

Hypoxic Pulmonary Vasoconstriction and Regional and Whole-lung PEEP in the Dog

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In open-chested (Group I) and closed-chested (Group II) dogs, the authors examined the effects of the application of regional and whole-lung PEEP (10 torr) on the partitioning of electromagnetically measured blood flow between a normoxic and a hypoxic compartment of the lung. In both Group I and Group II when the left lower lobe (LLL) was made the hypoxic compartment 1, by ventilation with nitrogen, 95 per cent, CO₂, 5 per cent, and 2, by causing complete absorption atelectasis, LLL blood flow-to-total pulmonary blood flow ratio (\dot{Q}_{LLL}/\dot{Q}_t) decreased 32-56 per cent. PEEP to the normoxic compartment (rest of the lung) during LLL hypoxia increased \dot{Q}_{LLL}/\dot{Q}_t significantly in both Group I (from 12 ± 2 to 35 ± 7 per cent) and Group II (from 8 ± 1 to 11 ± 1 per cent), but the increase was much greater in Group I, and transmural pulmonary arterial pressure increased significantly (6 ± 1 torr) in Group I only. PEEP to both the hypoxic LLL and the normoxic rest of the lung increased \dot{Q}_{LLL}/\dot{Q}_t significantly in Group I only (from 12 ± 2 to 19 ± 4 per cent) and transmural pulmonary arterial pressure increased significantly (7 ± 1 torr) in Group I only. PEEP to just the hypoxic LLL decreased \dot{Q}_{LLL}/\dot{Q}_t significantly in both Group I (from 12 ± 2 to 7 ± 1 per cent) and Group II (from 8 ± 1 to 5 ± 0.4 per cent). It is concluded that, in addition to the usual increase in regional functional residual capacity, the effect of PEEP on diseased lung is a summation of its beneficial and deleterious regional effects on the partitioning of blood flow between hypoxic and normoxic compartments of the lung. (Key words: Hypoxia; Lung; blood flow; hypoxic pulmonary vasoconstriction; intravascular pressures; shunting. Ventilation: positive end-expiratory pressure.)

IMPROVED MATCHING of ventilation to perfusion (\dot{V}/\dot{Q}) and decreased transpulmonary shunting (\dot{Q}_s/\dot{Q}_t) can be achieved by positive end-expiratory pressure (PEEP). Conversely, PEEP, when inadequately or inappropriately applied to abnormal lungs, might result in worsening of \dot{V}/\dot{Q} relationships.^{1,2} For example, inadequate PEEP that fails to improve ventilation in low \dot{V}/\dot{Q} and atelectatic regions could oppose hypoxic pulmonary vasoconstriction (HPV) (increase \dot{Q}_s/\dot{Q}_t) by diverting blood flow from well-ventilated regions to poorly ventilated regions by

selectively increasing pulmonary vascular resistance in well-ventilated lung. Conversely, a localized increase in airway pressure, such as caused by a foreign body or mucous plug one-way valve, could selectively increase vascular resistance in poorly ventilated lung and thereby enhance regional HPV. The purpose of this study was to investigate quantitatively the effects of regional and whole-lung PEEP on the partitioning of blood flow between a hypoxic compartment (left lower lobe, LLL) and a normoxic compartment (rest of lung).

Methods and Materials

Our experimental preparation has been described³⁻⁵ and is only summarized here. Sixteen mongrel dogs of either sex were anesthetized with pentobarbital, 25 mg/kg, and paralyzed with gallamine, 4 mg/kg, both given intravenously, their tracheas intubated with a cuffed endotracheal tube, and their lungs ventilated with a dual-piston Harvard respirator with 100 per cent O₂. Following a left thoracotomy, the LLL bronchus was cannulated distal to a ligature and ventilated independently and synchronously with the rest of the lung using the second piston of the respirator. The expiratory hoses were immersed in water to provide a positive end-expiratory pressure (PEEP) of 2 torr to both sides. Appropriate ventilation of the LLL relative to the rest of the lung was achieved by adjusting tidal volume and external dead space values until end-tidal CO₂ concentrations were 40 torr and peak airway pressures were equal.

Total cardiac output (\dot{Q}_t) and LLL blood flow (\dot{Q}_{LLL}) were measured with electromagnetic flow probes attached to the main pulmonary artery and LLL pulmonary artery, respectively. Pulmonary arterial pressure (P_{pa}) and left atrial pressure (P_{la}) were measured directly. Systemic blood pressure and blood for determination of arterial blood gas values (PaO₂, PaCO₂, and pH) were obtained from a catheter in a femoral artery.

