Cardiovascular Pressures With Venous Gas Embolism And Decompression

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Venous gas embolism (VGE) is reported with decompression to a decreased ambient pressure. With severe decompression, or in cases where an intracardiac septal defect (patent foramen ovale) exists, the venous bubbles can become arterialized and cause neurological decompression illness. Incidence rates of patent foramen ovale in the general population range from 25–34% and yet aviators, astronauts, and deepsea divers who have decompression-induced venous bubbles do not demonstrate neurological symptoms at these high rates. This apparent disparity may be attributable to the normal pressure gradient across the atria of the heart that must be reversed for there to be flow patency. We evaluated the effects of: a) venous gas embolism (0.025, 0.05 and 0.15 ml · kg^{-1} · min^{-1} for 180 min.); b) hyperbaric decompression; and c) hypobaric decompression on the pressure gradient across the left and right atria in anesthetized dogs with intact atrial septa. Left ventricular end-diastolic pressure was used as a measure of left atrial pressure. In a total of 92 experimental evaluations in 22 dogs, there were no reported reversals in the *mean* pressure gradient across the atria; a total of 3 transient reversals occurred during the peak pressure gradient changes. The reasons that decompression-induced venous bubbles do not consistently cause serious symptoms of decompression illness may be that the amount of venous gas does not always cause sufficient pressure reversal across a patent foramen ovale to cause arterialization of the venous bubbles.

VENOUS GAS EMBOLISM (VGE) is commonly reported with decompression to lowered ambient pressures, as experienced by divers, astronauts, and aviators. These circulating bubbles ultimately become trapped within the lungs where they are excreted via the airways or dissolved in the blood. Although decompression-induced venous bubbles may be associated with lung injury (10), even at moderate doses these events are less severe than those reported with arterial gas embolism. Arterialization of the VGE can occur via: a) the lung microcirculation (8,9,11,30); b) anatomical shunts located within the lung parenchyma (21,25); or c) intracardiac septal defects (3,4,23,24,31,32). An atrial septal defect (ASD), often manifested as a patent foramen ovale (PFO) located between the atria of the heart, may provide an anatomical route for the venous gas bubbles to access the systemic arterial circulation. These arterial bubbles can result in cerebral or myocardial embolization.

It is generally accepted that VGE commonly occur with even moderate decompressions either from elevated hydrostatic pressures or increasing altitude. With the reported incidence of ASD's ranging from 25–34% in the adult population (17,20), a disparity exists between these values and the actual cases of serious decompression illness (DCI) in aviators and astronauts who experience VGE. This disparity may be explained in part because the normal pressure gradient across the right and left atria usually must be reversed for VGE to cross into the left heart via a PFO. In subjects who have a PFO and experience VGE after decompression, yet have no symptoms of any neurological involvement, it is likely that the extent of bubbling was inadequate to cause a reversal in the atrial pressure gradient, and thus to effect the abnormal transport of bubbles across the anatomical shunt.

Recent studies re-examining the likelihood of serious hyperbaric DCI in individuals with an ASD revealed a greater incidence (23,24,32), although this finding did not correlate with altitude decompression (12). These observations do, however, raise the question of the validity of screening divers, aviators, and astronauts for the presence of ASD's to determine their acceptability and fitness for diving or flight duty.

The aim of this study was to determine the effects of VGE, as well as decompression to altitude or from hyperbaric pressures, on the intracardiac pressures of anesthetized dogs with intact atrial septa, and to deter-

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mine at what point the left to right atrial pressure gradients were likely to reverse.

MATERIALS AND METHODS

Venous Gas Infusions

Surgery: Twenty-two mongrel dogs (22 ± 6 kg) of both sexes were fasted for 24 h, anesthetized with pentobarbital sodium (25 mg • kg^{-1}, IV) and maintained with 10 mg • h^{-1}. The dogs were intubated and mechanically ventilated with air at a tidal volume (~15 ml • kg^{-1}) and frequency (~10–14 breaths • min^{-1}) adequate to maintain baseline arterial carbon dioxide (P_aCO_2) tensions between 30–45 mm Hg. Polyvinyl catheters were placed into the abdominal aorta via the left femoral artery for measurement of mean arterial blood pressure (MAP), in the right atrium (RAP), and the pulmonary artery via the right jugular vein (PAP), the right ventricle (RVP; mean, systolic and diastolic), the left ventricle via the right carotid artery for left ventricular end-diastolic pressure (LVEDP), as an indirect measure of left atrial pressure (LAP), and the inferior vena cava via the left femoral vein for venous access. Airway pressure was measured from the proximal end of the endotracheal tube. The catheters, excepting the airway, were fluid-filled with degassed heparinized saline and connected to calibrated pressure transducers, zero referenced at the right atrial level. Cardiac output ($\dot{Q}$) was measured using thermodilution techniques. Arterial blood gases were measured at baseline and hourly thereafter. End-tidal carbon dioxide ($P_{et}CO_2$) and arterial oxygen saturation (S_aO_2) were continuously measured (Nellcor, N-1000, Pleasanton, CA).

