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Hemodynamic Effects of Positive End-expiratory Pressure during Continuous Venous Air Embolism in the Dog

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Positive end-expiratory pressure (PEEP) may decrease venous air embolism (VAE) by increasing venous pressure at the incision level. Because PEEP and VAE can both increase pulmonary vascular resistance, it is possible that the application of PEEP during VAE may increase right atrial pressure (RAP) relative to left atrial pressure (LAP) and thereby reverse the normal interatrial pressure gradient, allowing paradoxical air embolism in patients with a probe-patent foramen ovale. We studied atrial pressures during 0, 4, and 8 mmHg PEEP before and during continuous VAE in both supine and upright tilted dogs. Both PEEP and VAE increased pulmonary artery pressure and resistance. Prior to VAE, PEEP increased both RAP and LAP but did not affect the interatrial pressure gradient. VAE alone did not affect RAP, LAP, or the interatrial pressure gradient. Application of PEEP during VAE had similar effects as at baseline, namely an increase in RAP and LAP with no change in the interatrial pressure gradient. Although RAP exceeded LAP more frequently in the upright than in the supine dogs, the effects of PEEP and VAE on atrial pressures were similar in both groups. Our finding that PEEP and VAE did not disproportionately increase RAP compared with LAP is consistent with other studies demonstrating preservation of right ventricular function in situations of increased right ventricular afterload. (Key words: Anesthesia: neurosurgical. Embolism: air, paradoxical. Heart: cardiac output; vascular pressures. Monitoring: left atrial pressure; right atrial pressure. Position: sitting. Ventilation: PEEP.)

VENOUS AIR EMBOLISM (VAE) may occur whenever venous pressure at the incision level is below atmospheric pressure and hence is a major risk for patients undergoing neurosurgical procedures in the sitting position.[1–3] VAE may also occur during head and neck or pelvic procedures if the patient is positioned with the operative site above the right atrium.[4] The frequency and severity of VAE should be decreased by maneuvers that increase venous pressure at the incision level, such as lowering the operative site relative to the right atrium, expanding intravascular volume by fluid administration or the antigravity suit, using positive pressure ventilation, and in the case of the neurosurgical patient, compressing the jugular veins.[2,5–7]‡ Positive end-expiratory pressure (PEEP) has also been recommended as a means to prevent and treat VAE.[2,5,8,9] By increasing intrathoracic pressure, PEEP increases both central and peripheral venous pressures.[10,11] Although PEEP may have adverse cardiovascular effects in selected patients,[10,11] the major concern when PEEP is used in the treatment of VAE is a possible increase in the frequency of paradoxical air embolism. PEEP may increase pulmonary vascular resistance, thereby increasing right ventricular end-diastolic pressure and right atrial pressure (RAP). Under normal conditions, left atrial pressure (LAP) is greater than RAP. If PEEP disproportionately increases RAP compared with LAP, reversal of the normal interatrial pressure gradient may occur. This might allow for direct access of venous air to the systemic circulation (paradoxical air embolism) in some patients, particularly the 25% of adult patients with a probe-patent foramen ovale.[12–15] Although a rare event, the morbidity and mortality from systemic air embolism is markedly increased over VAE. Therefore, reversal of the interatrial pressure gradient with PEEP should constitute a major contraindication to the use of PEEP in patients prone to VAE.

Whereas the cardiovascular effects of PEEP have been studied extensively under normal and abnormal hemodynamic conditions in animals and humans,[10,11] the effects on the interatrial pressure gradient are largely unknown. Because both PEEP and VAE can increase pulmonary vascular resistance, the potential for reversal of the interatrial gradient may be increased when PEEP is applied during VAE. The cardiovascular effects of air embolism alone, including the effects on the interatrial pressure gradient, have been studied, primarily using bolus air embolism models.[16–19] However, a continuous venous air embolism model may be more applicable to the usual clinical situation.[20] The effects of PEEP during air embolism have not previously been investigated. We, therefore, studied the effects of PEEP, the effects of VAE, and the interaction between PEEP and VAE in a canine model. Because the interatrial pressure gradient may vary with body position,[21] we studied both supine and upright tilted dogs.

