The effect of patient position during trauma surgery on fat embolism syndrome: An experimental study

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Abstract

Background: The aim of this study was to compare the effect of supine versus lateral position on clinical signs of fat embolism during orthopedic trauma surgery. Dogs served as the current study model, which could be extended and/or serve as a basis for future *in vivo* studies on humans. It was hypothesized that there would be an effect of position on clinical signs of fat embolism syndrome in a dog model.

Materials and Methods: 12 dogs were assigned to supine (*n* = 6) and lateral (*n* = 6) position groups. Airway pressures, heart rate, blood pressure, cardiac output, pulmonary artery pressure, pulmonary artery wedge pressure, right atrial pressure, arterial and venous blood gases, white blood count, platelet count and neutrophil count were obtained. Dogs were then subjected to pulmonary contusion in three areas of one lung. Fat embolism was generated by reaming one femur and tibia, followed by pressurization of the canal.

Results: No difference was found in any parameters measured between supine and lateral positions at any time (0.126 < *P* < 0.856).

Conclusions: The position of trauma patients undergoing reamed intramedullary nailing did not alter the presentation of the features of the lung secondary to fat embolism.

Key words: Canine, fat embolism syndrome, position, trauma surgery

Introduction

Fat embolism syndrome (FES) can lead to morbidity in trauma patients undergoing reamed intramedullary nailing of long bone fractures.[1-14] Embolization of fat is common in long bone fractures, however, FES rarely manifests. There is an additive effect of FES and pulmonary trauma which can cause pulmonary injury, e.g. adult respiratory distress syndrome (ARDS), whereas FES itself can worsen the effects of pulmonary contusion and lead to further pulmonary injury, e.g. ARDS.[15]

FES may have a mechanical cause with fat being lodged in the end capillaries and arterioles thus blocking blood flow to parts of the lung.[16-18] An immunologic basis for fat embolism has also been postulated.[19] Fat lodged in the lung parenchyma activates an immunologic response leading to damage to the lung parenchyma and an acute respiratory distress syndrome ensues.[16,20-22] The exact mediators and mechanism of this are unknown; however, one can utilize surrogate markers of inflammation to study its severity.

FES has an effect on patient physiology.[21,23,24] It is always accompanied by a drop in blood pressure (BP) and an increase in the pulmonary wedge pressure. It also alters gas exchange in the lungs leading to a rise in partial pressure of carbon dioxide ($PaCO_2$) and a drop in the partial pressure of oxygen (PaO_2) in the arterial blood. The change in these parameters can be used to indicate FES severity.

Patients undergoing reamed intramedullary nailing can be positioned in supine or lateral positions. Left versus right lateral position of trauma patients influence pulmonary volume and ventilation-perfusion relationships.[25,26] By

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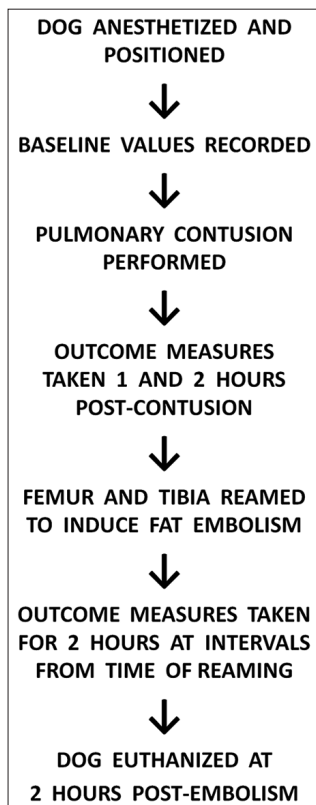E-mail: zderor@smh.ca

placing the contused lung in the dependent position, blood flow can be preferentially diverted to the injured lung. Position also affects autoregulation of blood flow. The interaction between these effects influences FES severity. However, the effect of position on FES severity has not been investigated systematically in comparing supine versus lateral orientation during orthopedic trauma surgery.

In this study, the effect of position on clinical presentations of FES was evaluated in a dog model. Changes were measured in the physiologic parameters in supine and lateral positions undergoing fat embolism and lung contusion. Immunologic response was noted by measuring the levels of markers of inflammation and platelet (PLT) activation. It was hypothesized that there would be an effect of position on clinical presentations of FES in a dog model.