Gas infusions: Following stabilization (30–45 min) and collection of baseline data, air was infused into the right atrium for 180 min using a volume-controlled reciprocating servo pump (Harvard, South Natick, MA). The dogs in the gas infusion studies were subdivided into three experimental groups (n = 6 each), depending upon the gas infusion dose and one control group (n = 4). The three gas doses were 0.025, 0.05 and 0.15 ml • kg^{-1} • min^{-1}. Hemodynamic measurements were collected throughout the gas infusion and for a 60 min post infusion period. $\dot{Q}$ and blood gases were measured every 60 min. Each dog received the VGE infusion for 180 min only once. The hearts were inspected post mortem for the presence of an ASD. Arterialization of the VGE was not examined in any of the experimental groups.

Hyperbaric Decompression

Six dogs were prepared as previously described with the addition of placement of an ultrasonic Doppler probe around the inferior vena cava via laparotomy to detect VGE that formed as a result of the decompression. The probe signal was range gated to maximize the reflected audible signal representing bubble recordings. Decompression bubble signals were evaluated semiquantitatively according to Grades 1–4 using a modified Spencer code (29) which consisted of periodic audio sampling at resting conditions and following passive deep knee bends, with the bubble score recorded as the peak value obtained in the two conditions. Although passive knee bends do not fully simulate their active counterpart, in all cases significant bubble showers were detected by Doppler. In some cases, the signals were recorded on cassette for playback analysis or digitized directly for computer-assisted evaluation. The instrumented animals were placed in the experimental compression chamber, ventilation was switched to a pneumatic-driven time cycled ventilator (Bird, Mark 14, Palm Springs, CA) and compressed to 2.84 bar (60 ft of sea water, fsw) at 0.37 bar • min^{-1} (12 fsw • min^{-1}) for 120 min, then decompressed to sea level at 0.92 bar • min^{-1} (30 fsw • min^{-1}). The animals were then immediately removed from the chamber and monitored post dive for 90 min.

Altitude Studies

Six dogs were prepared as previously described, including the vena caval Doppler probe. LVEDP was measured with a non fluid-filled transducer-tipped catheter (Millar Instr., Houston, TX). Tetanic muscle stimulation was used while at altitude to release venous bubbles trapped within the capillary beds of the left hind limb for the Doppler detection. The dogs were placed into the altitude chamber and all pressure and Doppler monitors connected to through-pass devices for continuous recordings. Following baseline data collection the dogs were decompressed to 40,000 ft (4,000 ft • min^{-1}) for 180 min. The animals were ventilated with room air to 20,000 ft and then switched to 100% oxygen thereafter. No oxygen pre-breathing was administered. The animals were then recompressed to sea level at 10,000 ft • min^{-1}. Monitoring was continued throughout the altitude simulation and until no further VGE could be detected by the Doppler, usually not exceeding 45 min. The breathing gas was switched back to air at 20,000 ft during decent.

All procedures were approved by The University of Texas-Houston Animal Care and Use Committee, and the animals were handled in accordance with the National Institutes of Health "Guide for the Care and Use of Laboratory Animals."

Statistics

Data are expressed as mean ± SEM. Data were analyzed using analysis of variance (ANOVA) with post-hoc comparisons made using Bonferroni-corrected Student's t test; $p < 0.05$ was considered statistically significant.

RESULTS

Venous Gas Infusions

The hemodynamic data from the VGE studies are given in Tables I–III. Fig. 1 shows the time course of changes for PAP and RAP in both the VGE and altitude simulated decompression. PAP increased significantly with each gas dose, beginning within the first 5 min of the infusion and remaining elevated for the 180 min period. Peak increases were dose dependent with the maximum value reaching 104% above baseline (0.15 ml • kg^{-1} • min^{-1}). RAP values were unchanged at the 0.025 dose, decreased (nonsignificant) with the 0.05

TABLE I. VENOUS GAS INFUSION AIR DOSE: 0.025 ml · kg^{-1} · min^{-1}.

	Baseline	60 Min	120 Min	180 Min
MAP	165 ± 7	157 ± 6	155 ± 5	148* ± 6
PAP	13.1 ± 1.2	16.3* ± 1.7	16.5* ± 1.3	17.3* ± 1.5
RAP_p	1.3 ± 1.0	2.7 ± 1.4	2.0 ± 0.8	1.5 ± 0.6
$LVEDP_m$	4.7 ± 1.2	4.6 ± 0.7	4.4 ± 0.6	5.1 ± 1.0
$LVEDP_p$	5.0 ± 1.4	5.6 ± 1.1	5.8 ± 1.1	5.7 ± 1.0
RVP_m	8.0 ± 0.5	10.0 ± 1.9	8.4 ± 1.1	8.9 ± 1.3
RVP_s	20.3 ± 1.7	22.2 ± 2.9	20.8 ± 1.8	21.5 ± 1.6
RVP_d	1.6 ± 0.5	2.3 ± 1.1	1.8 ± 0.5	2.2 ± 0.7
$LVEDP\text{-}RAP_m$	5.1 ± 0.9	4.6 ± 1.1	4.8 ± 0.4	5.7 ± 0.7
$LVEDP\text{-}RAP_p$†	3.7 ± 0.8	2.8 ± 1.2	3.8 ± 0.9	4.2 ± 0.7
CO (L · min^{-1})	3.22 ± 0.2	3.01 ± 0.3	2.48* ± 0.2	2.26 ± 0.2
PVR (dyn · s · cm^{-5})	217 ± 43	310 ± 21	395* ± 30	441* ± 38
SVR (dyn · s · cm^{-5})	4150 ± 276	4334 ± 365	5192 ± 525	5487 ± 609

Pressure units are mm Hg.
* $p < 0.05$ vs. baseline.
† LVEDP and RAP values taken at peak inspiration.
m = mean; s = systolic; d = diastolic; p = peak.

