

# The Effect of Pre-existing Pulmonary Vascular Disease on the Response to Mechanical Ventilation with PEEP Following Open-heart Surgery

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The effects of mechanical ventilation with and without positive end-expiratory pressure (PEEP) on hemodynamic performance and blood-gas exchange were studied in ten patients following open-heart surgery. Ventilation at constant tidal volume (15 ml/kg body weight) with 10 cm H<sub>2</sub>O PEEP following aortic valve replacement (AVR) in five patients without pulmonary vascular disease was associated with the following significant changes: a rise in arterial P<sub>O<sub>2</sub></sub>, a fall in the alveolar-arterial P<sub>O<sub>2</sub></sub> gradient when F<sub>I<sub>O<sub>2</sub></sub></sub> = 1.0, decreases in calculated Q<sub>v</sub>/Q<sub>t</sub> and cardiac index. Using a similar pattern of ventilation following mitral valve replacement (MVR) in patients with elevated pulmonary vascular resistance, we found a significant decrease in cardiac index (but less than in the AVR group), a significant elevation of calculated physiologic deadspace (V<sub>D</sub>/V<sub>T</sub>) and no change in Q<sub>v</sub>/Q<sub>t</sub>. An hour after removal of PEEP, intravascular pressures, blood flow and blood-gas exchange values of all patients with AVR had returned to control levels; patients with MVR had persistently significantly low cardiac indices, while

V<sub>D</sub>/V<sub>T</sub> returned to pre-PEEP values. These findings suggest that evaluation of responses to different ventilation patterns must take into account pre-existing V/Q abnormalities secondary to pulmonary vascular disease, particularly when these are secondary to chronic congestive heart failure. Following AVR, Q<sub>v</sub>/Q<sub>t</sub> changed in the same direction as cardiac index (CI) irrespective of ventilatory pattern: CI decreased and rose as CI increased. The authors conclude that with increasing severity of pulmonary vascular disease, changes in airway pressure will have an unpredictable effect on cardiac index unless the level of myocardial competence is taken into account. In the presence of ventricular failure, changes in pleural (and therefore transmural) pressures will be minimal compared with the high filling pressures and exert no influence on stroke volume.

Although pulmonary venous hypertension was more pronounced in the MVR than in the AVR group, there was no significant difference between the postoperative values for Q<sub>v</sub>/Q<sub>t</sub> (F<sub>I<sub>O<sub>2</sub></sub></sub> = 1.0), a condition probably fostered by marked differences in pre-existing V/Q. (Key words: Ventilation, mechanical; pulmonary vascular disease and; Heart: vascular heart disease and mechanical ventilation; Lung: pulmonary perfusion in heart disease.)

MECHANICAL VENTILATION with positive end-expiratory pressure (PEEP) is known to be of particular value when pulmonary blood-gas exchange is impaired by a decrease in lung volume.<sup>1,2</sup> Unfortunately, the responses of the cardiac output and pulmonary vascular resistance are not consistently beneficial. Our past experience with patients in whom acute respiratory failure of non-cardiac origin is associated with an increase in pulmonary vascular resistance has suggested that addition of PEEP to the ventilatory pattern is associated with a minimal change in cardiac output. This impression has led us

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to investigate the effects of added PEEP on hemodynamic performance and blood-gas exchange in patients with or without documented pulmonary vascular disease at a time when respiratory failure was not a prominent element of their clinical status.

### Methods

We studied a total of ten patients, five following aortic valve replacement (AVR) and five following mitral valve replacement (MVR) (table 1). Every MVR patient had a documented abnormally high pulmonary vascular resistance index (PVRI) preoperatively; this index was normal in every AVR patient. Detailed evaluation was carried out within 24 hours after operation at a time when elective mechanical ventilation was still being provided. All patients had received morphine intravenously as the principal anesthetic drug in combination with muscle relaxants. Although this technique provides extensive analgesia postoperatively, a few patients required additional intravenous sedation with small quantities of fentanyl (0.02–0.04 mg), diazepam (2–5 mg), or morphine (2–4 mg) during the course of the study. To support hemodynamic function, all patients were treated in routine manner, which included blood volume replacement and/or intravenous administration of drugs with myocardial inotropic properties. Thus, three patients were receiving isoproterenol and seven, either whole blood or salt-poor albumin to maintain left atrial and mean arterial pressures in a clinically satisfactory range. These patients were randomly distributed between the two groups.

