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Parameters Affecting Occurrence of Paradoxical Air Embolism

Susan Black, M.D., Roy F. Cucchiara, M.D.,† Rick A. Nishimura, M.D.,‡ John D. Michenfelder, M.D.†*

The effects of different patterns of ventilation and intravascular volume infusion on the occurrence of paradoxical air embolism (PAE) were evaluated in 15 pigs with a surgically created atrial septal defect (ASD). A balloon atrial septostomy was created transvenously in anesthetized pigs (mean diameter 8.6 mm ± 1 mm). Monitoring included transesophageal echocardiography (TEE) of the right and left heart, ECG, EEG, direct arterial pressure, right and left atrial pressures (RAP and LAP), pulmonary artery pressure, and pulmonary capillary wedge pressure (PCWP). With the animal in a head up tilt, air was infused into the superior vena cava at a rate of 0.27 ml · kg^{-1} · min^{-1} for 6 min or until PAE was identified on the TEE. Four situations were studied—intermittent positive pressure ventilation (IPPV), intermittent positive pressure ventilation with 10 cm H_2O positive end-expiratory pressure (PEEP), spontaneous ventilation, and IPPV following infusion of 500 ml hetastarch. The incidence of PAE was not different in any of the four situations. Release of PEEP resulted in an increase in the amount of PAE or new PAE in nine of 14 animals. PAE occurred both with and without mean RAP exceeding mean LAP and the incidence of PAE was not significantly different based on the atrial pressure gradient. In situations during which the mean LAP remained greater than mean RAP throughout the venous air infusion and PAE occurred, transient reversal of the right to left atrial pressure gradient during a portion of each cardiac cycle was demonstrated. (Key words: Embolism, air: incidence. Ventilation, PEEP: paradoxical air embolism.)

PARODOXICAL AIR EMBOLISM (PAE) can be a devastating complication which may occur in patients at risk for venous air embolism (VAE).[1] For air embolized to the venous system to enter the systemic arterial system, a communication between the venous and arterial systems as well as a pressure gradient favoring right to left passage of emboli must be present. Greater than 25% of patients with no history of cardiac disease have a probe patent foramen ovale (PFO) at autopsy.[2] These patients, as well as patients with other cardiac defects, would be at risk for the development of PAE during VAE. It is generally considered unlikely that significant volumes of air can pass from the venous system to the systemic arterial system through the pulmonary circulation.[3]

It has been suggested that the pattern of ventilation can influence both the occurrence of VAE as well as the development of PAE once VAE has occurred. Intermittent positive pressure ventilation with and without positive end-expiratory pressure (PEEP) as well as spontaneous ventilation have all been utilized in neurosurgical patients at risk for VAE. Spontaneous ventilation during sitting position neurosurgical procedures is not commonly used because of the potential for hypoventilation in the anesthetized patient with resultant hypercarbia, increased cerebral blood flow, and increased intracranial blood volume.[4] There is also concern that in a spontaneously ventilating patient, negative intrathoracic pressure during inspiration resulting in a lower central venous pressure and increased gradient for venous air entry could result in an increase in both the frequency and magnitude of VAE. The effect of spontaneous ventilation on the occurrence of PAE has not been addressed.

PEEP has been suggested as a means of decreasing VAE. PEEP, by increasing intrathoracic pressure and increasing central venous pressure, might decrease the pressure gradient in the venous system between the operative site and the right heart and therefore decrease the likelihood of VAE. However, concern exists that PEEP may increase the risk for PAE once VAE has occurred by increasing right atrial pressure relative to left atrial pressure, therefore increasing the likelihood of right to left passage of air.[5,6]

The effect of intravascular volume expansion on right atrial to PCWP gradients in sitting neurosurgical patients has also been examined.[7] In this study, the incidence of RAP exceeding PCWP was decreased in patients given an infusion of 10–30 ml/kg of lactated Ringer's solution. It was suggested, based on this finding, that such an infusion might decrease the risk for PAE.