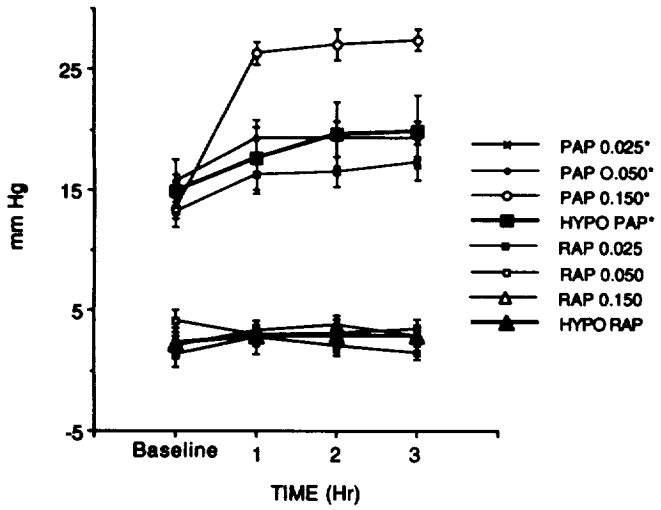

Fig. 1. Pulmonary artery pressure (PAP) and right atrial pressure (RAP) for the VGE studies and hypobaric decompression.

dose and elevated with the 0.15 ml · kg^{-1} · min^{-1} dose (nonsignificant). MAP decreased with each of the doses, reaching significance at particular intervals with each gas dose. LVEDP values were not significantly changed. RVP mean and systolic values increased significantly with the 0.15 ml · kg^{-1} · min^{-1} dose. The LVEDP-RAP mean gradient remained positive (i.e., non-reversed at each dose) (Fig. 2). Examining peak gradient pressure changes (maximum RAP and minimum LVEDP; i.e., $LVEDP\text{-}RAP_p$) throughout individual respirations and cardiac cycles did demonstrate two incidents of reversal; one dog at hour three in the 0.05 ml · kg^{-1} · min^{-1} group; one dog at hour two in the 0.15 ml · kg^{-1} · min^{-1} group. The mean $LVEDP\text{-}RAP_p$, however, was not reversed (Fig. 2). Three additional dogs had pressure gradients of 0–0.2 mm Hg during the experimental phases. Heart rate (HR) decreases were significant at hour three of the 0.15 ml · kg^{-1} · min^{-1} dose. $\dot{Q}$ was decreased (significant) at the 0.025 and 0.05 ml · kg^{-1} · min^{-1} doses. S_aO_2 and $P_{et}CO_2$ were decreased with each air infusion. Pulmonary vascular resistance (PVR) was increased at each dose, while systemic vascular resistance (SVR) was not changed. Arterial P_O_2 was decreased (significant) with the 0.05 and 0.15 ml · kg^{-1} · min^{-1} dose and P_aCO_2 was elevated with each dose, 0.025 and 0.15 ml · kg^{-1} · min^{-1} groups achieving significance.

Hyperbaric Decompressions

MAP and HR values were not significantly changed with hyperbaric decompression (Table IV). PAP values increased to a peak 30 min post decompression (nonsignificant), and returned to baseline values over the next 60 min; RAP values were unchanged (Fig. 1). LVEDP decreased within the first 10 min post decompression (nonsignificant) and remained slightly decreased. RVP pressures were slightly decreased (nonsignificant). $\dot{Q}$ steadily decreased, reaching significance 90 min post dive. PVR increases reached peak values at 30 min post dive (155%) and remained elevated throughout the 90 min. SVR increased progressively over the 90 min post dive period. The LVEDP-RAP mean gradient decreased post decompression while never achieving a reversal in the direction of the normal gradient (Fig. 2). Arterial P_aO_2 was elevated post decompression and P_CO_2 was unchanged. $P_{et}CO_2$ was decreased (significant) at 90 min, and S_aO_2 was unchanged.

Doppler detected venous bubbles were first recorded 12.3 ± 4 min (10–18 min, range) post decompression and persisted for up to 120 min. Spontaneous bubbles were detected at a peak Grade of 2 in two dogs and Grade 3 and 4 in one dog each. Grade 4 bubbles were detected in three dogs with deep knee bends.

Altitude Simulations

The hypobaric decompression data are presented in Table V. MAP increased at 20,000 ft, possibly due in part to the systemic vasoconstriction associated with the switch to 100% oxygen ventilation, and returned to lower than baseline values upon return to sea level pressures. PAP increased progressively (significant) to 20,000 ft, decreased momentarily with the switch to oxygen ventilation then continued to rise to a peak value (106%) 180 min into the simulated flight. RAP decreased during the decompression to altitude, then increased after 60 min at 40,000 ft. RAP values at 120 and 180 min

TABLE II. VENOUS GAS INFUSION AIR DOSE: 0.05 ml · kg^{-1} · min^{-1}.