Methods

Eight adult mongrel dogs, weighing 20–28 kg, were anesthetized with sodium pentobarbital, 30 mg/kg iv, intubated with a cuffed endotracheal tube, and mechanically ventilated with oxygen at a tidal volume of 15 ml/kg and a rate adjusted to maintain arterial blood carbon dioxide tension at 35–40 mmHg. Anesthesia was maintained by a continuous intravenous infusion of sodium pentobarbital at a rate of 7.5 $mg \cdot kg^{-1} \cdot h^{-1}$. Systemic arterial, inferior

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vena caval, and left atrial catheters were inserted by femoral cutdown. The left atrial catheter was inserted into the femoral artery and advanced retrograde into the left atrium using fluoroscopy and/or pressure waveform analysis. A triple-lumen, thermistor-tipped pulmonary artery catheter was inserted *via* the right external jugular vein. Four of the dogs were then tilted upright to a 30° angle by elevating the head of the table; the other four dogs remained horizontal in the supine position.

Following an additional hour for stabilization, baseline hemodynamic measurements were obtained at each of three levels (0, 4, and 8 mmHg) of PEEP; the order was randomized and measurements were obtained after 5 min at each level. Hemodynamic measurements included mean systemic arterial pressure (SAP), RAP, mean pulmonary arterial pressure (PAP), LAP, and cardiac output (CO). Transducers were zeroed at right heart level and recalibrated before each set of measurements. CO was recorded as the mean of three determinations by thermodilution technique, each using 10 ml of iced normal saline; the Edwards Laboratories 9520A Cardiac Output® Computer was used. RAP was measured from the proximal port of the pulmonary artery catheter. Cardiac index, systemic vascular resistance index (SVRI), and pulmonary vascular resistance index (PVRI) were calculated by standard formulae. The level of PEEP was regulated by placing an appropriate length of expiratory limb tubing under water; the level of PEEP was confirmed by continuous measurement of airway pressure from an orifice near the distal end of the endotracheal tube.

Following baseline measurements at each of the three levels of PEEP, VAE was begun at a rate of 0.1 $ml \cdot kg^{-1} \cdot min^{-1}$ through the inferior vena caval catheter using an infusion pump. The level of PEEP was changed every 5 min so that each of the three levels of PEEP occurred during each 15-min period; the order within each 15-min period was randomized. Hemodynamic data were obtained during the last minute of each level of PEEP. Following 1 h of VAE (four 15-min periods), the rate of VAE was increased to 0.2 $ml \cdot kg^{-1} \cdot min^{-1}$. One 15-min period of data collection (*i.e.*, three levels of PEEP) was obtained during this higher rate of VAE. The protocol was concluded at that point after initial experiments in two dogs resulted in severe hypotension (SAP < 50 mmHg) during a second 15-min period at this rate.

Statistics

Data were combined over 15-min periods so that one set of measurements was obtained at each level of PEEP during each 15-min period in each dog. Each hemodynamic variable (*e.g.*, LAP) was then analyzed by a three-factor, mixed-design analysis of variance with repeated measures on two factors (position × level of PEEP × 15-min period) with $P < 0.05$ considered significant.[22] Frequency data were analyzed by Chi-square test using Yates' correction.

Results

LAP was higher in the supine than in the upright dogs both at baseline and throughout the experiment ($P < 0.001$; table 1). PEEP increased LAP both at baseline and throughout the course of VAE ($P < 0.001$): the higher level of PEEP (8 mmHg) resulted in a greater increase in LAP. There was no effect of VAE on LAP and there was no interaction between PEEP and VAE.

RAP was higher in the supine than in the upright dogs ($P < 0.01$). PEEP increased RAP both at baseline and throughout the course of VAE ($P < 0.001$); the higher level of PEEP (8 mmHg) resulted in a greater increase in RAP. There was no effect of VAE on RAP and there was no interaction between PEEP and VAE.

The interatrial pressure gradient, LAP − RAP, was negative more frequently in the upright group (60%) than in the supine group (19%; $P < 0.01$). PEEP did not affect the interatrial gradient either at baseline or during the course of VAE. The change in interatrial gradient that occurred with 4 or 8 mmHg PEEP compared with no PEEP is presented in figure 1 (supine and upright groups combined); the average 95% confidence limits for the change in interatrial pressure gradient with 4 mmHg PEEP were −0.99 to 1.82 mmHg and with 8 mmHg PEEP were −0.81 to 1.79 mmHg. The frequency of a negative interatrial gradient was 59% with no PEEP, 33% with 4 mmHg PEEP, and 33% with 8 mmHg PEEP ($P > 0.05$). VAE did not affect LAP − RAP, consistent with the lack of effect of VAE on both LAP and RAP. There was no interaction between PEEP, VAE, and position.