In the current study, we examined the effects of intravascular volume expansion and of three patterns of ventilation: intermittent positive pressure ventilation with zero end-expiratory pressure (ZEEP), intermittent positive pressure ventilation with 10 cm water PEEP, and spontaneous ventilation on the incidence of PAE during venous air infusion in pigs with a surgically created atrial septal defect in the fossa ovalis.

Materials and Methods

The protocol was approved by the Institutional Animal Care and Use Committee. Fifteen pigs weighing 25–32.5 kg were anesthetized with pentobarbital 30 mg · kg^{-1} intravenously. Following induction of anesthesia, a 3.5 mHz transesophageal echocardiography (TEE) probe interfaced with a 3400 Diasonics® phased array sector ECHO instrument was inserted and positioned to obtain a four-chamber or long axis view of the heart, such that the left atrium and/or ascending aorta could be visualized. The

* Instructor in Anesthesiology.
† Professor of Anesthesiology.
‡ Assistant Professor of Medicine.

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Address reprint requests to Dr. Cucchiara: Mayo Clinic, 200 First Street SW, Rochester, Minnesota 55905.

trachea was then intubated. Anesthesia was maintained during the surgical preparation with 50% nitrous oxide (N_2O) in oxygen and halothane 0.5 to 1% inspired concentration. The left external jugular vein was exposed and an 8 French sheath inserted. Through a right groin incision, a 12 French sheath in the femoral vein and a femoral arterial catheter were inserted.

Under fluoroscopic guidance and following treatment with 1 $mg \cdot kg^{-1}$ of intravenous lidocaine, an atrial septostomy was performed at the level of the fossa ovalis.[8] From the right femoral vein, a transeptal puncture was performed utilizing an 8 French Mullin's sheath, dilator, and needle. Correct position in the left atrium was verified by aspiration of oxygenated blood and contrast injection. The Mullin's sheath was left in place in the left atrium and, following removal of the dilator and needle, a balloon-tipped catheter was advanced through the sheath into the left atrium. After confirmation of left atrial position by aspiration of oxygenated blood and contrast injection, the balloon was inflated with 1.5 ml of air. The sheath and the inflated balloon were then withdrawn through the atrial septum into the right atrium creating an atrial septostomy. An end-hole catheter was next passed from the femoral vein, through the right atrium and septal defect, into the left atrium to directly monitor left atrial pressure. A pulmonary artery catheter was inserted under fluoroscopic guidance through the external jugular vein sheath into either the left or right pulmonary artery and a wedge position obtained in a branch of the pulmonary artery below the level of the left atrium.

The animals were placed in the supine position and the table tilted 20° head up. Halothane was discontinued following surgical preparation and anesthesia was maintained with intermittent boluses of pentobarbital and 50% N_2O in O_2. Occasionally it was necessary to increase the inspired O_2 concentration to maintain arterial partial pressure of oxygen (Pa_{O_2}) above 100 mmHg. Mechanical ventilation was adjusted to maintain arterial partial pressure of carbon dioxide (Pa_{CO_2}) between 25 and 45 mmHg except during the spontaneous ventilation study period. The pulmonary arterial, right atrial, left atrial, and systemic arterial pressures were continuously monitored using Gould PE 23 transducers and recorded on a five-channel Gould ES recorder during all study and recovery periods. All transducers were zeroed at the level of the right atrium. In addition, a two-channel bilateral electroencephalogram (EEG) and electrocardiogram (ECG) were monitored and recorded. An echocardiographic image of the left atrium or aortic arch was monitored in all 15 pigs, using the TEE in 11 and a precordial ECHO in four pigs that had inadequate images on TEE. To obtain a view of the left atrium or aortic arch with the precordial ECHO probe, the probe was placed either along the left sternal border or in the subcostal position. Prior to beginning the study period, agitated saline containing microbubbles of air was injected into the pulmonary artery port of the pulmonary artery catheter and the left heart observed with TEE for evidence of transpulmonary passage of microbubbles. During all air infusion periods, the recorder was run at a paper speed of 25 mm/s. Cardiac cycles surrounding the occurrence of PAE and at periods of maximal hemodynamic changes and maximal air infused were examined for transient reversal of the atrial pressure gradient. Each animal was studied during five different conditions.

