of the right lung.

Regional Distribution of V_A in the Right Lung with Left Lung Atelectasis

Aerosolized microspheres measured in the left atelectatic lung averaged 1.5 ± 1.9% of that used to measure ventilation in the right lung, confirming insignificant ventilation to the left atectatic lung. In one dog ventilated with 10 cm H_2O PEEP, ventilation of the left atelectatic lung was 26% of the right lung ventilation. The resulting gas exchange data were excluded from the pooled data.

Discussion

The major findings of this study are as follow. First, compared to previous results with air ventilation (11), ventilation with 100% O_2 increased Q to the dependent left lung in the LLD posture (control). This supported the conclusion that HPV occurred in the dependent left lung in the LLD posture with air ventilation. Second, with left lung atelectasis, HPV caused a shift of blood flow from the atelectatic lung to the ventilated lung. Blood flow to the atelectatic left lung was greater with the left lung in the dependent position with and without PEEP. Third, left lung atelectasis resulted in a right lung FRC that was greater in the LLD than RLD posture. This was evidence that compression of the dependent right lung resulted from the weight of the atelectatic left lung, heart and abdomen in the RLD posture. Fourth, any impairment in gas exchange associated with left lung atelectasis was reduced with ventilation of the right lung with 100% O_2. However, PEEP increased (A-a)DO_2 in the LLD posture, a result of an increased shunt measured as an increased blood flow to the atelectatic lung.

Methodological Issues

On isolation from the chest cavity, the atelectatic left lung showed no visual evidence of edema and was easily expanded by ventilation with 5 cm H_2O PEEP and by inflation to TLC. Cardiac output was maintained constant by administering normal saline intravenously during the experiment. This was done to eliminate the cardiac output-induced effects on regional blood flow distribution. The accurate measurement of total ventilation to the ventilated right lung by the FMS with left lung atelectasis depended on the complete isolation of the two lungs by the double lumen tube intubation. Aerosolized microspheres detected in the atelectatic lung was only substantial (> 5% of total) in the RLD posture with 10 cm H_2O PEEP in one animal. These data were not included in the pooled data.

The use of 100% O_2 ventilation to the right lung with left lung atelectasis allowed the evaluation of the shift of Q to the right lung caused by changes in vascular pressure (zonal conditions) and distortion of the right lung by the weight of the atelectatic lung, independent of the effects of HPV.

The atelectatic lung was gas free and had a density of 1 g/ml. Like the abdominal contents the atelectatic lung has a low shear modulus (19) and is incompressible. The distortion due to the heart and abdominal weight on the atelectatic lung is unknown and we assumed that it was isotropically expanded. Because it is incompressible (no volume change), we assumed that a nonuniform distortion did not change blood flow. Accordingly, we attributed the change in blood flow with position and PEEP to changes in zonal conditions.

Volume adjustment to FRC and for vertical Ptp gradient during bilateral ventilation. Both injected and aerosolized microspheres were delivered in vivo near FRC, while the fluorescent signal was measured in vitro in dried lung pieces inflated to TLC. Therefore, several adjustments were made to express regional ventilation and perfusion as V_A and Q per unit regional volume at FRC. As in a previous study (12) for the ventilation of both lungs, the dimensions of the lung at FRC was obtained from measurements of the borders of the lung at FRC and TLC (20).

Volume adjustment to FRC and for vertical Ptp gradient with left lung atelectasis. In the absence of reported data, we assumed that the atelectatic lung was isotropically expanded. The volume of the atelectatic lung was the sum of the tissue and blood. Blood volume was computed using transit time across a normally expanded lung. Transit time in the atelectatic lung might be greater than that of the normally expanded lung since transit time increases as flow decreases (43). Thus we might have underestimated the atelectatic lung volume. Blood volume varied with posture and PEEP in the left atelectatic lung and represented the major part of the atelectatic lung volume.

Effect of Posture on Lung Volume

FRC of the dependent lung was smaller than that of the nondependent lung in the LLD posture but equal in the RLD posture after adjusting for the smaller weight of the left lung, a behavior consistent with previous results in the anesthetized dog ventilated with air (12) and in anesthetized humans (37, 38). This behavior indicated that lung compression due to heart and abdominal weight in conjunction with the vertical Ptp gradient was greater in the smaller dependent left lung in the LLD posture than in the dependent right lung in the RLD posture.

