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Positive Pressure Inspiration Differentially Affects Right and Left Ventricular Outputs in Postoperative Cardiac Surgery Patients

Paul C.M. Van den Berg, Cornelis A. Grimbergen, Joseph A.E. Spaan, and Michael R. Pinsky

Purpose: The purpose of this study was to determine the dynamic changes in right ventricular (RV) and left ventricular (LV) output during positive airway pressure inspiratory hold maneuvers so as to characterize the interaction of processes in creating steady-state cardiac output during positive pressure ventilation.

Materials and Methods: We examined the disparity of RV and LV outputs at 5 seconds (early) and 20 seconds (late) into a 25-second inspiratory hold maneuver in 14 subjects in the intensive care unit immediately following coronary artery bypass surgery. RV output was measured by the thermodilution technique, whereas LV output was measured by the arterial pulse contour method. RV and LV volumes were also measured by thermal and radionuclide ejection fraction techniques, respectively.

Results: As P_{aw} was progressively increased from 0 to 20 cm H₂O in sequential inspiratory hold maneuvers, both RV and LV outputs changed differently both at 5 seconds and 20 seconds into the inspiratory hold maneuvers. When expressed as change in cardiac output (L/min) for every cm H₂O P_{aw} increase relative to end-expiratory values, RV output increased at 5

seconds (0.05 ± 0.15 L/min) then decreased at 20 seconds (-0.08 ± 0.21 , $P < .05$). LV output decreased slightly at 5 seconds (-0.14 ± 0.22) and did not change from this minimal depressed level at 20 seconds ($P < .05$). Changes in RV and LV output were paralleled by changes in RV and LV end-diastolic volumes, respectively.

Conclusion: Positive pressure inspiration induces time-dependent changes in central hemodynamics, which are dissimilar between RV and LV function. Initially, inspiration increases RV output but decreases LV output, such that intrathoracic blood volume increases. However, sustained inspiratory pressures induce proportionally similar decreases in both RV and LV outputs. Thus, the hemodynamic effects of positive pressure ventilation will depend on the degree of lung inflation, the inspiratory time, and when measurements are made within the ventilatory cycle. These data also suggest that positive pressure ventilation with up to 20 cm H₂O P_{aw} does not significantly impair ventricular performance in humans.

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THE APPLICATION of positive pressure ventilation can have significant hemodynamic effects.^{9,11,14,18,53} Prior studies on the hemodynamic effects of intermittent positive pressure ventilation (IPPV) and positive end-expiratory pressure (PEEP) suggest that decreases in cardiac output that are usually seen are paralleled by decreases in intrathoracic blood volume owing to the associated decrease in systemic venous return.^{5,18} Furthermore, the decrease in cardiac output is proportional to the increase in mean airway pressure (P_{aw}).¹⁸ These conclusions are often derived from hemodynamic comparisons made between steady-state control conditions off-PEEP and on-PEEP conditions.³⁷ However, positive pressure inspiration may not

affect the right and left ventricles equally. Nor may dynamic changes in intrathoracic blood volume be accurately modeled by analyses of steady-state hemodynamics. Recent animal studies suggest that continuous positive airway pressure (CPAP) and PEEP may not induce hemodynamically significant decreases in systemic venous return despite inducing increases in right atrial pressure (P_{ra}).¹³ However, these observations have not been duplicated in humans. In part, duplication of such analyses in humans is hindered by difficulties in measuring instantaneous changes in right ventricular (RV) and left ventricular (LV) outputs and function during ventilation.

When P_{aw} and lung volume are increased, some determinants of RV and LV performance may be altered in the same direction, whereas others may be altered in opposite directions. For example, both ventricles are subjected to the same extrinsic compression by the expanding lungs, possibly increasing ventricular interdependence.^{6,10,41,54,57} However, positive pressure inspiration may increase pulmonary vascular resistance,⁵² but the associated increase in intrathoracic pressure will decrease LV afterload augmenting LV ejection.⁸ Thus, increases

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in lung volume and intrathoracic pressure may initiate intravascular volume shifts, which result in a transient dissimilarity between RV and LV output.

Accordingly, we examined the transient disparity between RV and LV outputs after observing stepwise increases in P_{aw} induced by airway inflation. Taking into account the time constants of the pulmonary and systemic vascular beds, we chose to examine differential RV and LV volumes and outputs at 5 and 20 seconds into an inspiratory hold maneuver.¹⁸ This analyses allowed us to examine both early and late cardiovascular changes during inspiratory hold maneuvers.

MATERIALS AND METHODS

Fourteen postoperative cardiac surgery patients were selected for the study. The study was approved by the ethical committee for human experimentation of the hospital, and all patients gave informed consent before surgery. No complications occurred as a result of the study. All patients underwent uncomplicated coronary artery bypass grafting, were functionally and clinically free of congestive heart failure, and had a normal preoperative contraction pattern on left ventriculography.

Patients were excluded from the study if they had an LV end-diastolic pressure >15 mm Hg, LV ejection fraction $<50\%$, atrioventricular conduction defects, arrhythmias, unstable angina pectoris, profoundly impaired myocardial pump function, or a preoperative diagnosis of myocardial infarction. All subjects had no more than mild obstructive pulmonary disease (forced expiratory volume 1 second [FEV₁] $>75\%$ of expired vital capacity). None of the subjects received β -adrenergic receptor blocking agents at the time of the study. The mean age of the 14 subjects was 59 ± 9 years, and their mean weight was 78 ± 11 kg.