Continuous Venous Air Infusion

Three respiratory patterns were studied with continuous venous air infusion of 8 $ml \cdot min^{-1}$ ($\sim$0.27 $ml \cdot kg^{-1} \cdot min^{-1}$) for a maximum of 6 min or until the occurrence of PAE. IPPV with ZEEP, IPPV with 10 cm H_2O PEEP, and spontaneous ventilation were studied in random sequence. The fourth condition included a 500 ml infusion of hetastarch over 30 min followed by continuous venous air infusion of 8 $ml \cdot min^{-1}$ at IPPV-ZEEP for 6 min or until detection of PAE. Following establishment of each of these four conditions (IPPV-ZEEP, IPPV-PEEP, spontaneous ventilation, and volume infusion) for 5 min, baseline measurements of mean arterial pressure (MAP), mean right atrial pressure (RAP), mean left atrial pressure (LAP), pulmonary artery systolic pressure (PASP), pulmonary artery diastolic pressure (PADP), pulmonary capillary wedge pressure (PCWP), end-tidal CO_2 partial pressure (ET_{CO_2}), and arterial blood gases were recorded. Venous air infusion into the superior vena cava at a rate of 8 $ml \cdot min^{-1}$ (0.27 $ml \cdot kg^{-1} \cdot min^{-1}$) was then begun. The ECHO image of the left heart was continuously observed for evidence of PAE during and following venous air infusion by an anesthesiologist experienced in the use of echocardiography. MAP, RAP, LAP, PASP, PADP, and HR were recorded every minute and PCWP every 2 min during air infusion and for the first 5 min postinfusion. Thereafter, the pressures were recorded every 5 min until they returned to baseline levels or stabilized. Air infusion was terminated at the time PAE was detected or after 6 min if no PAE occurred. ET_{CO_2} was measured following termination of venous air infusion. The PEEP was released in the IPPV-PEEP condition 15–60 s following discontinuation of the air infusion. The animals were allowed to recover for a minimum of 20 min after termination of venous air infusion before beginning the next study condition. All measured intravascular pressures returned to baseline levels or remained unchanged for at least 5 min prior to proceeding to the next study condition.

Single Bolus Venous Air Infusion

The fifth study condition involved a single bolus dose of venous air. Following completion of the four study

conditions utilizing continuous venous air infusion, the pigs were divided into two groups, each to receive an air injection of 2 ml · kg^{-1}, one group at IPPV-ZEEP and the other at IPPV-PEEP. Baseline measurements (MAP, RAP, LAP, PASP, PADP, PCWP, HR, ET_{CO_2}) were obtained 5 min after establishing the study condition. The injection of air was then given over 30 s. The ECHO image was monitored for PAE. MAP, RAP, LAP, PASP, PADP, and HR were recorded at 30 s and then every minute for 5 min and the PCWP every 2 min. All measurements were recorded every 5 min thereafter until the animal's vital signs stabilized or until it died. ET_{CO_2} was also recorded.

In order to evaluate the incidence of gross neurologic deficits in animals with PAE, those animals not dying as a result of VAE or PAE were awakened and observed following completion of the study period. Animals surviving were given 1.5 million units penicillin im, catheters were removed and the wounds closed. They were allowed to recover from anesthesia and their trachea extubated once they were able to maintain adequate ventilation. Neurologic exams were performed every 2 h until stable and at 24 h. The animals were then anesthetized with pentobarbital (30 mg · kg^{-1} iv) and given a lethal injection of intravenous potassium chloride. Following autopsy of all animals, the maximum diameter of the atrial septal defect (ASD) was determined. Animals dying during the study period were also examined for the presence of air bubbles within the coronary arteries.