The application of 10 cm H_2O PEEP doubled the

FRC of both left and right lung but maintained the left-right differences in FRC observed without PEEP, consistent with results in anesthetized humans in the lateral posture (37). This behavior in conjunction with the elimination of the vertical Ptp gradient with PEEP (2) suggests that nonuniform lung distortion independent of the vertical Ptp gradient was involved, and this occurred in spite of the PEEP-induced stiffer lung (37, 39). A role for the abdomen with a passive diaphragm has been implicated (18). Studies of lung deformation using finite element models have implicated the weight of the lung (46), the heart (5) and abdomen (19) as a contributor to the vertical Ptp gradient. Similar effects in the lateral decubitus posture need to be evaluated.

Effect of left lung atelectasis and posture on the right lung volume. FRC of either the left or right lung was reduced with inversion from the nondependent to dependent position. A similar effect occurred in the right lung with left lung atelectasis. With left lung atelectasis, the right lung expanded to fill the space in the thoracic cavity previously occupied by the expanded left lung, the result of a reduced pleural pressure (13). Right lung FRC was smaller with the lung positioned dependent because of compression by the weight of the atelectatic left lung, heart and abdomen. This behavior observed with unilateral atelectasis was similar to that which occurred in left lung pneumonectomized rabbits studied in the LLD and RLD postures (32) and in pneumonectomized dogs (22).

Effect of PEEP, Left Lung Atelectasis and Posture on Blood Flow and PVR

Effect of PEEP on PVR. That PEEP caused a shift of blood flow from the nondependent lung to the dependent lung in the LLD and RLD posture in the control lung ventilated with 100% O_2 is in line with previous studies in dogs (20, 36) and humans (23, 24, 37). The major effect of PEEP on the blood flow distribution in the absence of HPV was attributed to the increased lung regions in zone 2 relative to zone 3 and increased PVR in the nondependent regions relative to dependent regions.

Effect of left lung atelectasis on Q and PVR. Previous studies (9, 15, 28, 29, 33) have demonstrated that the diversion in blood flow from a lung made atelectatic was caused primarily by the increased PVR due to HPV. That HPV was involved was supported by our experimental results.

First, in the absence of ventilation, the blood flowing through the atelectatic lung maintained a P_RO_2 equal to P_VO_2 (60 mm Hg) that was below the level (100 mmHg) needed to trigger a HPV response (15). The absence of ventilation to the atelectatic lung was indicated by the absence of aerosolized microspheres in the atelectatic lung and confirmed by the blood flow to the atelectatic lung detected as shunt by the MIGET data for the whole lung.

Second, studies of unilateral hypoxia indicated a shift (40%) of blood flow from the hypoxic lung to the contralateral lung (26, 27) and an increase in perfusion pressure of 30%. This shift in blood flow was somewhat less than the 60% observed with left lung atelectasis. The greater reduction in blood flow caused by left lung atelectasis might be related to the dynamic response of the HPV (16, 42) or the lung nonuniform distortion caused by lung atelectasis per se and by the weight of the mediastinal contents and the abdomen in the intact chest.

Effect of posture on Q and PVR to atelectatic left lung. Blood flow to the dependent atelectatic left lung was reduced by half when it was positioned nondependent. This reduced blood flow to the atelectatic lung was consistent with increased PVR and zone 2 conditions in the nondependent position. By contrast, the greater blood flow to the atelectatic lung in the dependent than in the nondependent position was opposite to that expected from the greater nonuniform lung distortion in the dependent position. Accordingly, the differences in blood flow to the atelectatic lung between the LLD and RLD posture was primarily due to changes in the zonal conditions. The contribution of lung distortion to the reduction of blood flow to an atelectatic lung has been invoked in previous studies (10, 30, 35, 41) and its importance needs to be evaluated.