	Baseline	60 Min	120 Min	180 Min
MAP	160 ± 5	142 ± 9	150 ± 6	154 ± 4
PAP	15.7 ± 1.8	19.2* ± 1.6	19.2* ± 1.5	19.2* ± 1.5
RAP_p	4.1 ± 0.9	3.0 ± 0.5	3.1 ± 0.5	3.4 ± 0.8
$LVEDP_m$	6.2 ± 1.1	4.5 ± 0.7	4.2 ± 0.3	6.5 ± 1.0
$LVEDP_p$	7.6 ± 1.3	6.2 ± 1.1	6.0 ± 0.4	7.2 ± 1.4
RVP_m	12.5 ± 1.5	14.0 ± 1.8	12.3 ± 1.5	11.8 ± 1.0
RVP_s	25.1 ± 1.6	26.5 ± 0.8	26.7 ± 2.2	25.5 ± 2.3
RVP_d	0.3 ± 1.1	2.0 ± 0.6	1.4 ± 0.8	2.0 ± 1.4
$LVEDP\text{-}RAP_m$	5.1 ± 0.9	4.7 ± 0.6	4.2 ± 0.4	6.3 ± 1.1
$LVEDP\text{-}RAP_p$†	3.5 ± 0.9	3.1 ± 1.2	2.9 ± 0.7	3.8 ± 1.6
CO (L · min^{-1})	4.21 ± 0.5	3.55 ± 0.4	3.13* ± 0.4	2.69* ± 0.3
PVR (dyn · s · cm^{-5})	193 ± 28	363 ± 82	437* ± 103	426* ± 98
SVR (dyn · s · cm^{-5})	3267 ± 409	3338 ± 283	4048 ± 405	4956 ± 767

Legend same as Table I.

TABLE III. VENOUS GAS INFUSION AIR DOSE: 0.15 ml · kg^{-1} · min^{-1}.

	Baseline	60 Min	120 Min	180 Min
MAP	155 ± 8	129* ± 14	134 ± 11	139* ± 9
PAP	13.4 ± 0.9	26.3* ± 0.9	27.0* ± 1.3	27.4* ± 0.9
RAP_p	2.1 ± 0.7	3.3 ± 0.5	3.8 ± 0.8	2.9 ± 0.9
$LVEDP_m$	5.7 ± 0.7	5.3 ± 0.9	5.6 ± 1.1	6.1 ± 0.9
$LVEDP_p$	7.2 ± 0.7	6.7 ± 1.1	6.5 ± 1.3	7.7 ± 1.0
RVP_m	8.5 ± 1.2	14.9* ± 0.4	19.6* ± 4.4	17.0* ± 1.7
RVP_s	16.7 ± 1.3	31.0* ± 3.3	32.1* ± 2.3	34.9* ± 1.5
RVP_d	3.1 ± 0.8	4.8 ± 1.4	3.6 ± 0.6	4.6 ± 2.2
$LVEDP\text{-}RAP_m$	6.4 ± 0.6	5.5 ± 1.1	5.8 ± 1.0	6.2 ± 0.9
$LVEDP\text{-}RAP_p$†	5.1 ± 0.2	3.3 ± 0.9	2.7 ± 1.1	4.8 ± 1.1
CO (L · min^{-1})	2.81 ± 0.1	2.87 ± 0.2	2.88 ± 0.1	2.87 ± 0.1
PVR (dyn · s · cm^{-5})	233 ± 30	601* ± 52	593* ± 40	594* ± 27
SVR (dyn · s · cm^{-5})	4468 ± 231	3636 ± 386	3761 ± 394	3921 ± 326

Legend same as Table I.

were decreased, although clotting of the venous pressure lines occurred in several incidences and were not corrected until descent (Fig. 1). RVP values increased upon ascent and remained elevated throughout the decompression. LVEDP increased over the duration of the simulated flight and during the period of maximal venous bubbling (non-significant) then returned towards baseline upon return to sea level. The LVEDP-RAP peak gradient increased throughout the decompression, returning towards baseline with recovery (Fig. 2). The LVEDP-RAP mean was never reversed, although one dog had a transient reversal upon arrival at a simulated altitude of 40,000 ft. $\dot{Q}$ was slightly decreased post decompression while PVR was increased (significant) as was SVR (non-significant). P_aO_2 and P_aCO_2 values were increased post decompression. Venous gas bubbles were recorded at Grades 2–4 during the simulated flights.

No animals from any of the experimental or control groups had an ASD detected at autopsy.

DISCUSSION

The results of this study demonstrated that the normal mean pressure gradient across the atria of the heart (LAP > RAP, using LVEDP as a measure of LAP) was not reversed with venous gas infusions of 0.025, 0.05 and 0.15 ml • kg^{-1} • min^{-1}, or with hypo- or hyperbaric decompressions in anesthetized dogs with an intact atrial septum. Examining peak gradient changes throughout individual respiratory and cardiac cycles revealed three incidences (3%) with momentary reversals occurring during the experimental gas infusions or decompressions, out of a total of 92 recorded measurements.