The dogs were divided into two groups. In the first group (Group I, n = 8, 18 ± 2 kg), the right mediastinal and diaphragmatic pleura was widely opened and both left and right chest allowed to remain open throughout the experiment. In the second group (Group II, n = 8, 24 ± 2 kg), large-bore

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($\frac{1}{8}$ – $\frac{1}{4}$ inch OD) rigid plastic catheters were placed in the left and right pleural spaces at the midaxillary line to measure pleural pressure (P_{pl}), and both chests were then closed with an airtight seal. Residual pleural air was removed through the chest tubes.

Both groups of dogs underwent the same experimental sequence. The rest of the lung was continuously ventilated with 100 per cent O_2 while the LLL could be selectively ventilated with either O_2 or a mixture of N_2 , 95 per cent, and CO_2 , 5 per cent.⁵ LLL absorption atelectasis could be induced by occluding the LLL bronchus after ventilation with 100 per cent O_2 . PEEP to the LLL and the rest of the lung could be varied independently. The experimental sequence was (see table 1): Step a) ventilate total lung with 100 per cent O_2 and PEEP of 2 torr; Step b) ventilate the LLL with N_2 , 95 per cent, and CO_2 , 5 per cent; Step c) increase rest of the lung PEEP to 10 torr; Step d) increase LLL PEEP to 10 torr; Step e) decrease rest of the lung PEEP to 2 torr; Step f) decrease LLL PEEP to 2 torr; Step g) ventilate total lung with 100 per cent O_2 ; Step h) induce LLL absorption atelectasis by plugging LLL bronchus; Step i) increase rest of the lung PEEP to 10 torr.

Since LLL blood flow (\dot{Q}_{LLL}) changes passively with changes in total pulmonary blood flow (\dot{Q}_t), we express \dot{Q}_{LLL} as a percentage of \dot{Q}_t (\dot{Q}_{LLL}/\dot{Q}_t). Both P_{pa} and P_{la} are expressed as transmural pressures (intraluminal pressure relative to atmosphere minus

pleural pressure relative to atmosphere). All results are reported as means \pm standard errors, and were analyzed by paired t analysis, with $P < 0.01$ considered significant.

Results

COMPARISON OF GROUP I WITH GROUP II DURING CONTROL CONDITIONS (STEP A)

The initial P_{la} and \dot{Q}_t were significantly greater and \dot{Q}_{LLL}/\dot{Q}_t was significantly less in Group II compared with Group I (table 1). The calculated pulmonary vascular resistances of the LLL were 563 ± 64 and 562 ± 67 dynes·sec·cm⁻⁵ in Group I and Group II, respectively. The calculated total pulmonary vascular resistances were 241 ± 35 and 102 ± 21 dynes·sec·cm⁻⁵ in Group I and Group II, respectively.

COMPARISON OF GROUP I WITH GROUP II DURING HYPOXIC CONDITION

When the LLL was made hypoxic by ventilation with N_2 (Step b), the decreases in \dot{Q}_{LLL}/\dot{Q}_t were 49 per cent for Group I and 40 per cent for Group II (table 1, fig. 1). The difference between the two groups was not significant. There was no significant change in transmural vascular pressure (P_{pa} or P_{la}) in either group. After the LLL was made atelectatic (Step h) both groups experienced decreases in

TABLE 1. Summary of Results for Both Open-chest and Closed-chest Preparations at Each Method Step, Expressed as Mean \pm SE

