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

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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 PEEP 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 PEEP 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 PEEP does not significantly impair ventricular performance in humans.

The application of positive pressure ventilation can have significant hemodynamic effects. 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. Furthermore, the decrease in cardiac output is proportional to the increase in mean airway pressure (Paw). These conclusions are often derived from hemodynamic comparisons made between steady-state control conditions off-PEEP and on-PEEP conditions. 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 (Paw). 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 Paw 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. However, positive pressure inspiration may increase pulmonary vascular resistance, but the associated increase in intrathoracic pressure will decrease LV afterload augmenting LV ejection. Thus, increases
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. This analysis allows 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 Holter monitor. Patients were excluded from the study if they had an LV end-diastolic pressure $>15$ mm Hg, LV ejection fraction $<30\%$, 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 in 1 second $[FEV_1]$ $>75\%$ of expired vital capacity). None of the subjects received $\beta$-adrenergic receptor blocking agents at the time of the study. The mean age of the 14 subjects was 59 $\pm$ 9 years, and their mean weight was 78 $\pm$ 11 kg.

A randomly selected subgroup of six subjects was checked by transesophageal echocardiography at zero and 20 cm H$_2$O of $P_{aw}$ to evaluate whether an increase in $P_{aw}$ to 20 cm H$_2$O 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 $P_{aw}$ 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 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 in 1 second $[FEV_1]$ $>75\%$ of expired vital capacity). None of the subjects received $\beta$-adrenergic receptor blocking agents at the time of the study. The mean age of the 14 subjects was 59 $\pm$ 9 years, and their mean weight was 78 $\pm$ 11 kg.

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stroke counts are minimal and average counts begin to decrease as previously described. 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 anesthetized 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. 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 (Pao2, Ppa, Pm, CO2, EF, 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 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 Pm and lung volume. During the first two duplicate inspiratory hold maneuvers, no gas was inflated in the lungs and the resultant Pm 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 Pm were compared. Lung inflation was performed with the same F1O2 used to ventilate the subject. Accuracy of the Pm data during inspiration as not reflecting West zone 1 conditions was validated by the associated increase in Pm being less than the increase in Ppa.

Each individual inflation challenge was divided into four phases as described in Fig 1. Phase I started at end-expiration and represents the pre-inspiratory 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 Pm had been reached. The height of the plateau Pm was determined by the inflated volume, the functional residual capacity, and the compliance of the lungs and chest wall. All comparisons of hemodynamic and Pm data were made between baseline values during phase I and 5- or 20-second measured values during phase III. The maximal plateau Pm we strove for was 20 cm H2O. Phase IV describes the period in which Pm 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 Pm was evaluated after the pressure peak caused by the inflation with gas was passed and when the Pm 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 Pm. Two different thermodilution curves were recorded in phase III, one initiated at 5 to 6 seconds and another initiated at 20 seconds after Pm 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. Between the inspiratory hold maneuvers, the hemodynamic status of the subject was controlled with fluid infusions as
required by monitoring $P_{ra}$ (RV taping pressure) and $P_{aer}$. 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 (Nellcor) 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 ±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 $P_{aer}$.

Linear regression analysis was performed, using the method of least squares. The effect of changes in $P_{aer}$ on the measured hemodynamic variables ($CO_2$, $CO_3$, $Pra$, $PCWP$) was made over the entire range of $P_{aer}$ changes and found to be linear. However, for illustration purposes, changes between 0 and 20 cm H$_2$O are described in the Figs 1 through 5. Analyses of the $P_{aer}$ 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$_2$O $P_{aw}$, in 14 patients (A) and the same for LVEDV (B).

Fig 5. Ratio of the changes in pulmonary artery pressure and in pulmonary capillary wedge pressure caused by an increase in $P_{aw}$. $P_{aw}$ and pulmonary capillary wedge pressure (PCWP or $P_{pwp}$) 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$_2$O. The $P_{aw}$ range during the experiments ranged from 0 to 19.01 ± 2.7 cm H$_2$O. 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$_2$O. 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

<table>
<thead>
<tr>
<th>Subject</th>
<th>MAP (mm Hg)</th>
<th>Pp (mm Hg)</th>
<th>Prr (mm Hg)</th>
<th>Pwe (mm Hg)</th>
<th>CO1 (L/min)</th>
<th>EFr (%)</th>
<th>CI (L/min/m²)</th>
<th>SVI</th>
<th>EDVI</th>
<th>PCWP</th>
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<td>9</td>
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<td>8</td>
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<td>8</td>
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<td>10</td>
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<td>14</td>
<td>71</td>
<td>19</td>
<td>0</td>
<td>8</td>
<td>5.21</td>
<td>0.38</td>
<td>2.56</td>
<td>33</td>
<td>86</td>
<td>16</td>
</tr>
<tr>
<td>Mean ± SD</td>
<td>75 ± 15</td>
<td>21 ± 5</td>
<td>9 ± 4</td>
<td>9 ± 6</td>
<td>5.74 ± 1.52</td>
<td>0.41 ± 0.09</td>
<td>2.93 ± 0.70</td>
<td>36 ± 10</td>
<td>88 ± 21</td>
<td>14 ± 2</td>
</tr>
</tbody>
</table>

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

Abbreviations: MAP, mean systemic blood pressure; Pp, mean pulmonary artery pressure; Prr, right atrial pressure; Pwe, abdominal pressure; CO1, right ventricular cardiac output; EFr, right ventricular ejection fraction; CI, cardiac index; SVI, stroke volume index; EDVI, end-diastolic volume index; PCWP, pulmonary capillary wedge pressure.