A randomly selected subgroup of six subjects was checked by transesophageal echocardiography at zero and 20 cm H₂O of P_{aw} to evaluate whether an increase in P_{aw} to 20 cm H₂O resulted in a pressure-dependent tricuspid insufficiency. In none of these subjects could a P_{aw} -dependent tricuspid insufficiency be detected. As a standard measure in all 14 subjects, the P_{ra} wave form was also evaluated to detect patterns consistent with tricuspid insufficiency. In none of the subjects was a pressure-dependent tricuspid valve insufficiency wave form seen.

The patients were instrumented with systemic arterial and pulmonary arterial catheters before the start of the surgical procedure to collect blood samples and measure pressures. A standard lead II ECG was used to monitor heart rate and detect arrhythmias. All patients were receiving controlled mechanical ventilation with oxygen-enriched air. Before the start of the experiments, arterial blood gases were collected anaerobically and measured (Radiometer ABL-3, Copenhagen, Denmark) and ventilator settings were adjusted to maintain an $SpO_2 >96\%$, and a $PaCO_2$ between 35 and 45 mm Hg. To prevent a cold-induced reflex of the airways, care was taken to keep the temperature of inspired air at 34°C .²³ At the same time, this prevented a drift of the baseline temperature of the pulmonary artery thermistor.²⁵ RV ejection fraction (EF_{RV}) was measured using a fast-response thermistor pulmonary arterial catheter,

which has been validated against radionuclide techniques.¹⁹ Vascular and airway pressure measurements were made using high-fidelity transducers (HP Quartz transducers, Palo Alto, CA) and recorded on line as well as displayed on a video monitor (HP monitor 78342A, Palo Alto, CA) with a zero accuracy of ± 1 mm Hg and a full-scale accuracy of $+3\%$ after calibration. Pulmonary artery occlusion pressure (P_{pao}) measured at end-expiration was used as an estimate of LV end-diastolic pressure as validated by others.^{4,12,24} When P_{pao} was measured, it was done during inflation hold maneuvers in which cardiac output measures were not simultaneously measured. Systemic blood pressure was measured from a radial artery catheter. The intra-abdominal pressure (P_{abd}) was measured via a transurethral bladder catheter according to a technique described by Kashtan et al²⁶ and validated in both animals and humans.^{21,22}

Arterial Pulse Contour Method

A pulse contour method was used for the determination of instantaneous LV output (CO₁). The basic principle of this method is the analysis of the arterial pulse pressure profile. This method of determining cardiac output assumes a constant relationship between arterial pressure, aortic blood flow, and LV stroke volume.^{27,34} The pulse contour method has been compared with other cardiac output measuring methods, both in animals and humans.^{27,40,46,47,50} The correlation coefficient between the thermodilution and the pulse contour method is reported as .90.⁴⁰ We used the specific method of Wesseling et al.^{55,56} The advantage of this pulse contour method, compared with other methods,^{27,34} is that it adjusts for changes in mean arterial pressure, heart rate, and age-dependent characteristics of aorta compliance. Using this method, the systolic area of the arterial pressure waveform is integrated and multiplied by the characteristic impedance of the aorta. Because the characteristic impedance of the aorta of each subject was not known, it was cross-referenced and calibrated by thermodilution cardiac output method during periods of prolonged apneic steady states (15 seconds). During such a steady state, this cardiac output value represents both RV and LV output, whereas during non-steady state, the thermodilution method only represents RV cardiac output (CO_r). The computation constant of the pulse contour method was then adjusted so that the thermodilution method and pulse contour method gave the same cardiac output results during apneic baseline measurements.

Nuclear Stethoscope Method

Relative changes of LV end-diastolic volume were measured using a nuclear probe (Nuclear Stethoscope, Bois Inc., Cleveland, OH). The nuclear probe is a nonimaging scintillation probe with a maximum count rate capacity of 140,000 counts/sec. Recordings of counts over the precordium were made of a 99m-technetium compound in the vascular pool. The high count rate of this marker allows the continuous beat-to-beat analysis of LV volume changes. Positioning of the nonimaging probe over the precordium requires orientation of the detector based on stroke counts (end-diastolic minus end-systolic) and average counts (end-diastolic plus end-systolic divided by two) as recorded by the probe. The LV region of interest was chosen as the position with the maximum ratio of stroke counts to average counts. The background region of interest is chosen as a position immediately inferolateral to the LV region of interest, where

stroke counts are minimal and average counts begin to decrease as previously described.³ This technique was used to estimate LV ejection fraction, which, when interfaced with CO₂-derived stroke volume data during apneic steady-state conditions, allowed for calculation of baseline LV end-diastolic volume as the ratio of LV ejection fraction to stroke volume. Similarly, the ratio of this dynamically changing LV ejection fraction to matched aortic pulse contour-derived stroke volume estimates allowed calculation of beat-to-beat changes in LV end-diastolic volume during inspiratory hold maneuvers.

Protocol

Patients were anaesthetized with high-dose fentanyl. This anesthetic technique was used because of its stabilizing effects on the cardiovascular system during both the intraoperative and postoperative intervals.³⁴ After the coronary bypass operation, all patients were transported to the intensive care unit, and after a stabilization period of at least 2 hours and at maximum 5 hours, a baseline hemodynamic analysis was performed. At that moment all hemodynamic variables (P_{ra} , P_{pa} , P_{pao} , CO_2 , EF_{rv} , heart rate, and systemic blood pressure) had to be within 10% of the therapeutic goals determined by the operating team, otherwise the patient was not included in the study. All 14 subjects met these criteria. The experiments were started when the central body temperature was at least 37°C. During the experiments, all subjects were still under the sedative effects of fentanyl given during the operation.