	Left Lower Lobe (LLL) Ventilation	PEEP (torr)		Open-chest Results (Group I)					Closed-chest Results (Group II)				
		LLL	Rest of Lung	P_{pl} (torr)	P_{pa}^* (torr)	P_{la}^* (torr)	\dot{Q}_t (ml/min)	$\dot{Q}_{LLL}/\dot{Q}_t^\dagger$ (Per Cent)	P_{pl} (torr)	P_{pa}^* (torr)	P_{la}^* (torr)	\dot{Q}_t (ml/min)	$\dot{Q}_{LLL}/\dot{Q}_t^\dagger$ (Per Cent)
Step a	O_2 , 100 per cent	2	2	0	11.9 ± 0.8	4.5 ± 0.8	2460 ± 260	22.8 ± 3.0	-3.6 ± 0.8	14.4 ± 0.8	8.9 ± 0.8	4310 ± 360	13.1 ± 1.6
Step b	N_2 , 95 per cent CO_2 , 5 per cent	2	2	0	12.5 ± 0.2	4.7 ± 0.9	2490 ± 240	11.6 ± 1.7	-3.1 ± 0.5	15.0 ± 1.4	8.0 ± 0.5	4180 ± 290	7.9 ± 1.0
Step c	N_2 , 95 per cent CO_2 , 5 per cent	2	10	0	18.4 ± 1.2	7.3 ± 0.9	1720 ± 270	35.3 ± 7.0	+1.2 ± 1.0	15.6 ± 2.1	7.9 ± 1.2	2910 ± 330	10.7 ± 0.9
Step d	N_2 , 95 per cent CO_2 , 5 per cent	10	10	0	19.5 ± 1.0	7.8 ± 1.2	1730 ± 270	18.6 ± 4.2	+1.0 ± 1.3	17.6 ± 1.5	8.5 ± 1.4	3030 ± 290	8.2 ± 0.5
Step e	N_2 , 95 per cent CO_2 , 5 per cent	10	2	0	13.2 ± 1.4	5.2 ± 0.7	2480 ± 520	6.7 ± 1.1	-3.0 ± 0.9	14.9 ± 1.7	7.5 ± 1.0	4150 ± 293	5.0 ± 0.4
Step g	O_2 , 100 per cent	2	2	0	12.0 ± 1.0	5.5 ± 0.8	2600 ± 450	24.1 ± 2.4	-3.0 ± 0.9	14.1 ± 1.4	6.2 ± 1.1	4290 ± 350	13.9 ± 1.8
Step h	Atelectasis	0	2	0	12.2 ± 1.1	5.4 ± 0.8	2370 ± 300	10.2 ± 1.8	-6.0 ± 1.3	17.6 ± 1.9	9.9 ± 1.7	3960 ± 440	9.5 ± 1.1
Step i	Atelectasis	0	10	0	20.6 ± 1.4	7.4 ± 0.9	1680 ± 240	23.0 ± 5.4	-1.4 ± 1.6	19.1 ± 1.4	11.0 ± 2.0	2690 ± 370	12.3 ± 1.6

* Transmural pressures.

† \dot{Q}_{LLL}/\dot{Q}_t = percentage of the cardiac output perfusing the left lower lobe.

\dot{Q}_{LLL}/\dot{Q}_t , but the extents of this response were significantly different for the two groups. In Group I \dot{Q}_{LLL}/\dot{Q}_t decreased 57 per cent with no significant change in P_{pa} or P_{la} . On the other hand, in Group II \dot{Q}_{LLL}/\dot{Q}_t decreased only 32 per cent during LLL atelectasis, while at the same time transmural vascular pressures increased, primarily because there was a 3-torr decrease in left-lung pleural pressure. Within each group of LLL vasoconstrictor responses were not different between Step b and Step h.

EFFECTS OF PEEP ON LLL HPV

When 10 torr PEEP were added to the rest of the lung during LLL hypoxia (Step c), the increases in \dot{Q}_{LLL}/\dot{Q}_t were dramatic in both groups, but much higher in Group I than in Group II. In Group I transmural P_{pa} and P_{la} were significantly increased above normoxic levels, whereas in Group II transmural P_{pa} and P_{la} were unchanged due to an increase in P_{pl} . \dot{Q}_t decreased significantly in both groups.

When 10 torr PEEP were applied to both the rest of the lung and the LLL (Step c and Step d), \dot{Q}_{LLL}/\dot{Q}_t was significantly increased compared with Step b in Group I only. The difference between Steps b and d were not significant in Group II. Transmural P_{pa} and P_{la} were increased significantly in Group I compared with Step b, but the transmural P_{pa} and P_{la} were unchanged in Group II due to maintenance of a positive P_{pl} .

When 10 torr PEEP were applied only to the hypoxic LLL (Step e), \dot{Q}_{LLL}/\dot{Q}_t was decreased dramatically in both groups, with only small changes in vascular pressures. Return to bilateral normoxia and PEEP 2 torr (Step g) resulted in hemodynamic values similar to those found with Step a.

When 10 torr PEEP were added to the rest of the lung during LLL atelectasis (Step i), \dot{Q}_{LLL}/\dot{Q}_t increased toward normoxic levels in both groups. As seen before, during LLL hypoxic ventilation, the addition of PEEP during LLL atelectasis caused a larger increase in transmural vascular pressures in Group I than in Group II. \dot{Q}_t was decreased significantly in both groups.

Discussion

Our results show that the partitioning of blood flow between a normoxic and a hypoxic compartment is altered by changes in regional and whole-lung PEEP. Before discussion these results, consideration should be given to differences between the open-chested (Group I) dogs and close-chested (Group II) dogs.