The study was divided into three distinct periods, and all patients were ventilated with 100 per cent oxygen throughout. Tidal volumes were set at 15 ml/kg body weight with a constant-volume ventilator (Emerson Ventilator, Model No. 3PV) at a rate predetermined to maintain  $P_{aCO_2}$  in the 35–45-torr range. During the control period all patients were ventilated with an end-expiratory pressure of zero for a minimum of 30 minutes or until a steady state had been achieved. The latter was defined as the time at which two consecutive samples of expired gas collected during 30 consecutive breaths in a Douglas

TABLE 1. Patient Material

	Age (years), Sex	Weight (kg)
Group 1, aortic valve disease		
Patient 1	67, F	66
Patient 2	52, M	84
Patient 3	71, M	62
Patient 4	59, M	85
Patient 5	64, F	51
Group 2, mitral valve disease		
Patient 1	48, F	67
Patient 2	53, M	60
Patient 3	62, F	72
Patient 4	57, F	70
Patient 5	45, F	59

bag had less than 2 per cent variation in mixed expired  $P_{CO_2}$ . At this point recordings were obtained of radial and pulmonary arterial as well as left atrial blood pressures; blood samples were obtained from the radial and pulmonary arterial lines and expired gas was collected again during 30 consecutive breaths. Cardiac output was determined by the dye-dilution technique using 5 mg indocyanine green dye with injection into the densitometer (Beckman Cardiodensitometer, Model SP284 and SP305).

At the end of the control period, 10 cm  $H_2O$  end-expiratory pressure was added to the ventilatory pattern by placing the tubing from the expiratory port under water. Ventila-

### ABBREVIATIONS

AVR = aortic valve replacement
CI = cardiac index
FRC = functional residual capacity
LLPV = left lower pulmonary vein
MVR = mitral valve replacement
PA = pulmonary artery
PAP = mean pulmonary arterial pressure
PEEP = positive end-expiratory pressure
PVR = pulmonary vascular resistance
$Q_p/Q_s$ = pulmonary right-to-left shunt
RA = radial artery
RLPV = right lower pulmonary vein
RUPV = right upper pulmonary vein
SWI = stroke work index
$V_D/V_T$ = deadspace-to-tidal volume ratio
$V_T$ = tidal volume

tion was continued until CO<sub>2</sub> output had reached a constant level. All measurements were then repeated as during the first control period, following which PEEP was removed. After further ventilation, until a steady-state was reached, samples and measurements were obtained for the second control period.

Airway and blood pressures were measured with appropriate transducers (Hewlett-Packard, Models 270 and 267AC), the former calibrated with water, the latter with mercury at the beginning of the study. Pressures were registered continuously on a Hewlett-Packard Model 7788A recorder. Before each measurement transducers and amplifiers were checked for zero and balance. Reading precision was 2.5 torr for arterial blood pressure, 1.25 torr for pulmonary arterial pressure, 0.5 torr for left atrial pressure, and 0.27 torr for airway pressure. Expired gas collected in a Douglas bag during 30 consecutive expirations was analyzed for CO<sub>2</sub> concentration with an infrared analyzer (Spinco Model LB1) that had a precision of 0.1 per cent for CO<sub>2</sub>.