The protocol consisted of repeated inspiratory hold maneuvers of 25 seconds duration. These inspiratory hold maneuvers were separated by 1-minute intervals to regain the same steady-state situation as before the first inspiratory hold. Resumption of a stable baseline was documented by restoration of all measured hemodynamic variables to within 10% of their initial baseline values. Then, the next maneuver was performed, with an inflation volume 250 mL greater than during the previous maneuver. In this way, a series of maneuvers resulted in a stepwise increase in both P_{aw} and lung volume. During the first two duplicate inspiratory hold maneuvers, no gas was inflated in the lungs and the resultant P_{aw} equaled ambient pressure. The hemodynamic measurements performed during these maneuvers were used to derive the baseline values of all variables against which changes induced by increased P_{aw} were compared. Lung inflation was performed with the same F_{IO_2} used to ventilate the subject. Accuracy of the P_{pao} data during inspiration as not reflecting West zone 1 conditions was validated by the associated increase in P_{pao} being less than the increase in P_{aw} .

Each individual inflation challenge was divided into four phases as described in Fig 1. Phase I started at end-expiration and represents the pre-inflation period. In this period, the electronic sampling of data was started. Data sampled during this period were used to evaluate the hemodynamic status of the subject, and to evaluate whether hemodynamic deterioration outside the 10% range, as described in the protocol, had taken place. During phase II, an extra volume of gas was inflated in the lungs and created a peak pressure in the trachea. After this peak pressure, phase III started at the moment a plateau in P_{aw} had been reached. The height of the plateau P_{aw} was determined by the inflated volume, the functional residual capacity, and the compliance of the lungs and chest wall. All comparisons of hemodynamic and P_{aw} data were made between baseline values during phase I and 5- or 20-second measured values during

Fig 1. Time course of one inspiratory hold maneuver showing some of the measured variables used to evaluate the effects of an increased P_{aw} on the circulatory system. Data collection starts during a stable apneic phase I. In this example, 1000 mL of oxygen-enriched air was inflated in the lungs at $t = 3$ seconds to start phase II. After about 1 second, a new inflation state is achieved, which is phase III. The increase in P_{aw} (cm H₂O) is transmitted to the right atrium (P_{ra}) (mm Hg), the pulmonary artery (P_{pa}) (mm Hg), the systemic circulatory system (P_{ar}) (mm Hg), and the abdominal cavity (P_{abd}) (mm Hg). Data are collected during phase III. Sharp peaks in pressure readings are artifacts caused by the automatic thermodilution cardiac output syringe. Cardiac output thermodilution measurement starts approximately 5 seconds after P_{aw} has been increased. Following removal of the increased airway pressure, lung volumes rapidly decrease during phase IV.

phase III. The maximal plateau P_{aw} we strove for was 20 cm H₂O. Phase IV describes the period in which P_{aw} was allowed to return to its pre-inspiratory pressure by passive exhalation of the extra volume from the lungs.

The effect of an increase in P_{aw} was evaluated after the pressure peak caused by the inflation with gas was passed and when the P_{aw} had reached a plateau. In practice, all data used for further analysis were derived either 5 to 6 or 20 seconds after lung inflation was started. The tracheal pressure was measured at the entrance of the endotracheal tube and was used to represent P_{aw} . Two different thermodilution curves were recorded in phase III, one initiated at 5 to 6 seconds and another initiated at 20 seconds after the P_{aw} had hit a plateau. Each thermal injection was done during a separate inspiratory hold maneuver. All thermal decay profiles were inspected for an exponential thermal decay and return to its baseline value. If this was not the case, the measurements were discarded and the procedure repeated.

A time of 1 minute between consecutive inspiratory hold maneuvers was chosen because the time constant of volume shifts between the thoracic, abdominal, and peripheral compartments of the circulation is well within the order of 1 minute.²⁷ Between the inspiratory hold maneuvers, the hemodynamic status of the subject was controlled with fluid infusions as

required by monitoring P_{ra} (RV filling pressure) and P_{pao} . In this way, subjects were kept in a hemodynamic steady state throughout the protocol. Data from three of the subjects were discarded because of inaccurate pressure measurements. SaO_2 was continuously measured with a pulse oximeter (Nelcor) and end-tidal CO_2 levels were checked with a capnograph (Hewlett-Packard, Palo Alto, CA). During all experiments SaO_2 did not change and the end-expiratory CO_2 was stable within $\pm 2\%$.

Data Analysis

All data were digitalized with a sample frequency of 100 Hz, the band width of the used signals being less than 50 Hz. The signals were converted with a 12 bits resolution and were stored

on hard disk for later evaluation. Sampling of data started just before the beginning of an inspiratory hold and was stopped 4 seconds after termination of phase III of the maneuver.

The analysis of the data was concentrated on the changes in the hemodynamic variables induced by the increase in P_{aw} . Linear regression analysis was performed, using the method of least squares. The effect of changes in P_{aw} on the measured hemodynamic variables (CO_l , CO_r , P_{ra} , PCWP) was made over the entire range of P_{aw} changes and found to be linear. However, for illustration purposes, changes between 0 and 20 cm H_2O are described in the Figs 1 through 5. Analyses of the P_{aw} effects on the measured hemodynamic variables were performed with repeated measurement analysis of variance using a post hoc

Fig 4. Relative changes of RVEDV after 5 seconds of increased P_{aw} per cm H_2O P_{aw} in 14 patients (A) and the same for LVEDV (B).