Group II had approximately twice the filling pressure and \dot{Q}_t than occurred in Group I. The reason

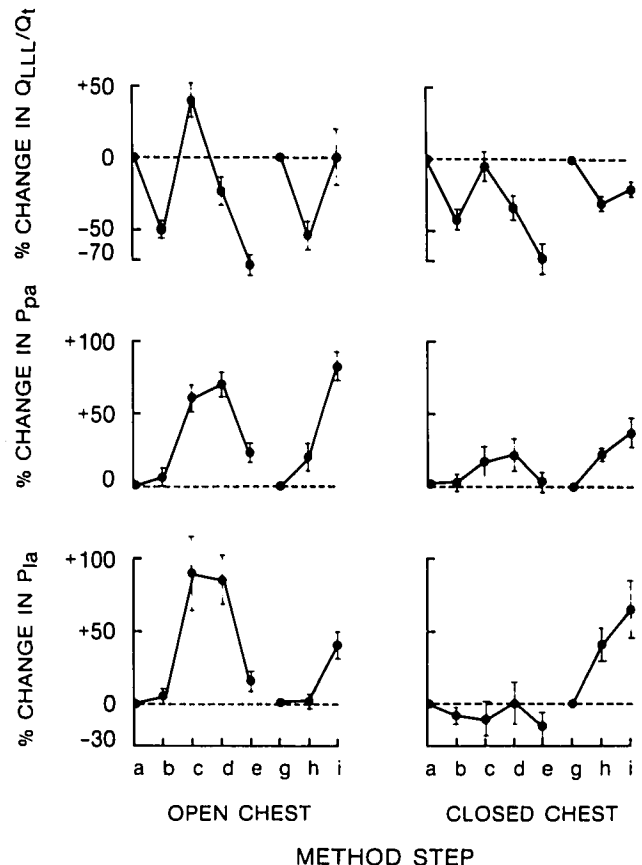


FIG. 1. \dot{Q}_{LLL}/\dot{Q}_t = percentage of the cardiac output perfusing the left lower lobe. In each method step the rest of the lung (RL) other than the left lobe (LLL) was ventilated with 100 per cent O_2 .

Methods steps:

Step a, ventilation of LLL with O_2 ; LLL PEEP = 2 torr, RL PEEP = 2 torr.

Step b, ventilation of LLL with N_2 , 95 per cent, and CO_2 , 5 per cent; LLL PEEP = 2 torr, RL PEEP = 2 torr.

Step c, ventilation of LLL with N_2 , 95 per cent, and CO_2 , 5 per cent; LLL PEEP = 2 torr, RL PEEP = 2 torr.

Step d, ventilation of LLL with N_2 , 95 per cent, and CO_2 , 5 per cent; LLL PEEP = 10 torr, RL PEEP = 10 torr.

Step e, ventilation of LLL with N_2 , 95 per cent, and CO_2 , 5 per cent; LLL PEEP = 10 torr, RL PEEP = 2 torr.

Step g, ventilation of LLL with O_2 ; LLL PEEP = 2 torr, RL PEEP = 2 torr.

Step h, atelectasis of LLL; LLL PEEP = 0 torr, RL PEEP = 2 torr.

Step i, atelectasis of LLL; LLL PEEP = 0 torr, RL PEEP = 10 torr.

for the difference in \dot{Q}_t is in part due to Group II dogs' being larger than those in Group I, and may, in part, be due to the possibility that positive-pressure ventilation caused total pulmonary resistance to be greater in Group I (no chest wall, greater compliance) than in Group II (intact chest wall, less compliant).⁶

For a flow probe to function correctly, it should cause a small constriction of the vessel. Since the same LLL pulmonary-artery flow probe (5 mm) was used in the two groups, the probe must have caused

greater vessel constriction in the larger Group II dogs. Consequently, control \dot{Q}_{LLL}/\dot{Q}_t was less in Group II (13 per cent) than in Group I (23 per cent). Although the difference is significant, we do not view this as a major experimental design defect because we are interested in changes in blood flow rather than absolute values of blood flow.