Effect of PEEP on Q and HPV in the atelectatic lung. With PEEP applied to the right lung ventilated with 100% O_2, blood flow (7%) shifted from the right lung to the atelectatic left lung in the LLD posture but not in the RLD posture. The reduced flow to the right lung with inversion from the RLD to LLD posture with PEEP was consistent with a larger fraction of the right lung positioned in zone 2 in the LLD posture than in the RLD posture, since the nondependent right lung is positioned lower relative to the mid chest level. The latter was exacerbated by the smaller FRC of the right lung in the RLD posture due to compression by the nondependent atelectatic lung and mediastinal contents. These effects on flow to the right lung were greater than any increase in HPV in the dependent atelectatic lung caused by the reduction of $P\bar{v}O_2$ with PEEP (from 57 to 46 mm Hg). A similar inhibitory effect on the increased HPV response with PEEP has been reported in open chest dogs (14).

Without PEEP, PVR to the whole lung ventilated with 100% O_2 increased with left lung atelectasis due to increased Ppa and Pcwp with cardiac output remaining constant. Similarly, with left lung atelectasis, PEEP increased PVR. This effect of PEEP with left

lung atelectasis was similar to the results in dogs ventilated bilaterally with 40% O_2 (25) or with 100% O_2 (14). In the latter studies PEEP had no inhibitory effect on the hypoxia-induced increase in PVR. Therefore, the effects of lung atelectasis and PEEP on PVR were additive.

Regional Distribution of Perfusion

Nongravitational perfusion heterogeneity. In the present study in both the LLD and RLD posture, a negative dorsal-ventral gradient of Q was observed in the left, right and whole lung with 100% O_2 ventilation, with the dorsal regions having a greater blood flow. By contrast, with air ventilation the dorsal-ventral gradient of Q was positive, with the dorsal regions having the lower Q (12). The positive dorsal-ventral gradient in Q was accompanied with a positive gradient in P_RO_2, with the dorsal regions having the lowest P_RO_2 (23). This difference between air and 100% O_2 ventilation is consistent with HPV occurring in the dorsal regions with air ventilation that was eliminated with 100% O_2 ventilation, resulting in a shift of Q from ventral to dorsal regions. The greater Q in the dorsal lung regions with 100% O_2 ventilation was similar to the finding in isolated dog lung ventilated with 95% O_2 (8). In the latter study, the greater Q in the dorsal lung region was attributed to a greater intrinsic vascular conductance. Because of the uncertainty regarding nonuniform lung distortion in the atelectatic left lung and the assumption that lung volume was uniform, the spatial gradients measured in the atelectatic lung were of questionable value and are not reported.

Effect of hyperoxia. In a previous study (31) with air ventilation, blood flow was lower in the dependent left lung than in the nondependent right lung in the LLD posture, opposite to the behavior expected from the effect of gravity. In our earlier study (12), simultaneous measurements of regional blood flow and ventilation indicated a positive vertical gradient in regional P_RO_2, with the dependent lung regions having a P_RO_2 value low enough to invoke an HPV response. The present experiments showed that blood flow measured with 100% O_2 ventilation was greater than that measured with air ventilation, supporting the conclusion that HPV was responsible for the reduced flow in the dependent lung ventilated with air. A similar conclusion was reached in studies of blood flow distribution measured using xenon-131 in supine humans breathing air and O_2-enriched gas (34). In these studies, blood flow in the human subjects breathing air was uniform up the lung, but shifted from the nondependent to dependent lung regions while breathing 100% O_2. The lower blood flow to the dependent lung region while breathing air was attributed to a dependent lung closing volume above FRC, a reduced ventilation, and HPV in the dependent lung. Breathing 100% O_2 abolished the HPV, shifting flow to the dependent lung regions.

Other factors might decrease blood flow to the dependent lung region. These include increases in PVR due to a reduced lung volume arising from the vertical Ptp gradient, to nonuniform lung distortion caused by the weight of the mediastinal contents, and to the compression of extra-alveolar vessels by an increased perivascular interstitial pressure (21).