Student-Neuman-Keules test (BMDP-V statistical package, Berkeley, CA). Statistical significance reports differences corresponding to a $P < .05$ unless otherwise stated. Data are presented as mean $\pm$ SD.

Fig 5. Ratio of the changes in pulmonary artery pressure and in pulmonary capillary wedge pressure caused by an increase in P_{aw} . P_{pa} and pulmonary capillary wedge pressure (PCWP or P_{pao}) were measured between 15 and 20 seconds after P_{aw} has been increased. Lines connect the values obtained in the same patient.

RESULTS

The baseline hemodynamic data of the 14 subjects before starting the protocol are given in Table 1. An example of the relation between the inflated lung volume and P_{aw} is given in Fig 2. The increase in P_{aw} is transmitted to intravascular structures within the thorax and abdominal cavity, as illustrated during one inspiratory hold maneuver. Per patient, a mean of 7 ± 2 duplicate inflations of the lungs were performed before P_{aw} increased to approximately 20 cm H_2O . The P_{aw} range during the experiments ranged from 0 to 19.01 ± 2.7 cm H_2O .

Lung inflation induced by increases in P_{aw} increased the intrathoracic vascular pressures and differentially altered the RV and LV outputs in a time-dependent fashion. From a baseline CO_r of 5.72 ± 1.5 L/min, right-sided cardiac output, as measured by CO_r 5 seconds after the initiation of the plateau phase, increased 0.05 ± 0.15 L/min/cm H_2O . This slight increase in CO_r was significantly different from the slight decrease in CO_l , simultaneously measured by the arterial pulse contour method. The change in CO_l was -0.14 ± 0.22

Table 1. Baseline Hemodynamic Data Before Lung Inflation

Subject	MAP (mm Hg)	P _{pa} (mm Hg)	P _{ra} (mm Hg)	P _{abd} (mm Hg)	CO _r (L/min)	EF _{rv} (%)	CI (L/min/m ²)	SVI	EDVI	PCWP
1	97	26	9	17	6.51	0.4	3.13	29	73	14
2	59	16	7	8	5.22	0.59	2.31	36	62	12
2	70	19	9	15	3.23	0.5	1.75	25	50	11
4	69	26	12	11	4.88	0.32	2.42	33	102	18
5	55	23	12	9	6.28	0.46	3.95	41	89	16
6	91	18	8	8	6.75	0.4	3.29	39	98	12
7	83	29	9	25	4.31	0.30	2.07	24	80	13
8	43	21	3	10	8.25	0.45	3.77	36	79	13
9	39	20	10	10	6.55	0.30	3.27	80	129	17
10	84	17	6	4	8.24	0.49	3.70	37	76	16
11	43	24	10	11	7.60	0.40	3.82	38	94	11
12	47	17	9	16	6.45	0.45	3.26	33	74	15
13	71	20	9	24	7.00	0.48	3.27	42	87	14
14	71	19	0	8	5.21	0.38	2.58	33	86	16
Mean ± SD	75 ± 15	21 ± 5	9 ± 4	9 ± 6	5.74 ± 1.52	0.41 ± 0.09	2.93 ± 0.70	36 ± 10	88 ± 21	14 ± 2

Hemodynamic profile of 14 patients, whose data were used for analysis.

Abbreviations: MAP, mean systemic blood pressure; P_{pa}, mean pulmonary artery pressure; P_{ra}, right atrial pressure; P_{abd}, abdominal pressure; CO_r, right ventricular cardiac output; EF_{rv}, right ventricular ejection fraction; CI, cardiac index; SVI, stroke volume index; EDVI, end-diastolic volume index; PCWP, pulmonary capillary wedge pressure.

L/min/cm H₂O ($P < .001$). These directionally dissimilar changes in RV and LV output decreased at 20 seconds into the inspiratory hold maneuvers. The change in CO_r from 5 to 20 seconds reversed direction decreasing significantly compared with baseline by -0.08 ± 0.12 L/min/cm H₂O ($P < .05$) (Fig 2). Whereas the mean CO_l did not change significantly from 5 to 20 seconds into the inspiratory hold maneuver (Fig 3), with a similar gain of CO_l of 0.16 ± 0.1 L/min/cm H₂O as P_{aw} increased compared with baseline CO_l. The correlation between changes in outflows from either ventricle and P_{aw} increases was linear across the entire P_{aw} spectrum at each time point, such that doubling the increase in P_{aw} doubled the effect it had on the measured variable and vice versa.

The changes in RV and LV outflows at 5 and 20 seconds into the pressure plateau phase of the inspiratory hold maneuver were associated with concomitant changes in ventricular volumes. After 5 seconds of increased P_{aw} RV end-diastolic volume increased, whereas LV end-diastolic volume decreased ($P < .05$) (Fig 5).

The increase in P_{aw} also increased in P_{pa} and P_{pao}. The increase in P_{pa} was 0.67 ± 0.16 mm Hg/cm H₂O, although the increase in P_{pao} was 0.40 ± 0.10 mm Hg/cm H₂O. The increase in P_{pa} was always greater than the increase in P_{pao}. Note that the P_{pao} measures were made in only seven subjects and were performed in between the thermodilution cardiac output measurements.