PAP was higher in the supine than in the upright group, both at baseline and throughout the experiment ($P < 0.01$, table 2). VAE markedly increased PAP ($P < 0.001$); the higher rate of VAE produced the greater increase in PAP. This rate of VAE increased PAP 227% over baseline (no PEEP data with both groups combined). There was a significant interaction between PEEP and VAE ($P < 0.01$) such that PEEP increased PAP at baseline but not during VAE.

PVRI did not differ significantly between the supine and upright groups. PEEP increased PVRI throughout the experiment ($P < 0.01$); in terms of per cent increase, this effect was most pronounced at baseline. VAE markedly increased PVRI ($P < 0.001$) and the higher rate of VAE resulted in the greater increase. At this rate of VAE, PVRI was increased 278% over control (no PEEP data with both groups combined). There was no significant interaction between PEEP and VAE.

Cardiac index tended to be lower in the upright than in the supine group ($P < 0.10$). PEEP decreased cardiac index at baseline and throughout the experiment (*P*

TABLE 1. Effects of Position, PEEP, and Venous Air Embolism on Left Atrial Pressure, Right Atrial Pressure, and the Interatrial Pressure Gradient

Variable	Position	PEEP	Baseline	Time of Air Embolism (min) 0–15	15–30	30–45	45–60	60–75
LAP	Supine	0	4.8 ± 0.2	4.5 ± 0.3	5.5 ± 0.3	5.2 ± 0.6	5.2 ± 0.5	5.2 ± 0.2
		4	6.5 ± 0.3*	7.5 ± 0.5*	6.8 ± 0.5*	6.2 ± 0.2*	6.8 ± 0.5*	7.0 ± 0.4*
		8	8.0 ± 0.4*	8.5 ± 0.6*	8.2 ± 0.6*	8.0 ± 0.4*	8.2 ± 0.2*	8.8 ± 0.5*
LAP	Upright	0	−2.0 ± 0.7†	−2.5 ± 0.3†	−2.2 ± 0.2†	−1.5 ± 0.9†	−2.2 ± 0.2†	−2.0 ± 0.4†
		4	0.0 ± 0.0*,†	0.0 ± 0.0*,†	−0.2 ± 0.2*,†	0.0 ± 0.4*,†	0.2 ± 0.2*,†	0.0 ± 0.0*,†
		8	0.8 ± 0.5*,†	0.0 ± 0.0*,†	0.0 ± 0.4*,†	1.0 ± 0.4*,†	0.2 ± 0.2*,†	1.2 ± 0.5*,†
RAP	Supine	0	3.0 ± 0.7	3.5 ± 1.0	4.5 ± 1.2	5.0 ± 0.7	3.8 ± 0.6	4.2 ± 1.1
		4	5.5 ± 1.3*	6.2 ± 1.4*	4.8 ± 1.1	6.0 ± 1.2	4.8 ± 0.8	6.2 ± 1.0*
		8	7.0 ± 1.5*	6.8 ± 1.3*	6.2 ± 0.5*	6.5 ± 1.0*	7.5 ± 0.3*	7.5 ± 0.9*
RAP	Upright	0	1.2 ± 1.1	0.8 ± 1.1‡	0.0 ± 1.4†	−0.2 ± 1.2†	0.0 ± 0.8‡	−1.2 ± 1.0†
		4	2.0 ± 2.0‡	1.2 ± 0.9†	1.5 ± 0.9*,‡	0.0 ± 0.7†	0.2 ± 0.6†	−0.2 ± 0.5†
		8	1.5 ± 1.7†	1.8 ± 1.0†	1.8 ± 0.8*,†	1.8 ± 1.0*,†	0.8 ± 0.9†	1.2 ± 0.5*,†
LAP − RAP	Supine	0	1.8 ± 0.8	1.0 ± 1.2	1.0 ± 1.6	0.2 ± 1.3	1.5 ± 1.0	1.0 ± 1.4
		4	1.0 ± 1.1	1.2 ± 1.8	2.0 ± 1.5	0.2 ± 1.4	2.0 ± 1.1	0.8 ± 0.5
		8	1.0 ± 1.3	1.8 ± 1.5	2.0 ± 1.0	1.5 ± 1.3	0.8 ± 0.5	1.2 ± 1.2
LAP − RAP	Upright	0	−3.2 ± 1.4†	−3.2 ± 0.9‡	−2.2 ± 1.3‡	−1.8 ± 0.9	−2.2 ± 1.0‡	−0.8 ± 1.2
		4	−2.0 ± 2.0	−1.2 ± 0.9	−1.8 ± 0.9‡	0.0 ± 0.7	0.0 ± 0.7	0.2 ± 0.5
		8	−0.8 ± 1.5	−1.8 ± 1.0†	−1.8 ± 0.5‡	−0.8 ± 1.1	−0.5 ± 1.0	0.0 ± 0.7