P<sub>O<sub>2</sub></sub>, P<sub>CO<sub>2</sub></sub>, and pH were measured with standard electrodes at 37°C and corrected to body temperature, if necessary.<sup>3</sup> Whole-blood O<sub>2</sub> content was determined with the manometric technique.<sup>4</sup> The following data were derived:

- 1) The alveolar-arterial oxygen difference:

$$D(A-a)P_{O_2} = [P_B - (P_{H_2O}^T + P_{aCO_2})] - P_{aO_2}$$

where

$$P_B = \text{atmospheric pressure and} \\ P_{H_2O}^T = \text{water vapor pressure at body} \\ \text{temperature (T)}$$

- 2) Intrapulmonary right-to-left shunt expressed as percentage of cardiac output:

$$\dot{Q}_r/\dot{Q}_t \times 100 \\ = \frac{(PA_{O_2} - Pa_{O_2}) \times 0.0031}{(Ca_{O_2} - Cv_{O_2}) + (PA_{O_2} - Pa_{O_2}) \times 0.0031} \times 100$$

- 3) Deadspace-to-tidal volume ratio:

$$V_D/V_T = \frac{Pa_{CO_2} - \bar{P}\bar{E}_{CO_2}}{Pa_{CO_2}}$$

where

$$\bar{P}\bar{E}_{CO_2} (\text{mean expired } P_{CO_2}) \\ = (P_B - P_{H_2O}) \times F\bar{E}_{CO_2}$$

- 4) Oxygen consumption (ml/min):

$$\dot{V}_{O_2} = \dot{Q} \times (Ca_{O_2} - Cv_{O_2})$$

- 5) Pulmonary vascular resistance index (units):

$$PVR = \frac{\bar{P}AP - \bar{L}AP}{\text{cardiac index}}$$

where  $\bar{P}AP$  and  $\bar{L}AP$  are the mean pulmonary arterial and left atrial pressures obtained by electronic integration.

Statistical analyses were performed using non-parametric statistical tests (U-test of Mann and Whitney and signs test).<sup>5</sup>

## Results

According to data obtained during the first control period (table 2), the postoperative alveolar-arterial P<sub>O<sub>2</sub></sub> gradient and intrapulmonary right-to-left shunt were elevated to above values found in normal patients but agreed with values previously found in patients with heart disease by us and other authors.<sup>6,7,8</sup> Following MVR, pulmonary arterial and left atrial pressures, as well as pulmonary vascular resistance indices, were significantly higher than normal and significantly different from those of patients with AVR. Although V<sub>D</sub>/V<sub>T</sub> was high and cardiac index low in the MVR group, they did not differ significantly from corresponding values in the AVR group.

Mechanical ventilation with positive end-expiratory pressure of 10 cm H<sub>2</sub>O was associated with different responses in the two groups. Following AVR, mechanical ventilation with PEEP decreased the mean alveolar-arterial P<sub>O<sub>2</sub></sub> gradient significantly (from 247 ± 28 to 188 ± 54 torr) and also decreased intrapulmonary right-to-left shunt (from 12.7 ± 4.2 to 8.1 ± 1.5 per cent of cardiac output) and cardiac index (from 3.13 ± 0.74 to 2.64 ± 0.67 l/min/m<sup>2</sup>) (figs. 1 and 2; table 2). Following mitral valve replacement, mechanical ventilation with PEEP led to significant elevations of Pa<sub>CO<sub>2</sub></sub> (from 36 ± 5 to 42 ± 4 torr) and V<sub>D</sub>/V<sub>T</sub> (from 0.43 ± 0.1 to 0.47 ± 0.11, while CI decreased

TABLE 2. Effects of Mechanical Ventilation with 10 cm H<sub>2</sub>O PEEP on Hemodynamic Performance and Blood-Gas Exchange Following Aortic or Mitral Valve Replacement