DISCUSSION

Our study demonstrates that positive-pressure inspiration induces time-dependent differential effects on RV and LV output. These data demonstrate that RV filling, CO_r, and intrathoracic blood volume increase during positive-pressure inspiratory effort of up to a P_{aw} of 20 cm H₂O. Although CO_l was less than apneic baseline values at both 5 and 20 seconds into an inspiratory hold maneuver, these decreases were most pronounced at 5 seconds returning toward apneic values at 20 seconds. These dynamic changes suggest a complex process by which mean cardiac output is determined by ventilatory phase-dependent changes in both RV and LV function. Although our study could not separate out the selective effects of increases in P_{aw} from increases in lung volume, these data demonstrate that mean cardiac output is not impaired by up to 20 cm H₂O P_{aw} increases to levels which would be clinically relevant (Table 2). Fessler et al¹³ demonstrated in dogs that the application of up to 15 cm H₂O PEEP did not alter the gradient for venous return. In support of these findings, they also observed a constant cardiac output. Their data agree with the flow data in our study in postoperative cardiac surgery patients.

Many prior studies in animals^{31,41,45} and humans^{11,36} have demonstrated that positive pressure inspiration decreases cardiac output. Braunwald et al⁵ demonstrated that PEEP decreased cardiac out-

Table 2. Mean Hemodynamic Data During Apneic CPAP

P _{aw} range	P _{aw} (cm H ₂ O)	P _a (mm Hg)	P _{pa} (mm Hg)	P _{ra} (mm Hg)	P _{abd} (mm Hg)	CO _r (L/min)	RV _{ef}	C _i	P _{pao} (mm Hg)	HR (beats/min)
0-3	0.42 ± 0.65	76.1 ± 11.8	21 ± 3.35	8.67 ± 2.69	9.52 ± 6.89	5.66 ± 2.28	0.4 ± 0.09	2.85 ± 0.96	11.5 ± 3.54	80.4 ± 12.9
3-6	5.08 ± 0.71	77.7 ± 10.5	22.1 ± 6.46	8.97 ± 2.32	11.5 ± 7.41	5.46 ± 1.06	0.41 ± 0.07	2.79 ± 0.48	11.7 ± 1.87	7.5 ± 13.1
6-9	7.66 ± 0.66	76.6 ± 14.2	23.7 ± 5.95	8.76 ± 3.61	8.85 ± 6.38	5.73 ± 1.32	0.39 ± 0.08	2.88 ± 0.66	11.2 ± 5.18	3.2 ± 13.5
9-12	10.6 ± 0.95	71 ± 16.7	25.9 ± 4.52	11.6 ± 3.17	11.9 ± 7.45	5.88 ± 1.89	0.4 ± 0.11	2.95 ± 0.81	12.3 ± 1.71	81.8 ± 14.4
12-15	13.7 ± 0.83	73.8 ± 16.1	27 ± 5	12.6 ± 2.86	11.7 ± 7.88	5.9 ± 1.94	0.4 ± 0.1	2.95 ± 0.85	13.7 ± 3.05	79.9 ± 13.8
15-18	16.4 ± 0.72	71.8 ± 16.2	28.8 ± 5.15	13.3 ± 2.59	12.8 ± 7.57	6.17 ± 1.81	0.41 ± 0.09	3.12 ± 0.79	14.9 ± 3.07	82.3 ± 13.2
18-21	19.5 ± 1.11	72.3 ± 20.1	30.5 ± 4.91	14.8 ± 3.53	13.3 ± 8.91	6.29 ± 1.71	0.43 ± 0.09	3.23 ± 0.77	18.7 ± 3.06	82.4 ± 13.4

Note: Pooled mean data for all subjects grouped by date achieving the desired P_{aw} threshold for each patient. Data are presented as mean ± SD. N = 14.

put by decreasing central blood volume. When cardiac output was returned to pre-PEEP levels by the infusion of a vasoactive compound, central blood volume also returned to baseline values despite the continued application of PEEP. Other studies have shown that the decrease in cardiac output is proportional to the increase in P_{aw}¹⁸ and presumably is caused by a decrease in both systemic venous return and intrathoracic blood volume. However, the mechanisms leading to this decrease in cardiac output are not well described.

Studies on the transient effects of positive pressure inspiration have contributed to this understanding because dynamic shifts in intrathoracic blood volume may not be reflected in steady-state blood pool volumes or mean blood flow but reflect the responses creating these steady-state conditions. Transient changes in venous return and intrathoracic blood volume have been described for selective increases in both P_{aw} and intrathoracic pressure induced by a Valsalva maneuver.⁸ However, a Valsalva maneuver is dissimilar to an inspiratory hold maneuver, where both intrathoracic pressure and lung volume increase. This distinction may be important because increasing lung volume can result in either an increase⁴² or a decrease³⁶ in lung blood volume. Morgan et al³³ noted in dogs that large tidal volume positive pressure inspiration increased pulmonary venous blood flow. Brower et al⁷ expanded these observations by demonstrating that lung blood volume shifts and pulmonary venous blood flow changes during inspiration depend on the pre-existent alveolar distention pressure (transpulmonary pressure) and the relative distention of the alveolar and extra-alveolar vascular spaces before inflation. In relatively under-resuscitated states, intrathoracic blood volume may increase as blood is pooled in the extra-alveolar vessels, whereas if the alveolar vessels have been distended before inspiration, increasing alveolar

pressure relative to pleural pressure will transfer blood from the alveolar to the extra-alveolar vessels increasing pulmonary venous blood flow. As transpulmonary pressure was increased in their isolated perfused canine lung model these fluid shifts became more pronounced. Our subjects were fluid resuscitated, such that they were hemodynamically stable with P_{pao} values of approximately 14 mm Hg. Furthermore, we examined the hemodynamic effects of progressive increases in lung volume and P_{aw}, thus we examined the hemodynamic effects of a wide range of transpulmonary pressures. We saw no directional changes in the 5- or 20-second response of either CO_r or CO_i across this range of lung distention pressures. Thus, our data do not support the hypothesis that the differential effects of positive pressure inspiration in our subjects reflects changes in intrathoracic vascular capacitances.