This relatively low rate for atrial pressure gradient reversal with VGE or decompression is consistent with reported findings that patients with a PFO who have VGE do not appear to be symptomatic of arterial embolism at rates predictable from the incidence rates of PFO's in the general population (12). The incidence of PFO's in individuals with no history of cardiac disease has been demonstrated at autopsy to be 27–35% (17). Using preoperative precordial echo ultrasound, the detection rate has been reported from 10–30% (16,20). Failure to demonstrate a PFO with echocardiography can still occur as a result of improper contrast technique, poor image resolution or inability to produce flow through the defect because of inadequate atrial pressure changes. An inadequate degree of sensitivity of precordial echocardiography can, for example, result in failure to correctly identify surgical patients at risk of arterial embolization (26), examples of which are reported where actual embolization did subsequently oc-

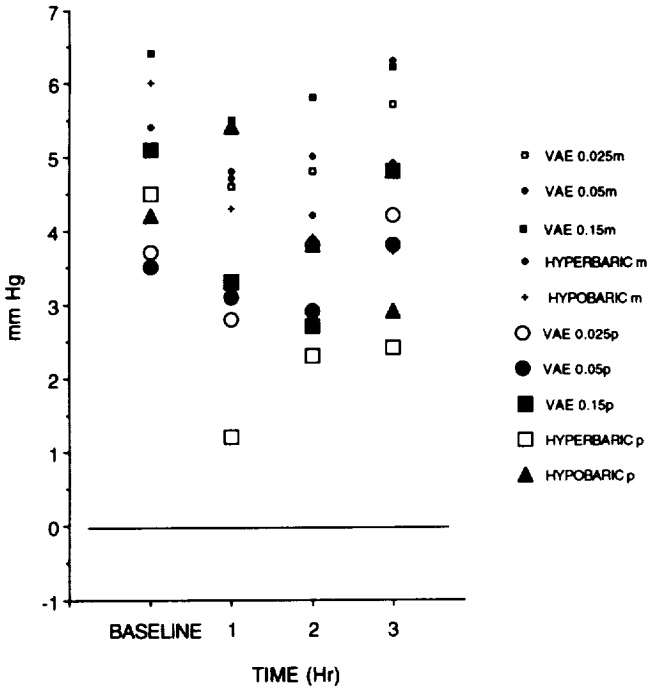

Fig. 2. Left ventricular end-diastolic pressure (LVEDP)—right atrial pressure (RAP) mean and mean peak gradient pressure change with VGE and decompression. Baseline represents measurement taken at 0 min at altitude. For the hyperbaric decompression baseline taken at predive; 1 represents 30 min., 2 represents 60 min., and 3 represents 90 min. post decompression.

cur (4,13). False negative results of preoperative screening for ASD's using precordial echocardiography are not uncommon (19), although superior sensitivity is reported with contrast imaging using transesophageal echo machines (26). Reported use of echocardiography for detection of flow across a PFO suggests that incidence rates range from 5–10% (4,16,18–20) for resting conditions and from 10–24% for provoked maneuvers (16,19). A review of these incidence rates and of the rates of false-negative transesophageal echocardiography saline-contrast studies is presented by Rafferty (28). From these data, Rafferty concluded that positive tests for a PFO are definitive in nature; however, a negative study does not necessarily preclude the possibility of flow patency, especially without proof that any provoked maneuver indeed caused a reversal in the atrial pressure gradient (18).

Venous gas bubbles will circulate into the pulmonary microcirculation resulting in both mechanical obstruction and vasoconstriction (9,10). The subsequent pulmonary hypertension and increase in vascular resistance can cause an increase in RAP relative to LAP that would result in a shunting of blood flow through an ASD, if present. However, even in the presence of venous bubbles, the interatrial pressures, and hence flow, may not always be reversed. It may thus be conjectured that even though significant VGE may occur as a result of decompression, trans-atrial movement of the bubbles as predicted by a reversal in the LAP-RAP gradient may not always occur. The duration of embolization or the speed at which the bubbles enter the pulmonary microcirculation may represent other factors influencing flow reversal through a PFO. In fact, Mehta et al. (22) reported that rapid bolus injections of air (0.5–1.5 $ml \cdot kg^{-1}$) into the right atria of dogs with intact atrial septa did not cause a pressure reversal, but that 2.0 $ml \cdot kg^{-1}$ did. This dose was 13.3 times the dose in the present study and far exceeded that normally seen with decompression (27). Vik et al. (31), reported arterial bubbles in anesthetized pigs receiving venous air infusions as small as 0.05 $ml \cdot kg^{-1} \cdot min^{-1}$, and who had PFO's detected by transesophageal echocardiography. Further, in their study the size of the PFO's (4.5 ± 3.1 mm dia.) were not related to the occurrence of the arterial bubbles and although RAP was elevated (nonsignificantly), they did not report left atrial values.

In the present study, MAP decreased with each VGE dose, and although statistically significant for the 0.025 and 0.15 $ml \cdot kg^{-1} \cdot min^{-1}$ doses, these values never exceeded 17% of baseline. ECG changes reported with VGE, such as S-T segment depression or T-wave inversion, have been associated with reductions in cardiac output and myocardial contractility (8). MAP was not significantly affected by the altitude or hyperbaric decompressions, although the decrease in heart rate likely contributed to the decrease in cardiac output. PAP was increased in a dose response fashion for the three VGE doses and closely approximated the hypobaric decompression values. These responses have been previously reported over a wider range of gas doses (7,9) and are likely attributable to increased mechanical obstruction, shunt, reflex vasoconstriction, and release of vasoactive mediators. These combined effects on the pulmonary microcirculation account for the significant elevations in pulmonary vascular resistance and to some degree the increase in peripheral vascular resistance as well. RVP values (mean, systolic, and diastolic) increased with VGE due to the increased pulmonary vascular resistance. This finding was previously reported by Powell, et al. (27), who correlated RVP values with decompression-induced venous gas loads to the pulmonary circulation based on an algorithm that was determined from calibrated venous gas infusions.