Effect of PEEP. In general with 100% O_2 ventilation, PEEP increased lung volume and reduced spatial nonuniformities in Q by redistributing blood flow from dependent and caudal regions to nondependent and cranial regions, confirming previous findings with air ventilation (12). However, the PEEP-induced shift in blood flow from ventral to dorsal regions measured previously with air ventilation was reversed with 100% O_2 ventilation. The PEEP-induced reduction in spatial nonuniformities in Q and V_A was most striking in the dependent left lung.

Regional Distribution of Ventilation in the Right Lung with Left Lung Atelectasis

Regional ventilation measured by the aerosolized microsphere technique with left lung atelectasis was observed only in the right lung. In previous studies of the whole lung ventilated with air (21), vertical gradients in V_A occurred in the right lung in both LLD and RLD postures. Left lung atelectasis with 100% O_2 ventilation reduced or abolished these gradients in the present study, similar to the effect of PEEP in the previous study. This effect of left lung atelectasis without PEEP was probably not predominantly caused by the increase in right lung volume which was small (10% and 30%) in the LLD and RLD posture, but by a change in right lung shape. The shape change would occur by a dependent and caudal expansion of the right lung (18) in conjunction with a cranial movement of the diaphragm opposed to the atelectatic lung. This issue requires experimental verification. The shape change of the right lung with left lung atelectasis might also be responsible for the elimination of any spatial gradients in Q in the LLD posture.

Without PEEP in the LLD posture, a negative caudal-cranial gradient in V_A that became more negative in the dorsal-ventral direction was observed, indicating better ventilation in the caudal-dorsal regions. In the LLD posture, PEEP produced a negative vertical gradient in V_A together with a negative dorsal-ventral gradient, indicating better ventilation in the dependent-dorsal regions. Thus, in the LLD