We favor the hypothesis that the instantaneous changes in blood flow reflect a combined effect of increasing lung volume on P_{abd} and thus increasing RV distention. The effect of positive pressure inspiration on RV volume is variable. RV volume has been reported to decrease,^{9,11,14,31,53,57} to be unaffected, and to increase during positive pressure inspiration.^{44,45,51} The mechanisms leading to these directionally different changes in RV volume are not agreed on. The increase in RV volume has been attributed to an increase both pulmonary vascular resistance^{2,10,20,29,38,49} and RV filling pressure. Whereas, a decrease in RV volume has been ascribed to a decrease in both RV compliance⁴³ and RV filling, the latter is caused by a decrease in venous return. Our data suggest that RV volumes remain constant or increase slightly associated with a maintenance in cardiac output. Our data do not support either of the two above-proposed mechanisms for RV volume change.

The reaction of the left ventricle to positive

pressure inspiration is also a matter of controversy. A decrease in LV volume during sustained increases in P_{aw} has been described in both animal⁵³ and human³⁹ studies. The decrease in LV end-diastolic volume was used to explain the decrease in cardiac output seen in these studies. However, increases in intrathoracic pressure induced by positive pressure ventilation will also decrease LV afterload,⁸ and this mechanism has been invoked to explain the observed increases in cardiac output in patients with heart failure following the application of PEEP.¹⁵ Additionally, an unchanged cardiac output during a Valsalva maneuver has also been reported and ascribed to squeezing of an overloaded pulmonary circulation.^{30,35} Our data support the hypothesis that if LV afterload was affected by these positive pressure inspiratory hold maneuvers, the effect was small. More likely, the decrease in CO_1 reflects decreasing LV end-diastolic volume owing to ventricular interdependence, since RV end-diastolic volume also increased.

Limitations of the Study

Although CO_r and CO_1 are measured with different techniques, a high correlation between the two methods has been established.^{3,4,12,24,28,58} Moreover, if the compliance of the vascular tree changed during the inspiratory hold maneuvers, it will most likely decrease when P_{aw} increased. This would result in overestimating CO_1 by the pulse contour method. We saw a decrease in CO_1 , thus, the actual decrease in CO_1 may have been even greater than observed. However, Versprille et al⁵² demonstrated that during changes in intrathoracic pressure, the aortic pulse contour method accurately reflects CO_1 when the mean arterial pressure does not change, as was the case in our studies. Clearly, CO_r and CO_1 , although starting at similar points before inspiration, change directionally in opposite directions with inspiration, demonstrate different time-dependent (5 and 20 seconds) phase changes, and demon-

strate that markedly different forces interact to define the outputs of the two ventricles. Also, the study of either RV or LV function alone will not accurately describe the dynamic forces determining the equilibrium seen during ventilation.

A discrepancy between radial or brachial artery compared with aortic pressure has been observed in the postoperative period of cardiac surgery subjects.^{1,48} However, this post-bypass difference in central and peripheral systemic blood pressure is transient and resolves with the administration of fluid.^{16,32} Gravlee et al¹⁷ found no difference in radial, brachial, or aortic pressures 20 minutes after cardiopulmonary bypass. Finally, autonomic tone could have changes during the course of these maneuvers, minimizing any hemodynamic deterioration associated with increasing P_{aw} . However, all subjects were under significant narcotic anesthesia during the time of study. Furthermore, both heart rate and calculated peripheral vascular resistance were constant. Accordingly, this human preparation reflects a model with almost no sympathetic responsiveness. In support of the argument that our subjects were markedly suppressed in their endogenous sympathetic responsiveness, six of the subjects had a baseline MAP of 60 mm Hg or less. However, in none of them was there evidence of tissue hypoperfusion, such as lactic acidosis oliguria, ECG changes of ischemia, or subsequent organ dysfunction.

SUMMARY

Our study demonstrates a differential effect of CPAP on RV and LV output, which is phase and time dependent. These changes in outflows are not predicted from assumptions based on selective changes in only P_{ra} , pulmonary vascular resistance, or LV afterload unless one assumes that CPAP differentially alters both RV and LV preload and afterload by affecting these variables, as well as maintains the pressure gradient for venous return.