Values are means ± SEM of four dogs.
PEEP = positive end-expiratory pressure (in mmHg); LAP = left atrial pressure (in mmHg); RAP = right atrial pressure (in mmHg); LAP − RAP = interatrial pressure gradient (in mmHg).

* $P < 0.01$ compared with corresponding 0 mmHg PEEP value.
† $P < 0.01$ compared with corresponding supine group value.
‡ $P < 0.05$ compared with corresponding supine group value.

< 0.01); the higher level of PEEP resulted in the greater decrease in cardiac index. VAE did not affect cardiac index and there was no interaction between VAE and PEEP.

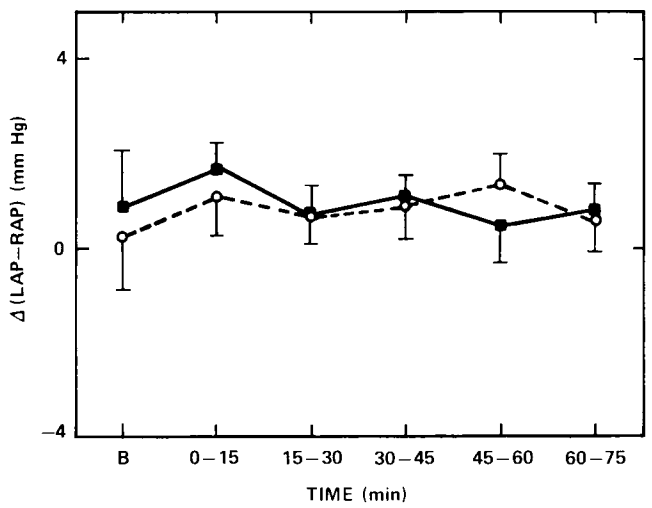

FIG. 1. The change in the interatrial pressure gradient, Δ (LAP − RAP), from the application of PEEP during venous air embolism. Values are means ± SEM of eight dogs. *B* refers to baseline values before venous air embolism; 0–15, 15–30, 30–45, and 45–60 min refer to values during 1 h of venous air embolism at a rate of 0.1 $ml \cdot kg^{-1} \cdot min^{-1}$; 60–75 min refers to values during 15 min of venous air embolism at a rate of 0.2 $ml \cdot kg^{-1} \cdot min^{-1}$. The open circles and dashed line represent changes with 4 mmHg PEEP; the closed squares and solid line represent changes with 8 mmHg PEEP.

PEEP decreased SAP ($P < 0.01$, table 3); the higher level of PEEP resulted in the greater decrease in SAP. Although the simple effects of position and time were not statistically significant, there was a significant interaction between position and time ($P < 0.05$) such that SAP decreased during VAE in the supine group only.

SVRI was higher in the upright compared with the supine group ($P < 0.05$). There were no significant effects of PEEP or VAE on SVRI.