	Aortic Valve Replacement (n = 5; Mean ± SD)				Mitral Valve Replacement (n = 5; Mean ± SD)			
	Period I Control		Period II 10 cm H <sub>2</sub> O PEEP		Period III Control		Period II 10 cm H <sub>2</sub> O PEEP	
Cardiac index (l/min/m <sup>2</sup> )	3.13 ± 0.74	2.64 ± 0.67*	3.11 ± 0.92	2.40 ± 0.62	2.40 ± 0.65*	2.34 ± 0.53*	2.34 ± 0.53*	
P <sub>ao</sub> (torr)	430 ± 23	502 ± 46*	461 ± 83	454 ± 53	471 ± 60	488 ± 81	488 ± 81	
D(A - v) P <sub>o</sub> (torr)	247 ± 28	188 ± 54*	221 ± 84	223 ± 55	205 ± 61	187 ± 78	187 ± 78	
Q̇ <sub>a</sub> /Q̇ <sub>v</sub> × 100	12.7 ± 4.2	6.1 ± 1.5*	10.8 ± 5.6	10.2 ± 2.9	9.6 ± 2.6	7.2 ± 2.7	7.2 ± 2.7	
C <sub>ao</sub> - C <sub>v</sub> (ml/100 ml)	4.76 ± 1.8	5.52 ± 1.4	4.90 ± 1.0	5.26 ± 0.65	4.92 ± 0.80	6.28 ± 1.05	6.28 ± 1.05	
Q̇ <sub>v</sub> (ml/min/m <sup>2</sup> )	234 ± 31	234 ± 53	240 ± 60	221 ± 33	207 ± 54	238 ± 42	238 ± 42	
Mean pulmonary arterial pressure (torr)	24.4 ± 1.5	26.5 ± 1.5	23.2 ± 1.3	30.6 ± 4.0	41.6 ± 4.0	37.8 ± 4.0	37.8 ± 4.0	
Pulmonary arterial diastolic pressure (torr)	19.37 ± 0.1	20.12 ± 7.31	19.87 ± 8.08	30.6 ± 2.63	33.0 ± 4.11	30.3 ± 2.20	30.3 ± 2.20	
Mean left atrial pressure (torr)	16.0 ± 1.1	17.2 ± 0.6	16.2 ± 1.2	23.5 ± 2.5	24.4 ± 2.4	22.8 ± 3.7	22.8 ± 3.7	
Pulmonary vascular resistance index (units/m <sup>2</sup> )	2.56 ± 0.51	3.82 ± 1.37	2.17 ± 0.76	6.43 ± 2.86	7.44 ± 3.27	6.77 ± 3.03	6.77 ± 3.03	
Heart rate (beats/min)	97 ± 4	95 ± 3	96 ± 4	100 ± 15	101 ± 13	102 ± 17	102 ± 17	
P <sub>ao</sub> /P <sub>v</sub> (torr)	31 ± 3	34 ± 2	31 ± 4	36 ± 5	42 ± 4*	37 ± 4	37 ± 4	
V <sub>a</sub> /V <sub>t</sub>	0.35 ± 0.07	0.34 ± 0.06	0.36 ± 0.05	0.43 ± 0.10	0.47 ± 0.11*	0.47 ± 0.06	0.47 ± 0.06	
V <sub>es</sub> (ml/min/m <sup>2</sup> )	198 ± 35	178 ± 29	207 ± 45	209 ± 20	195 ± 21	199 ± 27	199 ± 27	

\* Significant when compared with period I.

† Mean ± SD.

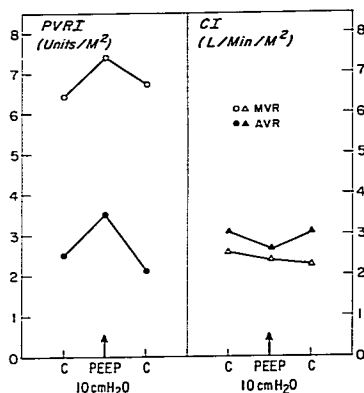


FIG. 1. Effects of mechanical ventilation with added PEEP on pulmonary vascular resistance and cardiac indices following open-heart surgery. Each point represents the mean for five patients. Standard deviations are given in table 2.