A chi-square test was utilized to compare incidence of PAE under different study conditions and to compare incidence of PAE at each study condition by presence or absence of a positive RA to LA pressure gradient. Rate of agreement between the PCWP-RAP and LAP-RAP gradients was assessed with a chi-square test. Changes in MAP, PCWP, PAP, LAP, and RAP from control were evaluated with paired *t* tests. Volume of air infused prior to PAE was compared with paired *t* tests. To compare changes in PCWP and LAP during venous air infusion, a straight line was fitted to both the PCWP and LAP over time for each animal during each venous air infusion. Paired *t* tests were used to compare the slopes. A *P* value less than 0.05 was considered significant.

Results

In the four study conditions utilizing venous air infusion, the incidence of PAE was not significantly different between patterns of ventilation or following intravascular volume expansion. Volume of air infused prior to development of PAE was also not different (table 1). Of the ten animals with PAE occurring at the time PEEP was discontinued, five had increased PAE from that observed during application of PEEP, four had new PAE which was not present during application of 10 cm H_2O PEEP, and one had a similar amount of PAE as during PEEP. One animal with PAE during ventilation with PEEP had no further PAE after the release of PEEP. The incidence of PAE following the bolus of venous air was very high and the same with IPPV-ZEEP and IPPV-PEEP.

TABLE 1. Incidence of Paradoxical Air Embolism during Different Study Conditions

Condition	Incidence Paradoxical Air Embolism*		Volume of Air* Infused Prior to VAE (ml ± SD)
Air infusion			
IPPV-ZEEP	11/14	(79%)	31.3 (11.9)
IPPV-PEEP	7/14	(50%)	29.7 (8.5)
PEEP release	10/14	(71%)	
Spontaneous ventilation	10/15	(67%)	28.0 (9.8)
Volume infusion (IPPV-ZEEP)	7/13	(54%)	26.6 (6.5)
Air Bolus (2 ml · kg^{-1} · 30 s^{-1})			
IPPV-ZEEP	5/6	(83%)	
IPPV-PEEP	5/6	(83%)	

* $P > .05$, chi-square test.

During venous air infusion, significant changes occurred in several hemodynamic variables (table 2). These variables returned to or near control values with termination of venous air infusion. In some circumstances, hemodynamic patterns were complicated by the development of myocardial ischemia secondary to PAE. With infusion of venous air, right atrial pressures (RAP) increased significantly in all situations and returned to or near control at 15 min postinfusion. Changes in left atrial pressure (LAP) varied between animals at the same condition and between conditions. Changes were in both directions, of shorter duration, and lesser magnitude than changes in RAP, but were statistically significant in three of the four conditions. PCWP increased with air infusion in all animals and all conditions. Rate of change in PCWP was significantly greater than rate of change in LAP in all conditions. Pulmonary artery systolic and diastolic pressures increased significantly during venous air embolism and returned to or near control levels within 15 min of completion of infusion in all conditions. Pulmonary artery pressure increases preceded development of PAE in all animals in all conditions (table 2). Mean systemic arterial pressure was unchanged during VAE unless PAE occurred and resulted in myocardial ischemia. The only exceptions to this were during VAE at IPPV-PEEP when MAP increased by 15 mmHg for 1–4 min during VAE and at IPPV-ZEEP when MAP increased a maximum of 11 mmHg at 1–2 min of VAE possibly due to increases in sympathetic nervous system activity. These changes returned to baseline with discontinuation of VAE.