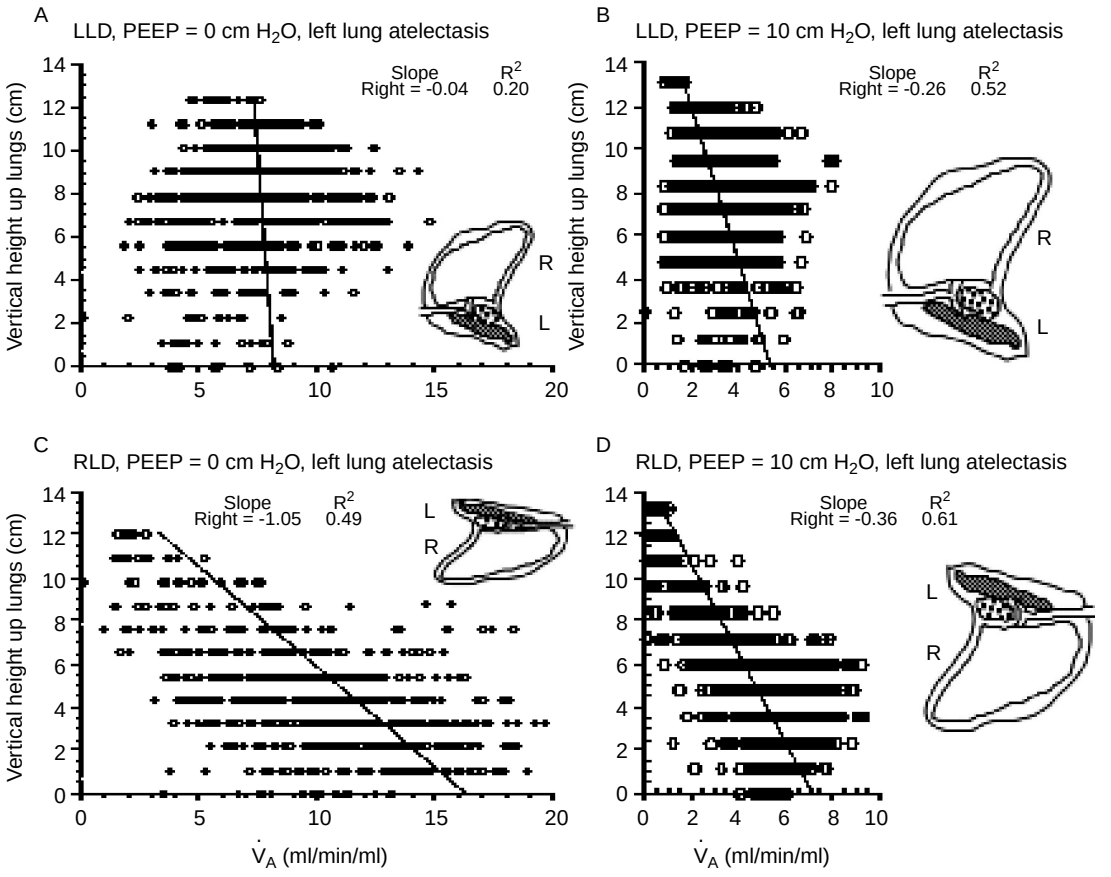

Fig. 4. Ventilation per unit regional lung volume (ml/min/ml) of right lung with left lung atelectasis *vs.* lung height for the representative animal in LLD without PEEP (A), LLD with 10 cm H_2O PEEP (B), RLD without PEEP (C), and RLD with 10 cm H_2O PEEP. The lines represent the best-fit values at center of mass from multiple linear regression analysis.

posture, PEEP caused a shift in ventilation form the caudal to the dependent lung regions.

In the RLD posture without PEEP, the most negative dorsal-ventral gradient was observed in the caudal regions and the most negative caudal-cranial gradients were observed in the dorsal regions, indicating a better ventilation in the caudal-dorsal regions. Without PEEP, the negative vertical gradient in V_A implied better ventilation in the dependent region. Thus in the RLD posture, PEEP caused a shift in ventilation from the caudal-dorsal to the dependent lung region. The major effect of PEEP in both postures was to shift ventilation to the dependent regions from the caudal regions.

The greater ventilation in the caudal than in cranial region of the right lung ventilated with 100% O_2 with left lung atelectasis was similar in behavior to that measured with the whole lung ventilated with air (12) and opposite to the that measured in conscious humans in the lateral decubitus posture (3). In the absence of a vertical Ptp gradient, PEEP produced negative vertical and dorsal-ventral gradients in V_A in both the LLD and RLD posture. The mechanism involved requires further study.

Ventilation and Perfusion Matching in the Right Lung after Left Lung Atelectasis

Despite considerable V_A and Q heterogeneity, V_A and Q were still matched in the ventilated lung in both LLD and RLD postures (Fig. 5). Addition of PEEP did not alter V_A and Q matching. V_A/Q was centered around $V_A/Q = 2$ in LLD, but between 1 and 2 in RLD. The probable cause was that total Q to the ventilated lung was increased in RLD, because of the redistribution of blood flow during left lung atelectasis.