Arterial oxygen tensions and saturation values decreased with each VGE dose (significant at the larger doses) due largely because of the development of physiological shunt by obstruction of pulmonary vessels by the gas bubbles. Further explanations reported earlier include: a) changes associated with lung injury that cause diffusion impairment such as edema or atelectasis; b) changes in the ventilation-perfusion ratio; or c) opening of pulmonary shunts (25). Obstruction of pulmonary vessels reduces the Co_2 tensions in the exhaled gases ($P_{et}CO_2$, thereby increasing the values in the arterial blood (P_aCO_2).

Certain conclusions drawn from the present study depend to some degree on the degree of confidence that can be placed in the approximation of LAP by LVEDP. Braunwald, et al. (6), reported that in normal individuals LVEDP exceeds LAP mean by an average of only 0.2 mm Hg. They further suggested that although atrial systole increased the ventricular filling rate, it did not cause LVEDP to further increase above LAP mean. In

TABLE IV. HYPERBARIC DECOMPRESSION.

	Baseline	Post Dive			
		10 Min	30 Min	60 Min	90 Min
MAP	128 ± 15	133 ± 7	126 ± 7	127 ± 9	126 ± 9
PAP	8.3 ± 1.8	7.1 ± 0.6	9.4 ± 1.9	7.6 ± 0.8	7.8 ± 1.4
RAP_p	0.0 ± 0.4	0.6 ± 0.8	0.5 ± 0.3	0.1 ± 0.3	0 ± 0.3
$LVEDP_m$	3.1 ± 0.3	2.0 ± 0.2	2.4 ± 0.2	2.7 ± 0.3	2.4 ± 0.4
$LVEDP_p$	3.5 ± 0.4	3.1 ± 0.9	2.1 ± 0.4	2.3 ± 0.4	2.3 ± 0.4
RVP_m	6.2 ± 1.7	7.5 ± 2.0	6.7 ± 1.3	5.3 ± 1.0	5.4 ± 0.7
RVP_s	20.6 ± 2.3	16.8 ± 1.9	17.5 ± 1.3	16.9 ± 2.5	16.1 ± 1.2
RVP_d	−1.4 ± 0.5	−0.9 ± 0.4	−0.6 ± 1.0	−0.5 ± 0.9	−0.9 ± 0.5
$LVEDP\text{-}RAP_m$	5.4 ± 0.8	4.6 ± 0.5	4.8 ± 0.5	5.0 ± 0.5	4.9 ± 0.5
$LVEDP\text{-}RAP_p$	4.5 ± 0.4	2.6 ± 0.9	1.2* ± 0.5	2.3* ± 0.4	2.4* ± 0.4
$\dot{Q}$ ($L \cdot min^{-1}$)	1.65 ± 0.7	1.21 ± 0.3	1.01 ± 0.1	1.06 ± 0.2	0.87* ± 0.1
PVR ($dyn \cdot s \cdot cm^{-5}$)	250 ± 81	368 ± 97	638* ± 228	408 ± 105	514* ± 117
SVR ($dyn \cdot s \cdot cm^{-5}$)	6392 ± 859	10,580 ± 2058	10,573 ± 1188	10,334 ± 1438	12,215* ± 1479

Legend same as Table I.

TABLE V. ALTITUDE DECOMPRESSION.

	Baseline	40,000 ft.				
		0 Min	60 Min	120 Min	180 Min	Post Flight
MAP	138 ± 4	144 ± 5	133 ± 3	134 ± 4	136 ± 5	128 ± 5
PAP	9.6 ± 1.1	14.9* ± 1.4	17.6* ± 2.6	19.6* ± 2.7	19.8* ± 3.0	11.5 ± 1.9
RAP_p	2.5 ± 0.7	2.3 ± 1.3	2.9 ± 0.9	1.8 ± 1.3	1.0 ± 0.9	2.5 ± 0.4
$LVEDP_m$	3.1 ± 0.5	5.5 ± 0.1	4.5 ± 0.5	5.0 ± 0.2	4.3 ± 0.3	4.1 ± 0.2
$LVEDP_p$	4.7 ± 0.8	6.5 ± 1.7	7.1 ± 1.4	6.3 ± 1.6	5.3 ± 1.7	6.0 ± 1.8
RVP_m	6.7 ± 1.7	8.2 ± 2.8	9.2 ± 2.5	10.2* ± 2.1	9.8* ± 2.0	5.9 ± 1.8
RVP_s	23.5 ± 1.7	27.0 ± 3.7	28.0 ± 6.6	37.5* ± 2.2	29.8 ± 3.9	21.3 ± 1.9
RVP_d	−0.1 ± 0.9	−0.4 ± 1.8	1.4 ± 2.6	5.1* ± 0.9	4.4 ± 1.4	−0.1 ± 1.4
$LVEDP\text{-}RAP_m$	3.5 ± 1.2	6.0 ± 1.2	4.3 ± 1.7	3.9 ± 1.7	3.7 ± 1.4	4.2 ± 1.6
$LVEDP\text{-}RAP_p$†	2.2 ± 0.9	4.2 ± 1.8	5.4 ± 2.8	3.8 ± 1.8	2.9 ± 1.3	3.4 ± 1.8
CO ($L \cdot min^{-1}$)	2.21 ± 0.5	—	—	—	—	1.84* ± 0.5
PVR ($dyn \cdot s \cdot cm^{-5}$)	333 ± 62	—	—	—	—	505* ± 115
SVR ($dyn \cdot s \cdot cm^{-5}$)	6145 ± 1096	—	—	—	—	7088 ± 1231