The relationship of the PCWP to RAP gradient to the LAP to RAP gradient in each circumstance both at control and during venous air infusion was examined. The gra-

TABLE 2. Hemodynamic Changes During Venous Air Embolism

Situation	Maximum Change in Pressure (mmHg) During VAE (±SD)						Percent $\overline{PAP}$ increase at PAE	Rate of Change (ΔP/ΔT) ± SD	
	MAP	RAP	LAP	PCWP	PAS	PAD		PCWP	LAP
IPPV-ZEEP	+10.7 (11.7)*	+3.8 (3.5)*	−4.0 (3.0)*	+12.2 (6.5)*	+53.7 (13.0)*	+35.7 (5.7)*	247% (164)*	3.79 (2.29)	−0.15 (0.61)†
IPPV-PEEP	+15.0 (15.3)*	+5.7 (4.2)*	−3.7 (4.6)*	+13.8 (9.6)*	+45.2 (13.3)*	+35.8 (6.3)*	196% (60)*	2.59 (1.04)	0.33 (0.80)†
Spontaneous ventilation	−9.8 (36)	+4.8 (1.7)*	−2.5 (4.3)	+15.3 (1.3)*	+43.8 (17.8)*	+31.8 (8.2)*	192% (74)*	2.82 (3.60)	0.11 (1.15)†
Volume infusion	+4.4 (4.6)*	+5.7 (3.6)*	−3.2 (4.1)*	+11.8 (7.9)*	+40.3 (15.4)*	+29.5 (8.1)*	139% (45)*	3.08 (2.37)	0.46 (0.84)†

* $P < 0.05$ compared with control values.

† $P < 0.05$ LAP ΔP/Δt compared with PCWP ΔP/Δt.

dients were said to agree if both PCWP and LAP were greater than RAP or if both PCWP and LAP were less than RAP. In these circumstances, PCWP to RAP gradient accurately reflected the LAP to RAP gradient. At control, the incidence of PCWP-RAP accurately reflecting the LAP-RAP was 57% at IPPV-ZEEP, 64% at IPPV-PEEP, 60% during spontaneous ventilation, and 77% following volume infusion. During venous air infusion, the incidence of agreement was 58% at IPPV-ZEEP, 57% at IPPV-PEEP, 60% during spontaneous ventilation, and 62% following volume infusion. The rate of agreement was not significantly different from the rate of disagreement (chi-square test).

Right atrial and left atrial pressures are usually reported as mean, rather than systolic and diastolic atrial pressures. The influence of the gradient between these mean pressures on the incidence of PAE was evaluated. The incidence of PAE was not different in a given study condition in animals with mean LAP greater than RAP throughout the venous air infusion as compared to those animals with mean RAP greater than mean LAP at some point during VAE (table 3).

When PAE occurred in spite of mean LAP exceeding mean RAP throughout the VAE, transient reversals of the atrial pressure gradient occurred such that RAP exceeded LAP during a portion of each cardiac cycle. Instantaneous atrial pressure gradients, rather than gradients between mean pressures, influenced occurrence of PAE. Pressure tracings when PEEP was discontinued in some animals that developed an increase in PAE revealed marked transient changes in the atrial pressure gradients such that RAP exceeded LAP during the majority of each cardiac cycle following discontinuation of PEEP. Prior to the discontinuation of PEEP, LAP exceeded RAP in these animals during all or most of each cardiac cycle. In other animals RAP exceeded LAP during most of each cardiac cycle during PEEP, and with the discontinuation of PEEP this gradient widened transiently.

TABLE 3. Incidence of PAE in Relation to RAP to LAP Gradient

Situation	Incidence PAE	
	$\overline{LAP} > \overline{RAP}$	$\overline{RAP} > \overline{LAP}$
IPPV-ZEEP	5/5 (100%)	4/7 (57%)
IPPV-PEEP	5/9 (5%)	2/5 (40%)
PEEP release	7/9 (78%)	3/5 (60%)
Spontaneous ventilation	5/5 (100%)	5/10 (50%)
Volume infusion	3/6 (50%)	4/7 (57%)
Bolus IPPV-ZEEP	1/1 (100%)	4/5 (80%)
IPPV-PEEP	2/2 (100%)	3/4 (75%)

$P > .05$ chi-square test in all situations.