Discussion

In this model PEEP increased both LAP and RAP but did not affect the interatrial pressure gradient. Additional hemodynamic effects of PEEP included an increase in PAP (prior to VAE), an increase in PVRI, and a decrease in SAP and cardiac index. These hemodynamic effects of PEEP are consistent with other reports.[10,11] The majority of investigations of the hemodynamic effects of PEEP have focused on the mechanisms by which PEEP decreases cardiac output. Although studies have differed, there is consensus that the decrease in CO is primarily caused by a decrease in venous return related to increased intrathoracic and intrapleural pressures.[10,11,23,24] A possible second and less important factor is reduced ventricular compliance or contractility.[25–30] In general, studies that have demonstrated such effects have found changes in left ventricular contractility and compliance to exceed those for the right ventricle. Right ventricular failure secondary to

TABLE 2. Effects of Position, PEEP, and Venous Air Embolism on Mean Pulmonary Arterial Pressure, Pulmonary Vascular Resistance Index, and Cardiac Index

Variable	Position	PEEP	Baseline	Time of Air Embolism (min) 0–15	15–30	30–45	45–60	60–75
PAP	Supine	0	11.2 ± 0.9	19.5 ± 2.0*	22.5 ± 1.6*	24.8 ± 0.2*	23.5 ± 1.2*	28.5 ± 2.3*
		4	13.2 ± 0.9†	17.0 ± 2.0*	23.2 ± 1.0*	23.2 ± 0.6*	22.0 ± 1.2*	25.8 ± 1.3*
		8	17.0 ± 1.6‡	19.8 ± 0.9**	23.0 ± 1.2*	23.0 ± 1.1*	22.2 ± 0.8*	27.2 ± 2.5*
PAP	Upright	0	4.5 ± 1.2§	10.5 ± 4.3*·§	14.8 ± 1.9*·§	16.8 ± 3.0*·§	16.2 ± 0.9*·§	23.0 ± 3.0*·¶
		4	6.2 ± 0.6§	10.0 ± 2.1*·§	14.5 ± 1.4*·§	16.0 ± 2.1*·§	15.8 ± 1.4*·§	22.2 ± 2.7*
		8	8.2 ± 0.6‡·§	10.2 ± 1.0§	14.0 ± 1.1*·§	15.0 ± 1.1*·§	17.8 ± 1.2*·¶	21.2 ± 2.0*·¶
PVRI	Supine	0	213 ± 37	442 ± 23*	526 ± 61*	565 ± 47*	528 ± 62*	792 ± 35*
		4	249 ± 39	323 ± 77	519 ± 68*	532 ± 57*	529 ± 115*	662 ± 57*
		8	429 ± 154‡	477 ± 68	568 ± 59	602 ± 115**	553 ± 143	762 ± 75*
PVRI	Upright	0	253 ± 24	627 ± 236	784 ± 135	746 ± 121	689 ± 27	971 ± 104
		4	335 ± 52	582 ± 164	854 ± 146	813 ± 111	722 ± 72	996 ± 124
		8	530 ± 65‡	712 ± 114	940 ± 116‡	885 ± 105†	893 ± 76‡	1091 ± 129†
CI	Supine	0	2.6 ± 0.5	2.8 ± 0.5	2.7 ± 0.4	2.8 ± 0.3	2.9 ± 0.5	2.7 ± 0.3
		4	2.4 ± 0.5	2.6 ± 0.4	2.7 ± 0.4	2.6 ± 0.3	2.6 ± 0.5†	2.4 ± 0.4†
		8	2.0 ± 0.4‡	2.0 ± 0.3‡	2.2 ± 0.3‡	2.2 ± 0.4‡	2.3 ± 0.4‡	2.0 ± 0.3‡
CI	Upright	0	2.1 ± 0.2	1.8 ± 0.3	1.8 ± 0.1	2.0 ± 0.1	2.2 ± 0.1	2.1 ± 0.3
		4	1.6 ± 0.2‡	1.5 ± 0.2†	1.5 ± 0.2†	1.6 ± 0.1‡	1.8 ± 0.2†	1.8 ± 0.1†
		8	1.2 ± 0.5‡	1.2 ± 0.2‡	1.2 ± 0.1‡	1.3 ± 0.1‡	1.6 ± 0.1‡	1.5 ± 0.1‡

Values are means ± SEM of four dogs.
PEEP = positive end-expiratory pressure (in mmHg); PAP = mean pulmonary arterial pressure (in mmHg); PVRI = pulmonary vascular resistance index (in dyne·sec·cm^{-5}·m^2); CI = cardiac index (in l·min^{-1}·m^{-2}).
* $P < 0.01$ compared with corresponding baseline value.
† $P < 0.05$ compared with corresponding 0 mmHg PEEP value.
‡ $P < 0.01$ compared with corresponding 0 mmHg PEEP value.
§ $P < 0.01$ compared with corresponding supine group value.
¶ $P < 0.05$ compared with corresponding supine group value.
** $P < 0.05$ compared with corresponding baseline value.