REFERENCES

1. Bazalar MG, Welch M, Golding LAR, et al: Comparison of brachial and radial artery pressure monitoring in patients undergoing coronary artery bypass surgery. *Anesthesiology* 73:38-45, 1990
2. Bemis CE, Serur JR, Borkenhagen D, et al: Influence of right ventricular filling pressure on left ventricular pressure and dimension. *Circ Res* 34:498-504, 1974
3. Berger HJ, Davies RA, Batsford WP, et al: Beat-to-beat left ventricle performance assessed from the equilibrium cardiac blood pool using a computerized nuclear probe. *Circulation* 63:133-142, 1981
4. Bouchard RJ, Gault JH, Ross JR Jr: Evaluation of pulmonary arterial end-diastolic pressure as an estimate of left ventricular end-diastolic pressure in patients with normal and abnormal left ventricular performance. *Circulation* 44:1072-1079, 1971
5. Braunwald E, Binion JT, Morgan WL, et al: Alterations in central blood volume and cardiac output induced by positive pressure breathing and counteracted by metraminol (Aramine). *Circ Res* 5:670-675, 1975
6. Brookhart JJ, Boyd TE: Local differences in intrathoracic

pressure and their relation to cardiac filling pressure in the dog. *Am J Physiol* 148:434-444, 1947

7. Brower R, Wise RA, Hassapoyannes C, et al: Effect of lung inflation on lung blood volume and pulmonary venous flow. *J Appl Physiol* 58:954-963, 1985

8. Buda AJ, Pinsky MR, Ingels NB, et al: Effects of intrathoracic pressure on left ventricular performance. *N Engl J Med* 301:453-459, 1979

9. Cournand A, Motley ML, Werko L, et al: Physiological studies of the effects of intermittent positive-pressure breathing on cardiac output in man. *Am J Physiol* 152:162-174, 1948

10. Culver BH, Marini JJ, Butter J: Lung volume and pleural pressure effects on ventricular function. *J Appl Physiol* 50:630-635, 1981

11. Dhainaut JF, Devaux JY, Monsallier JF, et al: Mechanisms of decreased left ventricular preload during continuous positive pressure ventilation in ARDS. *Chest* 90:74-80, 1986

12. Falicov RE, Resnekov L: Relationship of the pulmonary artery diastolic pressure to left ventricular end-diastolic and mean filling pressure in patients with and without left ventricular dysfunction. *Circulation* 42:65-73, 1970

13. Fessler HE, Brower RG, Wise RA, et al: Effects of positive end-expiratory pressure on the gradient for venous return. *Am Rev Respir Dis* 143:19-24, 1991

14. Fewell JE, Abendschein DR, Carlson CJ, et al: Mechanisms of decreased right and left ventricular end-diastolic volumes during continuous positive-pressure ventilation in dogs. *Circ Res* 47:467-472, 1980

15. Grace MP, Greenbaum DM: Cardiac performance in response to PEEP in patients with cardiac dysfunction. *Crit Care Med* 20:358-360, 1982

16. Gravlee GD, Brauer SD, O'Rourke MF, et al: A comparison of brachial, femoral and aortic intra-arterial pressures before and after cardiopulmonary bypass. *Anaesth Intensive Care* 17:305-311, 1989

17. Gravlee GP, Wong AN, Adkins TG, et al: A comparison of radial, brachial and aortic pressures after cardiopulmonary bypass. *Journal of Cardiothoracic Anesthesia* 3:20-26, 1989

18. Goldberg HS: Control of cardiac output by the circuit, in Snyder JV, Pinsky MR (eds): *Oxygen transport in the critically ill*. Chicago, IL, Year Book Medical, 1987, pp 36-45

19. Ham HR, Franken PR, Georges B, et al: Evaluation of the accuracy of steady-state Krypton-81m method for calculating right ventricle ejection fraction. *J Nucl Med* 27:593-601, 1986

20. Hobelmann CF, Smith DE, Virgilio RW, et al: Hemodynamic alterations with positive end-expiratory pressure: The contribution of the pulmonary vasculature. *J Trauma* 15:951-959, 1975

21. Iberti TJ, Kelly KM, Gentil DR, et al: A simple technique to accurately determine intra-abdominal pressure. *Crit Care Med* 15:1140-1142, 1987

22. Iberti TJ, Lieber CL, Benjamin E: Determination of intra-abdominal pressure using a transurethral bladder catheter. *Anesthesiology* 70:47-50, 1989

23. Ingenito EP, Pichurko BM, Lafleur J, et al: Breathing pattern affects respiratory heat loss but not bronchoconstrictor response in asthma. *Lung* 169:23-34, 1990

24. Jenkins BS, Bradley RD, Brainwaite MA: Evaluation of pulmonary arterial end-diastolic pressure as an indirect estimate of left atrial mean pressure. *Circulation* 42:75-78, 1970

25. Johnson RW, Normann RA: Central venous blood tem-

perature fluctuations and thermolulution signal processing in dogs. *Ann Biomed Eng* 17:657-669, 1989

26. Kashtan J, Green JF, Parsons EQ, et al: Hemodynamic effects of increased abdominal pressure. *J Surg Res* 30:249-255, 1981

27. Kouchoukos NT, Sheppard LC, McDonald DA: Estimation of stroke volume in the dog by pulse-contour method. *Circ Res* 26:611-623, 1970

28. Lappas D, Lell WA, Gabel JC, et al: Indirect measurement of left atrial pressure in surgical patients: Pulmonary-capillary wedge and pulmonary-artery diastolic pressures compared with left-atrial pressure. *Anesthesiology* 38:394-397, 1973

29. Liebman PR, Patten MT, Manny Y, et al: The mechanism of depressed cardiac output on positive end-expiratory pressure (PEEP). *Surgery* 83:594-598, 1978

30. Little WC, Barr WK, Crawford MH, et al: Altered effect of the Valsalva maneuver on left ventricular volume in patients with cardiomyopathy. *Circulation* 71:227-233, 1985