MATERIALS AND METHODS

Specimen selection and preparation

12 mongrel dogs (weight range 25-35 kg, age range 2-4 years) were used after approval of the Institutional Ethics Board in accordance with national laws. Dogs were randomly assigned to the supine position or the lateral position group [Figure 1]. Group size was determined based on the authors' financial constraints for this study, the practical limitations

DOG ANESTHETIZED AND POSITIONED

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BASELINE VALUES RECORDED

↓

PULMONARY CONTUSION PERFORMED

↓

OUTCOME MEASURES TAKEN 1 AND 2 HOURS POST-CONTUSION

↓

FEMUR AND TIBIA REAMED TO INDUCE FAT EMBOLISM

↓

OUTCOME MEASURES TAKEN FOR 2 HOURS AT INTERVALS FROM TIME OF REAMING

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DOG EUTHANIZED AT 2 HOURS POST-EMBOLISM

Figure 1: Flow chart of experimental procedure. Protocol followed from the time of dog anesthesia to euthanasia

of animal care provided by the authors' institution and the methodology of the authors' prior dog studies.[11,12,27,28] A standard anesthetic protocol was used with a respirator and paralyzing anesthesia.

Outcome parameters

An arterial line was inserted by ligating and cannulating the right carotid artery in the neck of each dog. The left internal jugular vein was ligated and cannulated and a pulmonary artery catheter was inserted with three ports.

To study the distribution of pulmonary blood flow, 1 million microspheres (10 µm diameter) were injected into the right atrium of each dog at baseline, with pulmonary contusion and after fat embolism. The microspheres were of a different color and hence, could be distinguished in postmortem lung tissue by color photometry. A blood sample was drawn at 7 ml/min starting 15 s prior to injection to 2 min after the spheres were injected. The concentration of the spheres reflected their rate of flow in the pulmonary vasculature.

The physiologic parameters that were measured presently included heart rate (HR), BP, respiratory rate, central venous pressure, pulmonary artery pressure, pulmonary wedge pressure, cardiac output (CO), arterial and venous partial pressures of oxygen and carbon dioxide. These measurements were taken at baseline, at 1 h and 2 h after lung contusion and at 1 min, 5 min, 15 min, 30 min, 1 h and 2 h after fat embolism.

The immunologic response to lung contusion and fat embolism was studied by using markers of inflammation and PLT activation.[29,30] Blood samples were obtained at baseline, at pulmonary contusion and after fat embolism was induced, as described above for physiological measurements. For flow cytometric evaluation of PLT and neutrophil (NEU) activation, blood samples were stained with fluorescence-conjugated antibodies against CD62P and CD11/18, respectively. PLTs and NEUs were identified from other cells by characteristic size, fluorescence and light scatter properties. White cell count, PLT count and hematocrit (HCT) in each of the blood samples were also measured.

Operative procedure

After induction of anesthesia, each dog was positioned in the supine or lateral position. In the lateral position, the left side was dependent. The carotid artery and internal jugular vein were isolated in the right-side of the neck of the animal. The artery and the vein were then ligated and cannulated. BP was monitored through the arterial catheter while a pulmonary artery catheter was inserted in the internal jugular vein. Baseline measurements of physiologic parameters, blood gases, blood counts and CD62P and CD11/18 levels were obtained. Blue microspheres were injected[31] and a right

atrial blood sample was obtained to determine the flow rate of the spheres in the pulmonary artery.

A right-sided thoracotomy was then performed in each dog and the seventh rib was resected. The right lung was exposed and then deflated for a total of 2 min. An area in each of the three lobes of the right lung was marked with a suture stitch. Using a similar approach from a prior study in a canine model, pulmonary contusion was performed in each of these three areas by using two metal discs with an interposed force transducer for measurement of applied pressure.[28] A compression force of 250 N was applied for 30 s in each of the three areas. This simulated pulmonary contusion in the trauma patient. Lung deflation allowed for compression, i.e., contusion, with the force clamp. A chest tube was then placed in the right chest and attached to an underwater seal. The thoracotomy was closed and the right lung was inflated. At 1 h after closure, a set of physiologic measurements was obtained. At 2 h after the closure of thoracotomy, another set of physiologic measurements was obtained as well as cell counts and blood gases. At the 2 h mark, pink microspheres were injected into the pulmonary artery and a blood sample was obtained from the right atrium to determine the rate of flow of the microspheres in the pulmonary vessels. The microsphere method has been used previously.[31] Fat embolism in the dog was then induced.