an increase in right ventricular afterload from PEEP is unlikely to be a significant factor at the low levels of PEEP used in this study.[25–27,30]

The effects of PEEP on the interatrial pressure gradient will depend on the baseline hemodynamic status and changes in venous return, ventricular compliance, ventricular function, and pulmonary vascular resistance. The major effect of PEEP, the increase in intrathoracic pressure, will produce equal increases in pressure in all four cardiac chambers. However, this effect will decrease ve-

TABLE 3. Effects of Position, PEEP, and Venous Air Embolism on Mean Systemic Arterial Pressure and Systemic Vascular Resistance Index

Variable	Position	PEEP	Baseline	Time of Air Embolism (min) 0–15	15–30	30–45	45–60	60–75
SAP	Supine	0	100 ± 10	90 ± 11	86 ± 10*	83 ± 5†	84 ± 7†	74 ± 6†
		4	101 ± 8	95 ± 8	81 ± 6†	84 ± 5†	80 ± 2†	71 ± 5†
		8	86 ± 7‡	88 ± 9	85 ± 2	78 ± 5	75 ± 7	68 ± 6†
SAP	Upright	0	106 ± 8	88 ± 15	91 ± 11	92 ± 10	98 ± 9	94 ± 10
		4	86 ± 14‡	87 ± 16	82 ± 12	89 ± 9	89 ± 10	92 ± 10
		8	66 ± 18‡	69 ± 16‡	65 ± 15‡	66 ± 14‡	85 ± 10§	77 ± 11‡
SVRI	Supine	0	3258 ± 564	2702 ± 494	2543 ± 474	2301 ± 347	2424 ± 524	2503 ± 462
		4	3651 ± 756	2935 ± 451	2428 ± 412	2472 ± 336	2548 ± 426	2296 ± 254
		8	3657 ± 948	3518 ± 619	3110 ± 498	2766 ± 340	2437 ± 243	2498 ± 243
SVRI	Upright	0	4099 ± 350	3850 ± 395	4082 ± 355¶	3698 ± 206¶	3619 ± 256	3714 ± 327
		4	4165 ± 322	4456 ± 572¶	4329 ± 321**	4431 ± 325**	4073 ± 294¶	4053 ± 248¶
		8	4100 ± 452	4261 ± 621	3973 ± 553	3926 ± 648	4200 ± 310¶	3964 ± 267¶

Values are means ± SEM of four dogs.
PEEP = positive end-expiratory pressure (in mmHg); SAP = mean systemic arterial pressure (in mmHg); SVRI = systemic vascular resistance index (in dyne·sec·cm^{-5}·m^2).
* $P < 0.05$ compared with corresponding baseline value.
† $P < 0.01$ compared with corresponding baseline value.
‡ $P < 0.01$ compared with corresponding 0 mmHg value.
§ $P < 0.05$ compared with corresponding 0 mmHg value.
¶ $P < 0.05$ compared with corresponding supine group value.
** $P < 0.01$ compared with corresponding supine group value.

nous return so that transmural filling pressures may decrease. Because both sides of the heart will have equal stroke volume, the net effect on the interatrial pressure gradient will depend on the reduction in venous return and the relative slopes of the Frank-Starling curves for each ventricle.[24-29] When stroke volume is returned to normal by volume expansion, there is usually little if any change in the interatrial pressure gradient.[24,25,27-29] If PEEP decreases left ventricular compliance and contractility more than right, then left ventricular end-diastolic pressure (and LAP) may increase more than right ventricular end-diastolic pressure (and RAP). If PEEP does cause right ventricular failure due to increased pulmonary vascular resistance, the net effect will be to decrease the interatrial pressure gradient[29]; this change may be limited by ventricular interdependence.