In none of the animals was PAE detected following pulmonary artery injection of agitated saline containing air microbubbles. Three animals died during the continuous air infusion, two as a consequence of PAE (one each at IPPV-PEEP and spontaneous ventilation), and one due to refractory hypotension during VAE (at the spontaneous ventilation condition) without evidence of PAE. Seven of the 12 animals receiving the 2 $ml \cdot kg^{-1}$ dose died. Six (two at IPPV-ZEEP, four at IPPV-PEEP) died as a result of PAE and one due to VAE without PAE (IPPV-ZEEP). Of the two animals that died due to VAE (without PAE), one had an ASD that was located in the posterolateral portion of the fossa ovalis with a large rim of tissue overhanging the ASD so that blood flow from the superior vena cava was directed toward the tricuspid valve, not over the ASD and the other had a small (4 mm) ASD. However, similar anatomy was present in other animals that developed PAE.

Ten of 15 animals developed evidence of coronary artery air embolism in the form of bradycardia (3), ventricular arrhythmias (2), ST segment changes (3), wall motion abnormalities on ECHO (2), and intracoronary air emboli at the time of autopsy (7). Signs of myocardial ischemia occurred in 9% of the animals developing PAE at IPPV-ZEEP, 9% at IPPV-PEEP, 10% at spontaneous ventilation, and 14% at the volume expansion condition during continuous air infusion. Following the 2 $ml \cdot kg^{-1}$ dose of air, 80% of animals developing PAE had evidence of myocardial embolism in both conditions; IPPV-ZEEP, IPPV-PEEP. Three animals had evidence of cerebral arterial air emboli in the form of unilateral EEG changes (2) and transient right upper extremity paresis (1). Two animals were unable to tolerate the application of 10 cm H_2O PEEP due to hemodynamic deterioration prior to the venous air infusion at IPPV-PEEP. These two pigs were

given the 500 ml of hetastarch, studied at the volume infusion situation, and then received the venous air infusion at IPPV-PEEP.

The mean (± standard deviation) diameter of the created ASD was 8.6 ± 3.7 mm as determined at autopsy. All of the defects were located in the region of the fossa ovalis. In some, the ASD was located in the superior portion of the fossa ovalis with a small rim of overhanging atrial septum, while in other animals, the ASD was located more centrally in the fossa ovalis without overhanging tissue.

Discussion

It is important to note the PAE did not occur in all circumstances in which both venous air embolism and an atrial septal defect were present. Failure of PAE to occur in all situations during VAE in the presence of an atrial septal defect is consistent with the relative infrequency of this complication. Although VAE occurs in approximately 45% of patients undergoing posterior fossa craniectomy while in the sitting position[9-11] and of these patients likely have a patent foramen ovale,[2] the observed occurrence of PAE based upon clinical signs is far less than the 10% that might be expected from these data.[9-11] This suggests that either the majority of episodes of PAE do not result in clinical signs or the frequency of occurrence is considerably less than 10%. The created atrial septal defects were frequently located just below the limbus of the fossa ovalis and some appeared to be shielded from superior vena cava blood flow (which was the source of VAE in this study and in sitting position patients). This is similar to the anatomy of a true patent foramen ovale. It has been demonstrated that right-to-left shunting at the atrial level consists primarily of inferior vena cava blood flow.[12,13] This may account in part for the failure of PAE to develop in all situations when VAE occurs in the presence of an interatrial communication even when the RAP at least transiently exceeds the LAP.

During venous air embolism in the presence of an ASD, PAE did not develop with the initial occurrence of the right atrial air. When PAE did occur, it followed the development of pulmonary hypertension. VAE causes pulmonary hypertension which in turn causes increased RAP relative to LAP.[14] Because PAE did not develop until after pulmonary artery pressure increased and because VAE can be detected by precordial Doppler prior to increases in pulmonary artery pressures,[15] it is unlikely that PAE would develop prior to detection of VAE.