Legend same as Table I.

another study, Braunwald, et al. (5), reported little difference between LAP mean, LAP z-wave (atrial pressure at onset of left ventricular contraction) and LVEDP. Additionally, the LAP a-wave peak (atrial contraction) was the same as the left ventricular a-wave which represents the transmission of the atrial contractile wave into the left ventricle (6). The tallest wave in the LAP pulse is the V-wave, which is the pressure at the time that the mitral valve opens. Although the apparent differences in LVEDP (obtained in a closed chested animal) and LAP (principally V waves, obtained by thoracotomy) pose some interpretative limitations on the determination of the atrial gradients, the relative advantage of using a closed-chested versus open-chested preparation presents a compelling argument for its use. Although mean LVEDP-RAP was not reversed in the present study, transient pressure changes during a cardiac or ventilation cycle need to be considered as well (4). Of the total number of VGE or decompression measurements in the present study, 3% showed transient reversals in the atrial pressure gradient. These data may also be affected by exaggerated respiratory maneuvers.

When any reversal of the atrial pressure gradient occurs during VGE in the presence of a PFO, the subject is at risk for arterial embolization with subsequent cerebral complications if the bubbles circulate into the brain. This risk factor has been previously recognized in hyperbaric decompression illness (23). In a later retrospective study of 90 divers, Moon et al. (24) found a statistically significant relationship between PFO and serious DCI. For the individuals with a resting PFO (i.e., Valsalva maneuver or cough was not required to provoke venous contrast transmission through the septal defect) they reported a five-fold increase in risk for serious DCI. Valsalva-induced shunts were not significantly correlated with an increased risk of DCI. Further, no data were reported on the incidence of neurologic DCI and with precordial bubble Grade and PFO. Wilmshurst, et al. (32), studied 61 divers with DCI and 63 controls without DCI and reported that the incidence of PFO did not affect onset of neurologic DCI more than 30 min after surfacing but did so for those with early symptoms. Interestingly, they reported that the group of symptom-free divers had a higher incidence of PFO's than reported in the echocardiographic studies of healthy individuals. Further, they also found that many divers with neurologic DCI and PFO's had undergone previous dives with more provocative pressure-time profiles, yet without complication. This finding, plus the fact that many symptomless divers had shunts, adds further evidence to the argument put forth in the present

study that the amount of gas phase present in the venous circulation is likely to be an important factor influencing a reversal of the atrial pressure gradient. Earlier studies have also suggested a relationship between PFO's and fatal hypobaric decompression illness (1), although in review of these cases, Fryer (14) emphasized that a disparity remains between the incidence rates of PFO's and decompression collapse.

CONCLUSION

It has been established that VGE may pose a significant risk to people undergoing decompression, and has been further postulated that a PFO may increase that risk factor. Reversal of the normal atrial pressure gradient can occur, at least transiently, with a release of a Valsalva maneuver, cessation of positive pressure breathing, cessation of the L-1 or M-1 anti-G straining maneuver, Müller maneuver, negative pressure breathing or even a cough (2,3,15). Further, pulmonary hypertension resulting from hypoxic pulmonary vasoconstriction as a consequence of altitude exposure (15) or following mediator release caused by VGE may also elevate RAP above LAP and contribute to an atrial pressure gradient reversal.

Altitude decompression resulting in the formation of venous bubbles and decompression illness has occurred for many years and is likely to continue as aircraft altitude capability increases. Continued exposure of individuals with a PFO to these environments requires a better understanding of their hemodynamic consequences.