The right knee of the dog was exposed and the femur and tibia were reamed with standard reamers 9 mm and 5 mm, respectively. Poly methyl methacrylate was injected into the femoral and tibial canals and pressurized by inserting a 4 mm Steinman pin into each of the femoral and tibial canals. The time frame for nailing using the pins was based on the approximate 2 h time frame within which long bone trauma is commonly treated in the authors' clinical practice. It was meant to simulate long bone nailing 2 h from the time of initial trauma, including the pulmonary contusion. Clear evidence of fat embolism was seen in each experiment with a drop in arterial pressure and a rise in wedge pressure with cement pressurization. The knee wound was then closed. Several measurements of physiologic parameters and blood gases were taken after induction of fat embolism. These were obtained at 5 min, 15 min, 30 min, 1 h and 2 h after fat embolization. At the 2 h mark, blood samples were obtained for cell counts, CD62P and CD11/18. Finally, red microspheres were injected into the pulmonary artery[31] and a blood sample was obtained from the right atrium to determine the rate of flow of the microspheres in the pulmonary vessels.

After obtaining physiologic measurements, blood samples and injecting red microspheres 2 h after fat embolization, dogs were euthanized using sodium pentobarbital.

Postmortem examination

All lung tissue samples were used for microsphere blood flow evaluation. Postmortem, bilateral thoracotomy was performed in each dog and three lung samples were taken from each of the lungs. On the right-side, the samples were taken from the contused areas, whereas on the left side the samples were taken from three equivalent areas. A sample of cardiac tissue was taken as control from each dog. All samples were weighed and sent to the manufacturer of the microspheres for quantification. By using the concentration of microspheres from the blood sample obtained at the time of injection, the regional blood flow to the left and right lung was determined. The microsphere technique is a validated method for determining regional pulmonary blood flow.

In this study, one dog died in the lateral position at the time of fat embolism induction. This dog was excluded from the study, since it had preexisting congestive heart failure, which was detected through hemodynamic monitoring during and after induction of anesthetic. The added stress of pulmonary embolism caused death. This was consistent with present hemodynamic monitor findings during the procedure. It was felt that this dog was probably not a good subject for the study due to preexisting heart failure and hence, this dog's exclusion would not bias the study.

Statistical analysis

Analysis was carried out using a P value of 0.05 to define significance. For the physiologic parameters and blood counts, a two-way analysis of variance (ANOVA) compared the two groups at different time points for each measurement. If the F value was significant, then least square means were used with the Bonferroni correction as a *post hoc* test. For CD62P and CD11/18 markers, the levels after contusion and fat embolization were compared versus baseline values within each group. The levels of these markers between the two groups were also compared. The blood flow data from the analysis of microsphere distribution and flow was used to obtain a relative blood flow measurement for each dog. This relative blood flow value was computed as blood flow to the contused lung/blood flow to the uncontused lung. The relative blood flow for each group after contusion and fat embolization was compared with the baseline to determine if there was a change with time. Moreover, relative blood flow was also compared between the two groups using two-way ANOVA.

RESULTS

The analysis of physiologic parameters and blood counts revealed no statistically significant difference between the supine and the lateral groups in any of the measurements at any time point [Tables 1 and 2]. Specifically, statistical analysis showed no differences ($0.126 > P > 0.856$) for