The pattern of ventilation and the use of volume infusion did not influence the incidence of PAE. This suggests that no pattern of ventilation markedly increases the risk for PAE or protects against the occurrence of PAE. Controversy surrounds the use of PEEP in neurosurgical patients at risk for venous air embolism. The application of PEEP as a method to increase central venous pressure has been advocated as a means to decrease the incidence of VAE[16-18] or to identify the site of air entry.[19-21] Studies examining the effectiveness of PEEP suggest that clinically applicable levels of PEEP may be ineffective in significantly increasing cerebral venous pressure and therefore decreasing the risk for VAE[6,22,23] and that jugular venous compression is more effective.[22] The adverse hemodynamic effects of PEEP in sitting patients (decreased mean arterial pressure and cardiac output, increased pulmonary vascular resistance) are also of concern.[6] Because of demonstration in humans that the application of PEEP resulted in a greater incidence of RAP exceeding PCWP[6] and the passage of contrast from the right to left atrium in some patients only with the application of PEEP,[5] it has been suggested that PEEP may increase the risk for PAE. Conversely, other studies in experimental animals and neurosurgical patients have failed to demonstrate an increase in the incidence of reversal of the interatrial pressure gradient with the application of PEEP.[14,24]

In this study, the incidence of PAE during IPPV-PEEP was similar to the incidence during IPPV-ZEEP and spontaneous ventilation. However, when PEEP was discontinued there was a surge of PAE in most animals occurring simultaneously with transient reversals of the atrial pressure gradient. This observation is consistent with the increased right to left shunting demonstrated during contrast echocardiography during the release phase of a Valsalva maneuver or following a cough.[25-28] It has been suggested that with increased intrathoracic pressure systemic venous return is impeded. With the discontinuation of PEEP (or Valsalva maneuver), the sudden increase in systemic venous return to the right atrium would increase RA pressure at a time when venous return to the left atrium remained lower.[26] Increases in RAP immediately following release of a Valsalva maneuver preceding similar increases in pulmonary capillary pressures by several seconds have been demonstrated.[28,29] This could account for the transient reversal of the atrial pressure gradients and surge of left-sided air bubbles observed in this study with the release of PEEP. This phenomenon may explain the apparent inconsistencies in results from studies examining the effects of PEEP on atrial pressure gradients and the influence of PEEP or the Valsalva maneuver on the incidence of right to left shunting. It is likely that increased intrathoracic pressure (PEEP or the strain phase of the Valsalva maneuver) does not alter the atrial pressure gradient. However, with the return of the intrathoracic pressure to lower levels, these gradients are transiently altered influencing the occurrence of right to left shunting. Because of the adverse hemodynamic changes that can be associated with PEEP, the ineffectiveness of PEEP in significantly increasing cerebral venous pressure compared with that of jugular venous compression, and the potential adverse influence of the release of PEEP on the

occurrence of PAE, we feel the use of PEEP in patients at risk for VAE is inadvisable.

Administration of a volume infusion in patients undergoing neurosurgical procedures in the sitting position has been demonstrated to decrease the incidence of RAP exceeding PCWP and has been suggested as a means to decrease the risk of PAE.[7] However, in this study, administration of a volume infusion of 500 ml of hetastarch (approximately 17 ml/kg) did not influence the incidence of PAE. This suggests that although intravascular volume expansion may alter pressure gradients, it does not eliminate the risk for PAE during VAE in the presence of an intracardiac defect.

The atrial septal defect created in the animals in this study was different from a patent foramen ovale in that it was not covered by a flap of tissue. In some animals, this was closely mimicked by the ASD lying underneath the superior rim of the fossa ovalis. The diameter of the ASD (mean 8.6 mm, range 4–18 mm) was similar to that reported in adult humans (mean 4.7 mm, range 1–19 mm).[2] There is controversy regarding the likelihood of significant volumes of venous air reaching the systemic circulation by passing through the pulmonary system.[3,30–33] However, it seems unlikely that the PAE observed in this study was due to transpulmonary passage of air because in all animals agitated saline injected into the pulmonary artery was not detected in the left heart.