The effect of PEEP on the interatrial pressure gradient is therefore difficult to predict *a priori*. The effect has not been the specific focus of prior animal investigations; attempts to draw conclusions from data in other studies are limited because other studies frequently have used high levels of PEEP (15–20 cmH_2O), have performed thoracotomies for instrumentation, have examined effects over a time course not applicable to the clinical situation, and have measured left-ventricular end-diastolic pressure, which may significantly underestimate LAP.[31] In general, the calculated effects of PEEP on the interatrial pressure gradient have been small. For example, Scharf and Brown[29] noted a 3.1 mmHg increase in LAP and a 2.9 mmHg increase in RAP with 15–20 cmH_2O PEEP, and Qvist *et al.*[24] noted a 4.5 mmHg increase in LAP and a 3.6 mmHg increase in RAP when 12 cmH_2O PEEP was applied. In the only clinical study that examined the effect of PEEP on the interatrial pressure gradient, Perkins and Bedford[32] reported that 10 cmH_2O PEEP increased RAP an average of 5.3 mmHg, did not significantly affect LAP, and reversed the mean interatrial pressure gradient. However, the PEEP measurements always occurred after the control measurements; a previous study from the same group documented reversal of the interatrial pressure gradient over time.[21] In addition, the 5.3 mmHg increase in RAP from the application of 10 cmH_2O (7.35 mmHg) PEEP is a larger change than expected based on other studies; similarly, finding no significant change in LAP with 10 cmH_2O PEEP is different from most other studies. Finally, it seems unlikely that the small increase in pulmonary vascular resistance that occurred with PEEP (from 124 to 192 dyne · sec · cm^{-5}) would have been sufficient to cause right ventricular failure and preferential elevation of RAP (see the following).

As in other experiments,[16-20] VAE in our study markedly increased PAP and PVRI. The increase in pulmonary vascular resistance is believed to be due to obstruction of pulmonary arterioles by air bubbles and to neurohumoral factors. The increase and then plateau in PAP seen in our study has been previously described[16,19,33,34] and may be due to a steady state in which the rate of infusion of air into the pulmonary circulation equals the rate of removal of air from the pulmonary circulation by diffusion into alveoli and surrounding blood. In our model, VAE had no effect on RAP despite marked increases in PAP and PVRI. The literature is not conclusive on the effects of VAE on RAP, particularly in a closed-chest model using positive pressure ventilation and continuous rather than bolus air embolism. In general, elevation of RAP is one of the very late findings in VAE and denotes impending right ventricular failure and cardiovascular collapse.[17,18] Right ventricular function is usually maintained with modest increases in right ventricular afterload, whether from PEEP,[27-29] partial ligation of the pulmonary artery,[30,35] or particulate pulmonary embolism.[36] Elevation of RAP and reversal of the interatrial pressure gradient may occur with more severe elevation in PVRI such as a faster rate of VAE, a higher level of PEEP, or a sustained Valsalva maneuver.[14,17,18,37]

The effects of PEEP during VAE in our study were similar to the effects prior to air embolism, namely an increase in LAP, RAP, and PVRI, a decrease in SAP and cardiac index, and no change in the interatrial pressure gradient. The increase in PAP which occurred with PEEP prior to air embolism did not occur during air embolism. This lack of effect of PEEP on PAP during embolism was seen in the individual as well as in the group data. The failure of PEEP to increase PAP during air embolism may be explained by the finding that PEEP produced only a relatively small percentage increase in PVRI during air embolism.

LAP, RAP, and PAP were lower in the upright than in the supine dogs. The interatrial pressure gradient, LAP − RAP, was negative more often in the upright dogs, similar to the result of a clinical study.[21] Although the interatrial pressure gradient was different in the two groups, neither group had a change in the interatrial pressure gradient related to either PEEP or VAE.

In this model of continuous VAE, PEEP significantly increased RAP but did not affect the interatrial pressure gradient; VAE did not affect atrial pressures and there was no interaction between air embolism and PEEP on atrial pressures. This lack of effect of air embolism on atrial pressures occurred at infusion rates that increased PAP 227% and PVRI 278%. Since PEEP increased RAP by approximately one-third of the level of PEEP, PEEP should be effective in decreasing the frequency and severity of VAE. In this model of continuous VAE, PEEP (at levels of 8 mmHg and below) did not result in reversal of the interatrial pressure gradient and would not have increased the risk of paradoxical air embolism. Clinical studies to determine whether this is also true in humans are in progress.

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