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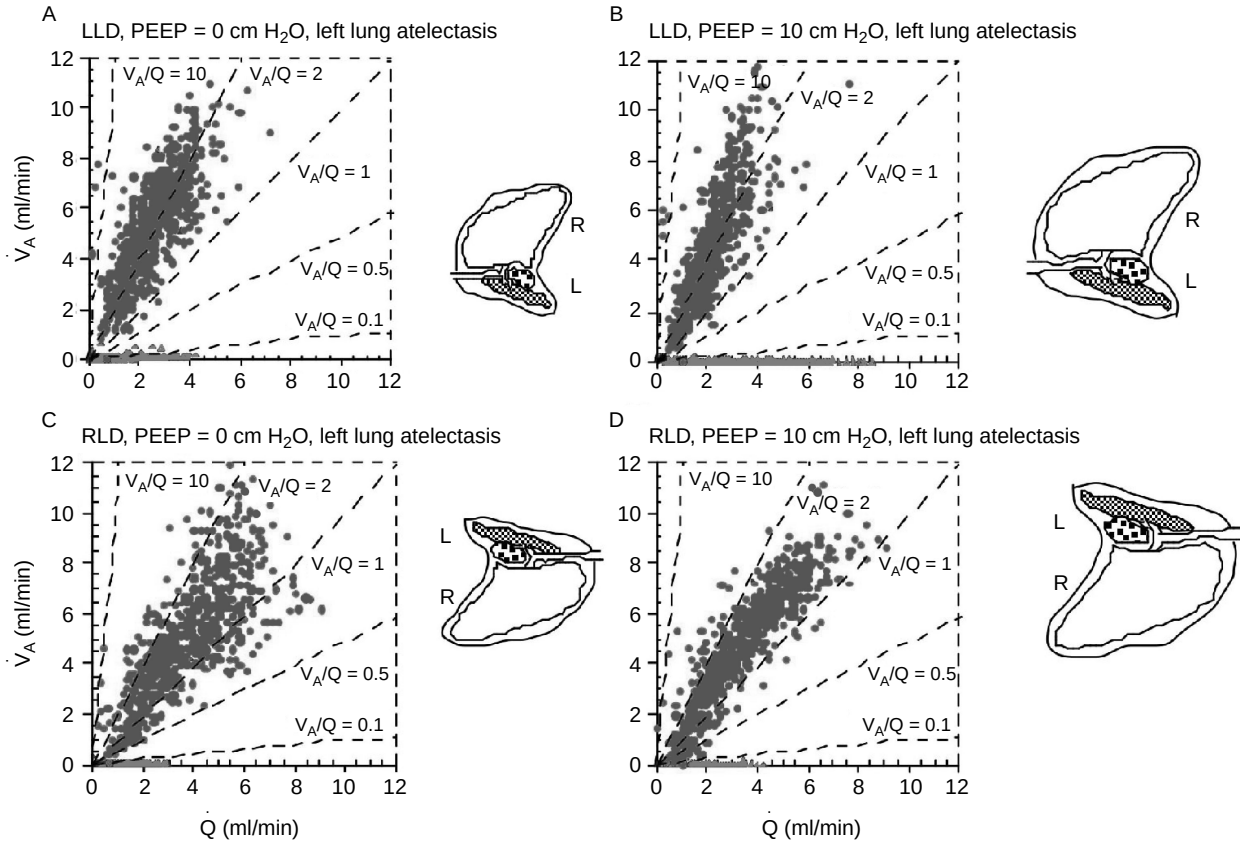

Fig. 5. Scattergram of regional ventilation plot against regional perfusion for a representative animal in LLD and RLD with and without PEEP during left lung atelectasis.

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References

1. Agostoni, E. and D'Angelo, E. Comparative features of the transpulmonary pressure. *Respir. Physiol.* 11: 76-83, 1970.
2. Agostoni, E., D'Angelo, E. and Bonanni, M.V. Topography of pleural surface pressure above resting volume in relaxed animals. *J. Appl. Physiol*. 29: 297-306., 1970.
3. Amis, T., Jones, J. and Hughes, J. Effect of posture on interregional distribution of pulmonary ventilation in man. *Respir. Physiol*. 56: 145-167, 1984.
4. Amis, T.C., Jones, H.A. and Hughes, J.M. Effect of posture on inter-regional distribution of pulmonary perfusion and V_A/Q ratios in man. *Respir. Physiol.* 56: 169-182, 1984.
5. Bar-Yishay, Hyatt, R. and Rodarte, J. Effect of heart weight on distribution of lung surface pressures in vertical dogs. *J. Appl. Physiol.* 61: 712-718, 1986.
6. Barer, G.R., Howard, P. and Shaw, J.W. Stimulus-response curves for the pulmonary vascular bed to hypoxia and hypercapnia. *J. Physiol.* (Lond) 211: 139-155, 1970.
7. Beck, K.C. and Lai-Fook, S.J. Pulmonary blood flow *vs.* gas volume at various perfusion pressures in rabbit lung. *J. Appl. Physiol.* 58: 2004-2010, 1985.
8. Beck, K.C. and Rehder, K. Differences in regional vascular conductances in isolated dog lungs. *J. Appl. Physiol*. 61: 530-538, 1986.
9. Benumof, J.L. Mechanism of decreased blood flow to atelectatic lung. *J. Appl. Physiol*. 46: 1047-1048, 1979.