The syndrome of PAE was first described in 1877 by Cohnheim.[34] With improved diagnostic techniques, such as echocardiography, paradoxical embolism is being identified more frequently as a possible etiology in ischemic stroke.[35] Paradoxical air embolism resulting in significant neurologic deficits and mortality in patients undergoing neurosurgical procedures at risk for VAE has also been reported.[1,9,30,31,36] Paradoxical embolism resulting in a transient neurologic deficit has also been reported following other operative procedures.[37] In patients suffering paradoxical cerebral embolism in whom the intracardiac defect is identified, a patent foramen ovale is most commonly found.[38,39]

A patent foramen ovale has been demonstrated at autopsy in 27–35% of individuals with no history of cardiac disease.[2,40] Therefore, approximately one-fourth of patients at risk for venous air embolism would also be at risk for paradoxical air embolism. With earlier diagnosis of VAE provided by sensitive monitors such as precordial Doppler and TEE,[15] prompt treatment and elimination of the source of air entry have reduced significant morbidity and mortality due to VAE. Even in neurosurgical patients with a high incidence of VAE such as those undergoing posterior fossa craniectomy in the sitting position (VAE incidence 45%) morbidity or mortality from VAE is rare.[9,10,11,41] The ability to prevent or decrease the risk for PAE in patients at risk for VAE would be expected to have a further positive effect on outcome in this group.

It had been suggested that in patients at risk for VAE, the PCWP to RAP gradient is a useful measurement as a predictor of risk for PAE.[42] This is based on the assumption that the PCWP to RAP gradient accurately reflects the LAP to RAP gradient and that a LAP (PCWP) lower than RAP increases the risk for the development of PAE during an episode of VAE. However, in this study, the PCWP to RAP gradient was not a reliable predictor of the LAP to RAP gradient either at control or during VAE. In addition, the incidence of PAE was not influenced by the mean RAP to LAP gradient. Although it appears that a RAP transiently greater than LAP during at least a portion of the cardiac cycle is necessary for PAE to occur, the gradient between the mean atrial pressures did not influence the occurrence of PAE. It is likely that other factors such as anatomy and direction of blood flow also influence the occurrence of PAE. Finally, although the PCWP correlated closely with the LAP at control, its rate of increase during VAE was greater than that for the LAP. The PCWP is less accurate at higher pulmonary pressures and in the presence of significant pulmonary hypertension PCWP is not a reliable measurement of left heart pressures. Based on these data, PCWP is not a useful measurement in predicting risk for PAE.

Observation of transient reversals in the atrial pressure gradients during each cardiac cycle is consistent with observations of bidirectional shunts in congenital heart disease[13] and experimental atrial septal defects.[43] Transient reversal of the pressure gradients accounts for the development of PAE even when mean RAP remains less than mean LAP during VAE. This finding points to persistent risk for VAE regardless of the measured atrial pressure gradients. It cannot be assumed that a LAP greater than RAP eliminates risk for PAE or that a RAP greater than LAP during VAE in a patient with an intracardiac shunt will always result in PAE. The only assurance that a given patient at risk for VAE is probably not at risk for PAE would be demonstration of the absence of a patent foramen ovale or other intracardiac defect as by preoperative diagnostic echocardiography. The sensitivity of contrast echocardiography using a Valsalva maneuver or cough in detecting a known patent foramen ovale has been reported to range between 64% and 100%.[26,44] We feel that to minimize the risk for PAE optimal management of patients at risk for VAE would include preoperative echocardiography to detect patent foramen ovale, use of sensitive monitors for VAE such as precordial Doppler or TEE, prompt elimination of source of VAE, and avoidance of positive end-expiratory pressure. Even with these measures, it is unlikely that the risk of PAE can be completely eliminated.

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