Table 1: Physiological parameter measurements

Parameter	Side	t=0	1 h pc	2 h pc	1 min pe	5 min pe	15 min pe	30 min pe	1 h pe	2 h pe
BP (mmHg)	Lat	79.33	82.50	85.17	71.00	86.17	84.00	83.33	82.00	84.00
		11.38	14.36	10.80	22.03	16.19	11.59	10.78	16.57	11.37
	Sup	102.00	103.33	109.33	59.00	95.17	99.33	82.50	104.33	100.33
		10.20	11.89	10.65	16.64	17.33	21.92	38.62	16.52	17.93
HR (beats/min)	Lat	73.83	94.50	93.83	118.40	111.50	107.67	104.67	104.83	107.33
		15.18	44.32	9.70	11.80	18.76	20.77	18.25	18.50	14.94
	Sup	103.83	121.67	109.17	116.33	117.33	112.00	97.50	118.50	118.50
		15.75	9.03	8.52	17.06	16.82	15.03	44.64	23.25	29.17
RR (breaths/min)	Lat	15.00	15.00	16.33	15.00	15.00	15.00	15.00	15.00	15.00
		4.86	4.86	4.97	4.86	4.86	4.86	4.86	4.86	4.86
	Sup	18.50	18.50	18.50	18.50	18.50	18.50	18.50	18.50	18.50
		1.22	1.22	1.22	1.22	1.22	1.22	1.22	1.22	1.22
PAP (mmHg)	Lat	13.00	13.67	14.67	26.20	24.00	22.67	22.00	21.17	21.67
		1.10	2.66	1.75	4.49	2.10	2.07	2.10	1.72	1.51
	Sup	14.83	16.33	17.67	27.83	24.17	24.00	23.83	24.00	25.00
		4.26	5.09	5.72	8.06	6.34	6.20	7.25	8.02	10.14
PAOP (mmHg)	Lat	7.67	7.50	7.67	7.00	7.83	7.83	8.00	7.80	8.00
		1.37	1.05	1.03	1.00	1.47	0.98	1.26	1.30	1.10
	Sup	9.00	10.00	9.50	8.67	10.50	10.50	10.83	9.00	9.00
		3.16	5.51	2.59	1.53	4.14	3.94	4.62	1.26	1.41
RAP (mmHg)	Lat	4.67	4.83	4.83	6.33	5.83	5.17	4.50	5.20	4.67
		2.07	1.72	1.72	2.08	1.83	1.47	1.05	1.10	1.37
	Sup	6.00	5.83	6.67	6.33	7.17	7.17	6.83	6.50	6.83
		1.41	1.60	1.97	1.53	1.83	1.47	1.17	0.84	1.47
CO (L/min)	Lat	3.91	4.67	4.86	4.90	4.75	4.93	4.68	4.36	3.91
		1.08	1.00	1.13	1.32	1.43	1.42	1.22	1.23	1.08
	Sup	3.77	4.40	4.06	4.10	4.03	3.83	4.20	3.67	3.77
		0.67	1.01	1.19	1.15	0.72	0.76	1.01	0.62	0.67
PvO_2 (mmHg)	Lat	49.30	55.77	52.33	-	48.25	48.72	50.00	47.93	46.68
		8.54	9.94	3.97	-	1.68	7.30	5.76	4.26	4.66
	Sup	50.27	54.75	50.57	-	45.87	46.23	47.58	47.70	46.65
		4.97	0.88	4.77	-	7.91	5.29	5.28	9.16	10.37
$PaCO_2$ (mmHg)	Lat	38.58	43.53	40.80	-	45.80	47.05	47.68	46.75	47.25
		5.30	2.97	3.21	-	3.69	4.15	4.17	6.13	5.56
	Sup	40.50	39.55	42.40	-	44.47	44.57	43.82	45.45	46.60
		3.62	3.74	3.02	-	3.59	5.30	5.55	3.99	7.39
PaO_2 (mmHg)	Lat	260.23	167.32	193.72	-	119.72	117.83	126.92	112.08	124.55
		12.55	44.49	37.87	-	47.78	50.99	50.66	47.68	52.01
	Sup	264.97	174.73	179.02	-	89.50	94.18	96.35	103.58	94.82
		21.13	22.64	37.28	-	27.01	24.44	31.46	44.57	30.53

Top number represents mean, whereas bottom number indicates one standard deviation. No statistical difference between lateral and supine groups was noted at any time point ($P>0.05$), Lat = Lateral position, Sup = Supine position, pc = Post-contusion, pe = Post-embolism, t = Time point, BP = Blood pressure, HR = Heart rate, RR = Respiration rate, PAP = Pulmonary artery pressure, PAOP = Pulmonary artery occlusion pressure, RAP = Right arterial pressure, CO = Cardiac output, PvO_2 = Mixed venous oxygen pressure, $PaCO_2$ = Partial pressure of carbon dioxide in arterial blood, PaO_2 = Partial pressure of oxygen in arterial blood. The 1 min data were not used in the analysis for any of the dogs in either group

BP, HR, respiration rate, pulmonary arterial pressure, pulmonary arterial occlusion pressure, right arterial pressure, CO, mixed venous oxygen pressure, $PaCO_2$, PaO_2, white blood cells (WBCs), PLTs, NEUs, hemoglobin, HCT and mean PLT volume.