10. Burton, A.C. and Patel, D.J. Effect on pulmonary vascular resistance of inflation of the rabbit lungs. *J. Appl. Physiol*. 12: 239, 1958.
11. Chang, H. *Spatial distribution of ventilation and perfusion in the lateral decubitus posture*. (Ph.D. Thesis). Seattle: University of Washington, 2001.
12. Chang, H., Lai-Fook, S., Domino, K., Schimmel, C., Hildebrandt, J., Robertson, H., Glenny, R. and Hlastala, M. Spatial distribution of ventilation and perfusion in anesthetized dogs in lateral postures. *J. Appl. Physiol*. 92: 745-762, 2002.
13. Chen, L., Williams, J.J., Alexander, C.M., Ray, R.J., Marshall, C. and Marshall, B.E. The effect of pleural pressure on the hypoxic pulmonary vasoconstrictor response in closed chest dogs. *Anesth. Analg.* 67: 763-769, 1988.
14. Domino, K.B. and Pinsky, M.R. Effect of positive end-expiratory pressure on hypoxic pulmonary vasoconstriction in the dog. *Am. J. Physiol.* 259: H697-H705, 1990.
15. Domino, K.B., Wetstein, L., Glasser, S.A., Lindgren, L., Marshall, C., Harken, A. and Marshall, B.E. Influence of mixed venous oxygen tension (PVO2) on blood flow to atelectatic lung. *Anesthesiology* 59: 428-434, 1983.
16. Dorrington, K.L., Clar, C., Young, J.D., Jonas, M., Tansley, J.G. and Robbins, P.A. Time course of the human pulmonary vascular response to 8 hours of isocapnic hypoxia. *Am. J. Physiol*. 273: H1126-H1134, 1997.
17. Fowler, W.S. Lung function studies II. The respiratory dead space. *Am. J. Physiol.* 154: 405-416, 1948.
18. Froese, A.B. and Bryan, A.C. Effects of anesthesia and paralysis on diaphragmatic mechanics in man. *Anesthesiology* 41: 242-255,