(from  $2.64 \pm 0.62$  to  $2.49 \pm 0.65$  l/min/m<sup>2</sup>).  $\dot{Q}_s/\dot{Q}_t$  did not change significantly (figs. 1 and 2; table 2).

An hour after discontinuation of PEEP (second control period), patients with MVR had persistently significantly decreased cardiac indices compared with the initial control values (first control:  $2.64 \pm 0.62$  l/min/m<sup>2</sup>; second control:  $2.34 \pm 0.53$  l/min/m<sup>2</sup>). This was in sharp contrast to the patients with AVR, in whom cardiac indices returned to control values once PEEP was discontinued. According to figure 3, patients with low or normal pulmonary vascular resistance indices had significantly greater percentage changes in PVR indices, CI, and  $\dot{Q}_s/\dot{Q}_t$  on addition or removal of PEEP than patients with high initial PVR indices.

On transition from one study period to another a decrease in cardiac index was associated with a decrease in  $\dot{Q}_s/\dot{Q}_t$ . The converse was also true. This relationship did follow consistently upon removal of PEEP, although the direction of change varied according to the underlying disease. For example, in the AVR group there was an increase in cardiac index with an increase in  $\dot{Q}_s/\dot{Q}_t$ .

Following MVR, removal of PEEP resulted in further decreases of both cardiac index and  $\dot{Q}_s/\dot{Q}_t$ .

The difference between pulmonary arterial diastolic and left atrial pressures was significantly greater in patients who had MVR, a reflection of the severity of their pulmonary vascular disease (table 2).

Oxygen uptake and CO<sub>2</sub> output remained unchanged in all patients during all study periods.

## Discussion

According to the findings of this study, an increase in airway pressure produced by adding PEEP to the pattern of mechanical ventilation is associated with lesser apparent hemodynamic perturbations whenever pulmonary vascular disease is present. Our patients, for whom elective ventilator support was provided following open-heart surgery, did not have a pronounced element of res-

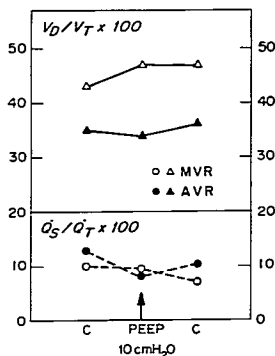


FIG. 2. Effects of mechanical ventilation with added PEEP on  $V_p/V_t$  and  $\dot{Q}_s/\dot{Q}_t \times 100$  during mechanical ventilation following open-heart surgery. Each point represents the mean for five patients.  $V_p/V_t$  ratios were significantly higher following mitral valve replacement (MVR).  $\dot{Q}_s/\dot{Q}_t \times 100$  dropped on addition of PEEP following aortic valve replacement (AVR); it did not change in patients whose pulmonary vascular resistance index was abnormally high (mitral valve replacement). Standard deviations are given in table 2.