BP, pulmonary arterial wedge pressure and PaO_2 data showed no statistically significant differences between lateral and supine groups [Figures 2-4]. Although the relative blood flow also showed no difference between positions, a trend of increasing blood flow to the contused lung was seen in the lateral group after pulmonary contusion and fat embolism [Figure 5]. Although this trend was not shown to be statistically significant, the trend of increasing blood flow was consistent with the original study hypothesis that there would be an influence of position on clinical signs of FES in a canine model. Blood flow to the contused and non-contused lungs in the supine group remained relatively unchanged.

Following pulmonary contusion and fat embolism, there was no significant difference ($P > 0.05$) for lateral versus supine in CD62P (PLT), which showed an increase by

a factor of 1.40 ± 0.20 versus 1.25 ± 0.25. Similarly, there was no difference ($P > 0.05$) for lateral versus supine in CD11/18 (NEU), which showed an increase by a factor of 0.90 ± 0.02 versus 1.01 ± 0.10. The lateral position group displayed significant changes in CD62P and CD11/18 percent expression compared to baseline ($P < 0.05$). CD11/18 decreased compared

to baseline in the lateral position, being accompanied by a significant decrease in WBC counts. All these are surrogate markers of inflammation, whose rise indicates that the pulmonary fat embolism-incited systemic inflammation occurred in dogs in the lateral position, but not in dogs in the supine position. Both groups showed significant drops in PLT counts, without any significant changes in HCT levels.

Table 2: Blood parameters

Parameter	Side	Baseline	2 h pc	2 h pe
WBC (10^9/L)	Lat	8.66	5.74	4.47
		3.96	2.90	3.01
	Sup	6.40	4.15	3.95
		2.63	1.86	1.06
PLT (10^9/L)	Lat	209.88	169.92	161.44
		35.41	80.00	26.89
	Sup	183.53	164.43	148.87
		56.89	54.09	46.55
NEU (%)	Lat	5.63	2.87	2.35
		6.54	4.03	3.48
	Sup	2.82	1.25	0.66
		3.67	1.83	1.54
HG (g/L)	Lat	122.83	124.95	134.24
		6.15	8.73	17.12
	Sup	118.47	128.72	124.45
		14.03	20.84	19.15
HCT	Lat	0.34	0.35	0.37
		0.03	0.03	0.05
	Sup	0.33	0.37	0.35
		0.05	0.06	0.06
MPV (10^{-15} L)	Lat	8.65	8.78	8.70
		1.05	0.97	0.60
	Sup	8.43	8.17	8.15
		1.33	1.07	1.09

Top number represents mean, whereas bottom number indicates one standard deviation. No statistical difference between lateral and supine groups was noted at any time point ($P>0.05$), Lat = Lateral position, Sup = Supine position, WBC = White blood cells, PLT = Platelets, NEU = Neutrophils, HG = Hemoglobin, HCT = Hematocrit, MPV = Mean platelet volume, pc = Post-contusion, pe = Post-embolism

DISCUSSION

Physiologic data showed no difference between supine and lateral groups. Changes that occur in physiologic parameters with induction of fat embolism are well-described.[1-14,16-19] A drop in mean arterial BP and CO as well as a rise in pulmonary capillary wedge pressure, are commonly observed. A rise in $PaCO_2$ and a fall in PaO_2 also accompany fat embolism. These changes were seen in our series, but without a statistical difference. This indicates that there was no effect on the degree of change in different patient positions. Even so, for polytrauma subject with fractures of the femoral shaft, surgical treatment with reaming and nailing while patients are in the lateral position is not associated with an increased risk of mortality or admission to the intensive care unit.[32]