1974.
19. Ganesan, S., Rouch, K.E. and Lai-Fook, S.J. A finite element analysis of the effects of the abdomen on regional lung expansion. *Respir. Physiol*. 99: 341-353, 1995.
20. Greenleaf, J.F., Ritman, E.L., Sass, D.J. and Wood, E.H. Spatial distribution of pulmonary blood flow in dogs in left decubitus position. *Am. J. Physiol*. 227: 230-244, 1974.
21. Hughes, J.M.B., Glazier, J.B., Maloney, J.E. and West, J.B. Effect of lung volume on the distribution of pulmonary blood flow in man. *Resp. Physiol*. 4: 58-72, 1968.
22. Johnson, R.L., Jr., Cassidy, S.S., Grover, R., Ramanathan, M., Estrera, A., Reynolds, R.C., Epstein, R. and Schutte, J. Effect of pneumonectomy on the remaining lung in dogs. *J. Appl. Physiol.* 70: 849-858, 1991.
23. Kaneko, K., Milic-Emili, J., Dolovich, M.B., Dawson, A. and Bates, D.V. Regional distribution of ventilation and perfusion as a function of body position. *J. Appl. Physiol*. 21: 767-777, 1966.
24. Landmark, S.J., Knopp, T.J., Rehder, K. and Sessler, A.D. Regional pulmonary perfusion and V/Q in awake and anesthetized- paralyzed man. *J. Appl. Physiol.* 43: 993-1000, 1977.
25. Lejeune, P., Vachiery, J.L., De Smet, J.M., Leeman, M., Brimioulle, S., Delcroix, M., Melot, C. and Naeije, R. PEEP inhibits hypoxic pulmonary vasoconstriction in dogs. *J. Appl. Physiol*. 70: 1867-1873, 1991.
26. Marshall, B.E. and Marshall, C. Continuity of response to hypoxic pulmonary vasoconstriction. *J. Appl. Physiol*. 49: 189-196, 1980.
27. Marshall, B.E., Marshall, C., Benumof, J. and Saidman, L.J. Hypoxic pulmonary vasoconstriction in dogs: effects of lung segment size and oxygen tension. *J. Appl. Physiol*. 51: 1543-1551, 1981.
28. McFarlane, P.A., Gardaz, J.P. and Sykes, M.K. CO_2 and mechanical factors reduce blood flow in a collapsed lung lobe. *J. Appl. Physiol.* 57: 739-743, 1984.
29. Miller, F.L., Chen, L., Malmkvist, G., Marshall, C. and Marshall, B.E. Mechanical factors do not influence blood flow distribution in atelectasis. *Anesthesiology* 70: 481-488, 1989.
30. Morgan, B. and Guntheroth, W. Pulmonary blood flow and resistnace during acute atelectasis in intact dogs. *J. Appl. Physiol.* 28: 609-613, 1970.
31. Mure, M., Domino, K.B., Robertson, T., Hlastala, M.P. and Glenny, R.W. Pulmonary blood flow does not redistribute in dogs with reposition from supine to left lateral position. *Anesthesiology* 89: 483-492, 1998.
32. Olson, L.E. Effect of posture on static lung volumes and pulmonary mechanics in pneumonectomized rabbits. *J. Appl. Physiol.* 74: 415-422, 1993.
33. Pirlo, A.F., Benumof, J.L. and Trousdale, F.R. Atelectatic lobe blood flow: open *vs*. closed chest, positive pressure *vs*. spontaneous ventilation. *J. Appl. Physiol*. 50: 1022-1026, 1981.
34. Prefaut, C. and Engel, L.A. Vertical distribution of perfusion and inspired gas in supine man. *Resp. Physiol*. 43: 209-219, 1981.
35. Quebbeman, E.J. and Dawson, C.A. Influence of inflation and atelectasis on the hypoxic pressor response in isolated dog lung lobes. *Cardiovasc. Res*. 10: 672-677, 1976.
36. Reed, J.H., Jr. and Wood, E.H. Effect of body position on vertical distribution of pulmonary blood flow. *J. Appl. Physiol*. 28: 303-311, 1970.
37. Rehder, K. and Sessler, A.D. Function of each lung in spontaneously breathing man anesthetized with thiopental-meperidine. *Anesthesiology* 38: 320-327, 1973.
38. Rehder, K., Wenthe, F.M. and Sessler, A.D. Function of each lung during mechanical ventilation with ZEEP and with PEEP in man anesthetized with thiopental-meperidine. *Anesthesiology* 39: 597-606, 1973.
39. Roussos, C.S., Martin, R.R. and Engel, L.A. Diaphragmatic contraction and the gradient of alveolar expansion in the lateral posture. *J. Appl. Physiol.* 43: 32-38, 1977.
40. Schimmel, C., Grazer, D. and Glenny, R. Extending fluorescent microsphere methods for regional organ blood flow to 13 simultaneous colors. *Am. J. Physiol: Heart Circ. Physiol*. 280: H2496-H2506, 2001.
41. Thomas, L.J., J.R., Griffo, Z.J. and Roos, A. Effect of negative-pressure inflation of the lung on pulmonary vascular resistance. *J. Appl. Physiol.* 16: 451, 1961.
42. Vejlstrup, N.G., O'Neill, M., Nagyova, B. and Dorrington, K.L. Time course of hypoxic pulmonary vasoconstriction: a rabbit model of regional hypoxia. *Am. J. Respir. Crit. Care Med*. 155: 216-221, 1997.
43. Wang, P.M., Fike, C.D., Kaplowitz, M.R., Brown, L.V., Ayappa, I., Jahed, M. and Lai-Fook, S.J. Effects of lung inflation and blood flow on capillary transit time in isolated rabbit lungs. *J. Appl. Physiol*. 72: 2420-2427, 1992.
44. West, J.B. and Dollery, C.T. Distribution of blood flow and ventilation-perfusion in the lung measured with radioacitve CO_2. *J. Appl. Physiol*. 15: 405-410, 1960.
45. West, J.B. and Dollery, C.T. Distribution of blood flow in isolated lung:relation to vascular and alveolar pressures. *J. Appl. Physiol*. 55: 1341-1348, 1964.
46. West, J.B. and Matthews, F.L. Stresses, strains, and surface pressures in the lung caused by its weight. *J. Appl. Physiol.* 32: 332-345, 1972.