31. Marini JJ, Culver B, Butler J: Mechanical effect of lung distention with positive pressure on cardiac function. *Am Rev Respir Dis* 124:382-386, 1981

32. Mohr R, Lavee J, Goor DA: Inaccuracy of radial artery pressure measurement after cardiac operations. *J Thorac Cardiovasc Surg* 94:286-290, 1987

33. Morgan BC, Abel FL, Mullins GL, et al: Flow-patterns in cavae, pulmonary artery, pulmonary vein and aorta in intact dogs. *Am J Physiol* 210:903-909, 1966

34. Nichols WW: Continuous cardiac output derived from the aortic pressure waveform: A review of current methods. *Biomed Eng* 8:376-379, 1973

35. Parisi AF, Harrington JJ, Askenazi J, et al: Echocardiographic evaluation of the Valsalva maneuver in healthy subjects and patients with and without heart failure. *Circulation* 54:921, 1976

36. Permutt S, Howell JBL, Proctor F, et al: Effect of lung inflation on static pressure-volume characteristics of pulmonary vessels. *J Appl Physiol* 16:64-70, 1991

37. Pinsky MR, Vincent JL, DeSmet JL: Estimating left ventricular filling pressure during positive end-expiratory pressure in humans. *Am Rev Respir Dis* 143:25-31, 1991

38. Powers SR, Mannal R, Nederio M, et al: Physiologic consequences of positive end-expiratory pressure (PEEP) ventilation. *Ann Surg* 178:265-272, 1973

39. Prewitt RM, Oppenheimer L, Sutherland JB, et al: Effect of positive end-expiratory pressure on left ventricular mechanics in patients with hypoxemic respiratory failure. *Anesthesiology* 55:409-415, 1981

40. Purschke R, Brucke P, Schulte HD: Untersuchung zur Zuverlässigkeit der Schlagvolumenbestimmung aus der Aorten-druckkurve. Teil II. Langzeitbeobachtung bei Patienten. *Der Anaesthesist* 12:525-534, 1974

41. Robotham JL, Lixfield W, Holland L, et al: The effects of positive end-expiratory pressure on right and left ventricular performance. *Am Rev Respir Dis* 121:677-683, 1980

42. Ruskin J, Backe RJ, Rembert JC, et al: Pressure-flow studies in man: Effect of respiration on left ventricular stroke volume. *Circulation* 48:79-85, 1973

43. Santamore WP, Bove AA, Heckman JL: Right and left ventricular pressure volume response to positive end-expiratory pressure. *J Appl Physiol* 15:H114-H119, 1984

44. Scharf S, Brown R: Influence of the right ventricle on canine left ventricular function with PEEP. *J Appl Physiol* 52:254-259, 1982
45. Scharf SM, Brown R, Saunders N, et al: Changes in canine left ventricular size and configuration with positive end-expiratory pressure. *Circ Res* 44:672-678, 1979
46. Smith NT, Wesseling KH: Cardiac output beat-to-beat: Evaluation of a new apparatus and method. *IRCS Journal* 2:1153-1155, 1974
47. Smith NT, Wesseling KH, Weber JAP, et al: Preliminary evaluation of a pulse contour cardiac output computer in man: Feasibility of brachial or radial arterial pressures. *Proceedings of the San Diego Biomedical Symposium* 13:107-113, 1974
48. Stern DH, Gerson JL, Allen FB, et al: Can we trust the direct radial artery pressure immediately following cardiopulmonary bypass? *Anesthesiology* 62:557-561, 1985
49. Stool EW, Mullins CB, Leskin SJ, et al: Dimensional changes of the left ventricle during acute pulmonary artery hypertension in dogs. *Am J Cardiol* 33:868-875, 1974
50. Tajimi T, Sunagawa K, Yamada A, et al: Evaluation of pulse contour methods in calculating stroke volume from pulmonary artery pressure curve (comparison with aortic pressure curve). *Eur Heart J* 4:502-511, 1983
51. Tittley JG, Fremes SE, Weisel RD, et al: Hemodynamic metabolic consequences of PEEP. *Chest* 88:4496-4502, 1985
52. Versprille A, Jansen JRC, et al: Negative effect of insufflation on cardiac output and pulmonary blood volume. *Acta Anaesthesiol Scand* 34:607-615, 1990
53. Viquerat CE, Righetti A, Suter PM: Biventricular volumes and function in patient with adult respiratory distress syndrome ventilated with PEEP. *Chest* 83:509-514, 1983
54. Wallis TW, Robotham JL, Compean R, et al: Mechanical heart-lung interaction with positive end-expiratory pressure. *J Appl Physiol* 54:1039-1047, 1983
55. Wesseling KH, de Wit B, Weber JAP, et al: A simple device for the continuous measurement of cardiac output. *Adv Cardiovasc Phys* 5:16-52, 1985 (suppl 2)
56. Wesseling KH, Smith NT, Nichols WW, et al: Beat-to-beat cardiac output from the arterial pressure pulse contour, in Feldman SA, Leigh JM, Spierdijk J (eds): *Measurement Anesthesia*. Leiden, the Netherlands, Leiden University Press 1974, pp 148-164
57. Wise RA, Robotham L, Bromberger-Barnea B, et al: The effect of PEEP on left ventricular function in right heart by passed dogs. *J Appl Physiol* 51:541-546, 1981
58. Yernault JC: Lung mechanics I: Lung elasticity. *Bulletin of the European Physiopathology and Respiratory Society* 19:28-32, 1983