DISCUSSION

Our study demonstrates that positive-pressure inspiration induces time dependent differential effects on RV and LV output. These data demonstrate that RV filling, CO1, and intrathoracic blood volume increase during positive-pressure inspiratory effort of up to a Pwe of 20 cm H2O. Although CO1 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 Pwe from increases in lung volume, these data demonstrate that mean cardiac output is not impaired by up to 20 cm H2O Pwe 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 animals31,41,45 and humans11,36 have demonstrated that positive pressure inspiration decreases cardiac output. Braunwald et al3 demonstrated that PEEP decreased cardiac out-
Table 2. Mean Hemodynamic Data During Apneic CPAP

<table>
<thead>
<tr>
<th>Paw range (cm H2O)</th>
<th>Paw (mm Hg)</th>
<th>Pao (mm Hg)</th>
<th>Pao (mm Hg)</th>
<th>Pao (mm Hg)</th>
<th>CO2 (L/min)</th>
<th>RV (mL)</th>
<th>CI (mm Hg/min)</th>
<th>Pao (mm Hg)</th>
<th>HR (beats/min)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0-3</td>
<td>0.64 ± 0.65</td>
<td>76.1 ± 11.8</td>
<td>21 ± 1.35</td>
<td>8.67 ± 2.69</td>
<td>9.52 ± 6.89</td>
<td>5.68 ± 2.28</td>
<td>0.4 ± 0.09</td>
<td>2.85 ± 0.96</td>
<td>11.5 ± 5.34</td>
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<tr>
<td>3-6</td>
<td>5.08 ± 0.71</td>
<td>77.7 ± 10.5</td>
<td>22.1 ± 4.46</td>
<td>8.97 ± 2.32</td>
<td>11.5 ± 2.41</td>
<td>5.48 ± 1.06</td>
<td>0.41 ± 0.07</td>
<td>2.79 ± 0.48</td>
<td>11.7 ± 1.97</td>
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<tr>
<td>6-9</td>
<td>7.66 ± 0.65</td>
<td>76.8 ± 14.1</td>
<td>23.7 ± 5.95</td>
<td>8.76 ± 3.61</td>
<td>8.65 ± 0.68</td>
<td>5.73 ± 1.32</td>
<td>0.39 ± 0.08</td>
<td>0.86 ± 0.92</td>
<td>11.2 ± 5.18</td>
</tr>
<tr>
<td>9-12</td>
<td>10.6 ± 0.95</td>
<td>71 ± 16.7</td>
<td>25.9 ± 4.52</td>
<td>11.6 ± 3.17</td>
<td>11.9 ± 7.45</td>
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<td>12-15</td>
<td>13.7 ± 0.83</td>
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<td>15-18</td>
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<td>12.8 ± 7.57</td>
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<td>18-21</td>
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<td>30.5 ± 4.91</td>
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<td>0.43 ± 0.09</td>
<td>0.32 ± 0.77</td>
<td>16.7 ± 3.06</td>
</tr>
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</table>

Note: Pooled mean data for all subjects grouped by date achieving the desired Paw 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 Paw 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 Paw and intrathoracic pressure induced by a Valsalva maneuver. 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 increase or a decrease in lung blood volume. Morgan et al noted in dogs that large tidal volume positive pressure inspiration increased pulmonary venous blood flow. Brower et al 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 Paw values of approximately 14 mm Hg. Furthermore, we examined the hemodynamic effects of progressive increases in lung volume and Paw, 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 CO2 or CO1 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 Paw and thus increasing RV distention. The effect of positive pressure inspiration on RV volume is variable. RV volume has been reported to decrease, to be unaffected, and to increase during positive pressure inspiration. 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 and RV filling pressure. Whereas, a decrease in RV volume has been ascribed to a decrease in both RV compliance 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
A decrease in LV volume during sustained increases in inspiration is also a matter of controversy. The decrease in LV end-diastolic volume 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, and this mechanism has been invoked to explain the observed increase in cardiac output seen in patients with heart failure following the application of PEEP. Additionally, an unchanged cardiac output during a Valsalva maneuver has also been reported and ascribed to squeezing of an overloaded pulmonary circulation. 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 reflects decreasing LV end-diastolic volume owing to ventricular interdependence, since RV end-diastolic volume also increased.

**Limitations of the Study**

Although CO and CO are measured with different techniques, a high correlation between the two methods has been established. Moreover, if the compliance of the vascular tree changed during the inspiratory hold maneuvers, it would most likely decrease when increased. This would result in overestimating CO by the pulse contour method. We saw a decrease in CO, thus, the actual decrease in CO may have been even greater than observed. However, Versprille et al demonstrated that during changes in intrathoracic pressure, the aortic pulse contour method accurately reflects CO when the mean arterial pressure does not change, as was the case in our studies. Clearly, CO and CO, 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 demonstrate 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. However, this post-bypass difference in central and peripheral systemic blood pressure is transient and resolves with the administration of fluid. Gravlee et al 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. 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 lactate 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 pulmonary vascular resistance, or LV afterload unless one assumes that CPAP differentially alters both RV ad LV preload and afterload by affecting these variables, as well as maintains the pressure gradient for venous return.

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