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REFERENCES

1. Adler HF. Neurocirculatory collapse at altitude. Randolph AFB, TX: USAF School of Aviat. Med., un-numbered report.
2. Alexander JA, Rembert JC, Sealy WC, Greenfield JC. Shunt dynamics in experimental atrial septal defects. J. Appl. Physiol. 1975; 39:281–5.
3. Black S, Cucchiara RF, Nishimura RA, Michenfelder JD. Parameters affecting occurrence of paradoxical air embolism. Anesthesiology 1989; 71:235–41.
4. Black S, Muzzi DA, Nishimura RA, Cucchiara RF. Preoperative and intra operative echocardiography to detect right-to-left shunt in patients undergoing neurosurgical procedures in the sitting position. Anesthesiology 1990; 72:436–8.
5. Braunwald E, Brockenbrough EC, Frahm CJ, Ross Jr. JR. Left atrial and left ventricular pressures in subjects without cardiovascular disease. Circulation 1961; 24:267–9.
6. Braunwald E, Frahm CJ. Studies on Starling's law of the heart. IV observation on the hemodynamic functions of the left atrium in man. Circulation 1961; 24:633–42.
7. Butler BD. Cardiopulmonary effects of decompression bubbles: physiology of bubbles in the pulmonary and systemic circulation. In: Pilmanis AA, ed. USAF special report: hypobaric decompression sickness. Brooks AFB, TX: Air Force Systems Command 1992:53–82.
8. Butler BD, Hills BA. The lung as a filter for microbubbles. J. Appl. Physiol. 1979; 47:537–43.
9. Butler BD, Hills BA. Transpulmonary passage of venous air emboli. J. Appl. Physiol. 1985; 59:543–7.
10. Butler BD, Conkin J, Luehr S. Pulmonary hemodynamics, extravascular lung water and residual gas bubbles following low dose venous gas embolism in dogs. Aviat. Space Environ. Med. 1989; 60:1178–82.
11. Butler BD, Katz J. Vascular pressures and passage of gas emboli through the pulmonary circulation. Undersea Biomed. Res. 1988; 15:203–9.
12. Clark JB, Hayes GB. Patent foramen ovale and type II altitude decompression sickness. [Abstract]. Aviat. Space Environ. Med. 1991; 62:445.
13. Cucchiara RF, Nishimura RA, Black S. Failure of preoperative echo testing to prevent paradoxical air embolism: report of two cases. Anesthesiology 1989; 71:604–7.
14. Fryer DI. Subatmospheric decompression sickness in man. Slough, UK: Technivision Services, 1969: AGARDograph No. 125.
15. Garrett JL. The role of patent foramen ovale in altitude-induced decompression sickness. In: Pilmanis AA, ed. The proceeding of the 1990 hyperbaric decompression sickness workshop, Brooks AFB, TX: Air Force Systems Command, 1992; A1-SR-1992-0005:81–93.
16. Guggiari M, Lechat P, Garen-Colonne C, Fusciardi J, Viars P. Early detection of patent foramen ovale by two-dimensional contrast echocardiography for prevention of paradoxical air embolism during sitting position. Anesth. Analg. 1988; 67:192–4.
17. Hagen PT, Scholz DG, Edwards WD. Incidence and size of patent foramen ovale during the first 10 decades of life: an autopsy study of 965 normal hearts. Mayo Clin. Proc. 1984; 59:17–20.
18. Konstadt SN, Louie EK, Black S, Rao TLK, Scanlon P. Intraoperative detection of patent foramen ovale by transesophageal echocardiography. Anesthesiology 1991; 74:212–16.
19. Lechat P, Mas JL, Lascault G, et al. Prevalence of patent foramen ovale in patients with stroke. N. Engl. J. Med. 1988; 318: 1148–52.
20. Lynch JJ, Schuchard GH, Gross CM, Wann LS. Prevalence of right-to-left atrial shunting in a healthy population: detection by valsalva maneuver contrast echocardiography. Am. J. Cardiol. 1984; 53:1478–80.
21. Marquez J, Sladen A, Gendell H, Boehnke M, Mendelow H. Paradoxical cerebral air embolism without an intracardiac septal defect. J. Neurosurg. 1981; 55:997–1000.
28. Mehta M, Sokoll MD. Relation of right and left atrial pressure during venous air embolism. Anesthesiology 1981; 55:A238.
23. Moon RE, Camporesi EM. Right-to-left shunting and decompression sickness. Undersea Biomed. Research 1988; 15(Suppl):18.
24. Moon RE, Kisslo JA, Massey RW, Fawcett TA, Theil DR. Patent foramen ovale (PFO) and decompression illness. Undersea Biomed. Res. 1991; 18(Suppl):15.
25. Niden AH, Aviado DM. Effects of pulmonary embolism on the pulmonary circulation with special reference to arteriovenous shunts in the lung. Circ. Res. 1956; 4:67–73.
26. Pearson AC, Labovitz AJ, Tatineni S, Gomez CR. Superiority of transesophageal echocardiography in detecting cardiac source of embolism in patients with cerebral ischemia in uncertain etiology. J. Am. Coll. Cardiol. 1991; 17:66–72.
27. Powell MR, Spencer MP, von Ramm O. Ultrasonic surveillance of decompression. In: Bennett PB, Elliott DH, eds. The physiology and medicine of diving. 3rd ed. London: Bailliere Tindall 1982:404–34.
28. Rafferty TD. Intraoperative transesophageal saline-contrast imaging of flow-patent foramen ovale. Anesth. Analg. 1992; 75: 475–80.
29. Spencer MP. Decompression limits for compressed air determined by ultrasonically detected blood bubbles. J. Appl. Physiol. 1976; 40:229–35.
30. Vik A, Brubakk AO, Hennessy TR, Jenssen BM, Ekker M, Slrdahl SA. Venous air embolism in swine: transport of gas bubbles through the pulmonary circulation. J. Appl. Physiol. 1990; 69:237–44.
31. Vik A, Jenssen BM, Brubakk AO. Paradoxical air embolism in pigs with a patent foramen ovale. Undersea Biomed. Res. 1992; 19:361–74.
32. Wilmshurst PT, Byrne SC, Webb-Peploe MM. Relation between interatrial shunts and decompression sickness in divers. Lancet 1989; 2:1302–5.