In the lateral position group, a trend was observed towards increased blood flow to the contused lung with pulmonary contusion and FES induction. This contradicts the notion of autoregulation of pulmonary blood flow, which redirects blood away from injured areas of the lung to uninjured parts in order to match ventilation and perfusion, especially when the normal lung is dependent (down) for patients with unilateral pulmonary disease. Although this is a known phenomenon[25,26] present data indicates the
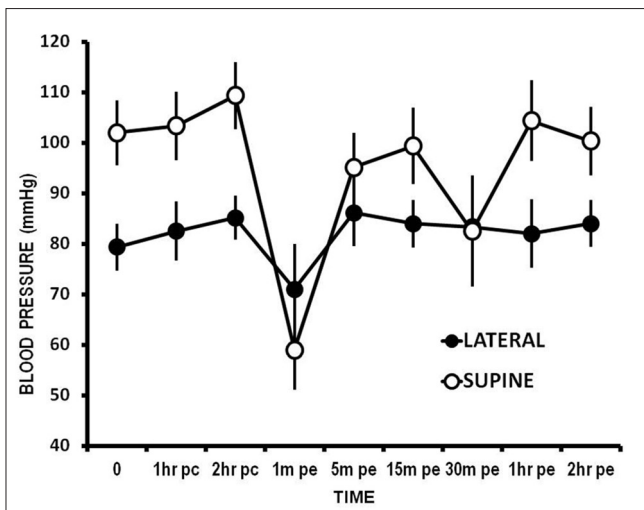
Figure 2: A trend line graph showing blood pressure measurements. The error bars represent one standard error of the mean
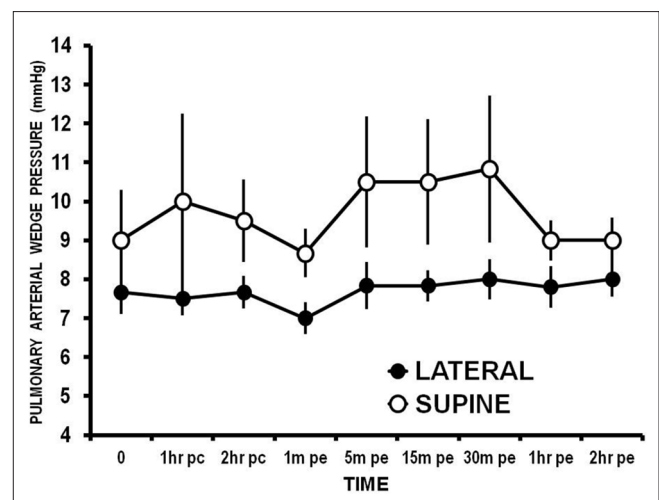
Figure 3: A trend line graph showing pulmonary arterial wedge pressure measurements. The error bars represent one standard error of the mean
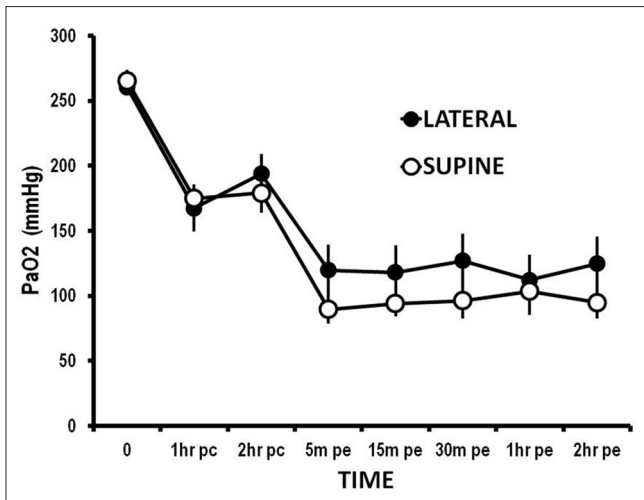
Figure 4: A trend line graph showing PaO$_2$ (arterial oxygen) measurements. The error bars represent one standard error of the mean
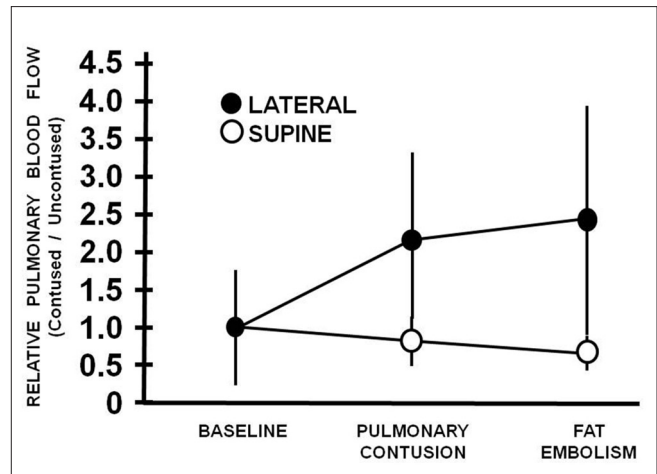