Comparison of Group I with Group II during hypoxia is not scientifically rigorous, because each animal could not serve as its own control. Nevertheless, we have done this to indicate possible important differences between, and similarities among, the two groups. There was no significant difference between Group I and Group II in the LLL vasoconstriction responses caused by ventilation hypoxia. With the rest of the lung exposed to 100 per cent O_2 and therefore maximally vasodilated, these LLL responses to hypoxia should be considered maximal. However, Group I had a significantly greater LLL vasoconstrictor response to LLL atelectasis (57 per cent) than did Group II (32 per cent). This result is expected in view of the pleural pressure changes we observed and similar previous findings by others.⁷ When a lobe of the lung was made atelectatic in a closed-chest preparation, the retraction of the lung caused regional pleural pressure to become more negative and transmural vascular pressure to increase.⁷ In Group II we found LLL atelectasis caused a 3-torr increase in P_{pl} and 3.5- and 3.7-torr increases in transmural P_{pa} and P_{la} , respectively. Increased transmural pulmonary vascular pressure inhibits hypoxic pulmonary vasoconstriction.³ There was no significant change in P_{pl} or P_{pa} in the animals whose chests were open during LLL atelectasis.

The principal finding of this study is that selective PEEP to the rest of the lung in clinically relevant dosage inhibits LLL HPV. However, the same amount of PEEP had a greater effect where the thorax was open, as compared with closed. There are two possible reasons for this difference. First, with a closed thorax, increases in pleural pressure could buffer or minimize changes in transmural pulmonary vascular pressure caused by rest of the lung PEEP. In Group II, when 10 torr PEEP were added to the rest of the lung, P_{pl} increased by 4.3 torr (43 per cent increase) and by 4.6 torr (46 per cent increase) during N_2 ventilation of the LLL and during LLL atelectasis, respectively. This agrees well with previous findings in normal lungs of 50 per cent transmission of PEEP to P_{pl} .[¶] Thus, rest of the lung PEEP increased

transmural pulmonary vascular pressure significantly more in the animals whose thoraces were open, which opposed LLL HPV to a greater extent.³ Second, it is possible that Group I was initially on a higher pressure-volume curve of the lung than Group II, and therefore had greater increases in vascular resistance when PEEP was applied. Selective PEEP to the hypoxic LLL (Step e) further decreased \dot{Q}_{LLL}/\dot{Q}_t (Group I more than Group II) by predictably and selectively increasing LLL pulmonary vascular resistance. Different initial positions along different pressure-volume curves of the lung between the two groups are compatible with this similarity between findings in the two groups.

Differences in initial lung volumes do not explain the effects of whole-lung PEEP on LLL HPV. Inhibition of lobar HPV by vascular pressure does provide an explanation for the increase in \dot{Q}_{LLL}/\dot{Q}_t during LLL hypoxic ventilation when 10 torr PEEP were added to both the rest of the lung and the LLL (whole-lung PEEP) in Group I. Normal pulmonary vessels markedly decrease their vascular resistance as pulmonary arterial pressure is increased to 16–17 torr, but only slightly decrease their vascular resistance at pressures above this level.^{6,8} However, actively constricted pulmonary vessels continue to decrease their pulmonary vascular resistance at pulmonary arterial pressures much higher than the limit at which normal vessels are no longer decreasing their resistance.^{6,9} In Group I the increase in P_{pa} from a control of 11.9 ± 0.8 torr to 19.5 ± 1.0 torr when 10 torr PEEP were added to the whole lung preferentially decreased pulmonary vascular resistance in the actively constricted vessels of the LLL and increased \dot{Q}_{LLL}/\dot{Q}_t . In Group II P_{pl} changes prevented a significant increase in P_{pa} following whole-lung PEEP and \dot{Q}_{LLL}/\dot{Q}_t did not increase.

Our experiment has ignored the usual increase in regional functional residual capacity caused by PEEP. However, the present findings have numerous potential clinical counterparts. First, these findings indicate that if low- \dot{V}/\dot{Q} regions (Step c) and atelectatic regions (Step i) persist following the application of 10 torr PEEP, an increase in transpulmonary shunt would occur. Second, these findings suggest that a localized increase in airway pressure in a low- \dot{V}/\dot{Q} region (Step e), such as might exist behind a one-way ball-valve foreign body or mucous plug,¹⁰ would result in a decrease in transpulmonary shunt. Thus, HPV and an increase in airway pressure can additively increase regional pulmonary vascular resistance. Third, when 10 torr PEEP are transmitted to the whole lung equally, including regions of low \dot{V}/\dot{Q} (Step d), our results from the more clinically relevant

¶ Chapin JC, Downs JB, Douglas ME, et al: Lung Expansion and Pressure Transmission with Positive End Expiratory Pressure (abstr), American Society of Anesthesiologists, Annual Meeting, 1975, pp 103–104.

closed-chest preparation suggest transpulmonary shunt would remain unchanged. We conclude that the effect of PEEP on abnormal lung is a summation of beneficial and deleterious regional effects of PEEP in low- \dot{V}/\dot{Q} atelectatic and undiseased regions of lung.

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