Figure 5: A trend line graph showing relative pulmonary blood flow measurements. The error bars represent one standard error of the mean

opposite, being in agreement with findings indicating that infants have improved ventilation when the affected lung is dependent (down).[31] This observation may be explained by preferential ventilation of the nondependent lung (up), which would lead to subsequent redirection of blood flow to match ventilation and perfusion. This has been noted when ventilating intensive care patients in the right and left lateral decubitus positions.[25,26] Presently, the increase in blood flow after fat embolism was due to more fat being lodged in the dependent (down) lung. This increase was small compared with the larger jump in relative blood flow to the nondependent lung after contusion was applied. This implies that the nondependent contused lung was responsible for more of the gas exchange.

The markers of PLT and NEU activation currently showed significant changes as compared with baseline only in the lateral position group. Pooling of blood to the dependent lung (down) during the lateral position period is gravity-driven, but is not overcome by hypoxemia.[25,26] The addition of pulmonary contusion may render lung tissue more susceptible to overall congestion and activation of PLTs. Furthermore, fat embolism plus pulmonary contusion may lead to pulmonary microvascular sequestration of leukocytes and possible leukopenia. Although PLT and NEU activation currently did not interfere with pulmonary oxygenation in this acute setting, the significance of PLT and NEU activation with lateral position may only become apparent after prolonged rest and may play a role in the development of posttraumatic acute lung injury.

Although no statistical differences between supine and lateral groups were seen in physiologic parameters, gas exchange or pulmonary blood flow, a trend of increased blood flow to the contused nondependent lung was observed. The authors hypothesize that this was due

to ventilation-perfusion matching in the face of better ventilation of the nondependent lung. In the markers of NEU and PLT activation, no difference was noted between supine and lateral groups. However, in the lateral group, there was a nonstatistically significant increase in PLT activation and a decrease in NEU counts. The leukopenia may be a result of pooling of blood and sequestration of NEUs in the dependent lung. Moreover, the increase in activated PLTs may reflect local inflammatory response and increased pulmonary blood flow to the nondependent contused lung.

There were several potential drawbacks in our study. First, although there was no significant difference in measured parameters between the supine and lateral groups, certain patterns may warrant further investigation. Second, a small number of dogs were employed due to logistical animal care issues and budgetary constraints. Third, the drop in arterial pressure in each experiment and the rise in wedge pressure with cement pressurization were taken as clinical presentations of fat embolization; however, this is not conclusive proof. Fourth, current findings may be specific to the study design, namely, a right-sided lung contusion with ipsilateral femoral and tibial reaming with the noninjured lung in the dependent position in the lateral group. Fifth, the 2 h observation from fat embolization to euthanization may have been too short to allow for physiological changes to progress adequately. However, the 2 h timeframe for the study was based on the authors' experience, which showed that this was adequate time for initial physiologic changes to occur. Sixth, no histological analysis of the lungs was performed, since all tissue samples that were taken had to be used for microsphere blood flow evaluation. Seventh, the left versus right lateral position of trauma patients may influence the volume and ventilation-perfusion relationships;[25,26] however, this effect was minimized by placing all dogs with their right-side

facing up. Eighth, although intramedullary pressure was not measured during femoral reaming, nailing, or cementing at present, such procedures may increase intramedullary pressure.[33-36] As such, it may be expected that the current long bones would have experienced the same trend. Finally, the addition of lung contusion could potentially be a confounding variable in this study of position and fat embolization.

To conclude, there were no statistical differences between supine and lateral groups regarding physiologic parameters. This preliminary study can provide a basis for a more comprehensive *in vivo* study on humans to determine whether the supine or the lateral position is superior.

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