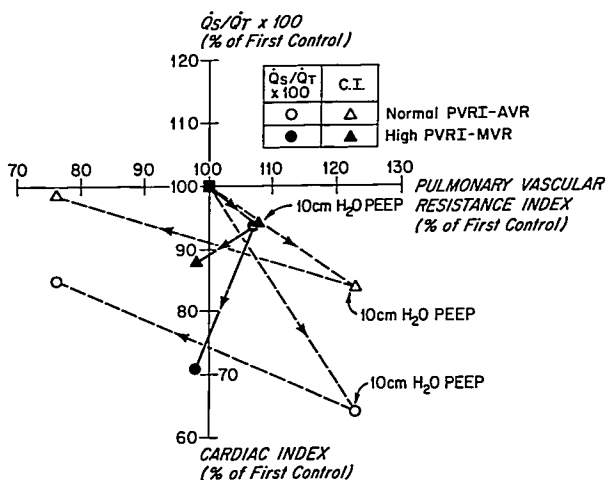


FIG. 3. Comparison of percentage changes in  $\dot{Q}_s/\dot{Q}_T \times 100$  and cardiac index upon addition of PEEP in patients with (MVR) and without (AVR) significant pulmonary vascular disease. PVR index (percentage of first control period) is drawn on the X axis and  $\dot{Q}_s/\dot{Q}_T \times 100$  and CI (per cent of first control period) on the Y axis. Addition of PEEP following AVR (open symbols) was associated with a large increase in PVR index and substantial decreases in both  $\dot{Q}_s/\dot{Q}_T \times 100$  and CI. Following MVR (closed symbols) the increase in PVR index and decrease in  $\dot{Q}_s/\dot{Q}_T \times 100$  as well as CI were markedly attenuated (i.e., the change in PVRI was considerably smaller when its control value was high).

piratory failure, and the persistent deficiency in oxygenation (i.e., mean  $\dot{Q}_s/\dot{Q}_T \times 100$  10 to 12 per cent) probably reflected the residual effect of left ventricular failure. The latter is supported by the finding of substantially higher than normal mean left atrial pressures with subnormal cardiac indices. In these cases the effects of added airway pressure on cardiac indices varied according to the calculated PRV indices.

We believe that appropriate evaluation of the patient's hemodynamic response to a change in airway pressure can be achieved only after consideration of three factors: 1) blood volume; 2)  $\dot{V}/\dot{Q}$  abnormalities produced by heart disease; 3) the state of myocardial contractility. Given normal pulmonary mechanics, high peripheral venous compliance, and normal myocardial contractility, a rise in mean airway pressure will be associated with a decrease in blood flow due

to diminution of right ventricular filling (pre-load). In the clinical setting, this diminution in flow is usually offset by an appropriate therapeutic increase in blood volume. With moderate hypervolemia and the decrease in venous compliance, right ventricular preload is increased and cardiac output will return to control levels. Experimental injury to the lung (e.g., oleic acid injection) is associated with severe hypoxemia, partially relieved by mechanical ventilation with added PEEP.<sup>8</sup> As gross and histologic examination indicates, the injury is associated with massive loss of erythrocytes, protein, electrolytes, and water into the lung, tantamount to an extensive loss of intravascular volume. If mechanical ventilation with PEEP is initiated in this hypovolemic setting, then the ensuing fall in cardiac output will be marked unless volume replacement is provided promptly. The suggested relationship between changes in

blood flow and increased airway pressure is supported by the findings of Sykes *et al.*,<sup>10</sup> who demonstrated no change in cardiac output in animals made hypervolemic with blood transfusion before the addition of 10 cm H<sub>2</sub>O PEEP to the ventilatory pattern. Also of interest with regard to this problem is their statement that a waveform utilizing positive pressure throughout the ventilatory cycle "produced no change in cardiac output . . . when the animal was in gross congestive cardiac failure."<sup>9</sup>

Second, evaluation of the results of added PEEP must consider the abnormal  $\dot{V}/\dot{Q}$  ratio introduced by changes in pulmonary vascular anatomy. Long-standing mitral valve disease is associated with regional changes in pulmonary vascular morphology, ultimately leading to abnormal distribution of blood flow.<sup>11,12,13</sup> The preponderance of vascular

changes in lower lobes has been demonstrated repeatedly since its original description by Parker and Weiss.<sup>14</sup> Other investigators, using radioactive gases, have shown that an increase in PVR index secondary to chronic mitral valve disease results in increased blood flow to the non-dependent lung (upper lobes).<sup>15,16</sup> The expected  $\dot{V}/\dot{Q}$  maldistribution was evident in our MVR patients, whose  $V_D/V_T$  ratios were significantly higher than those in the AVR group (PVR indices normal in the latter). Therefore, addition of PEEP will not result in the same response in the two groups. Although increased left atrial pressure secondary to left ventricular failure (*i.e.*, alveolar edema) will influence primarily the lower lobes in MVR and AVR patients, this part of the lung will receive less of the total pulmonary blood flow when affected selectively by changes in its

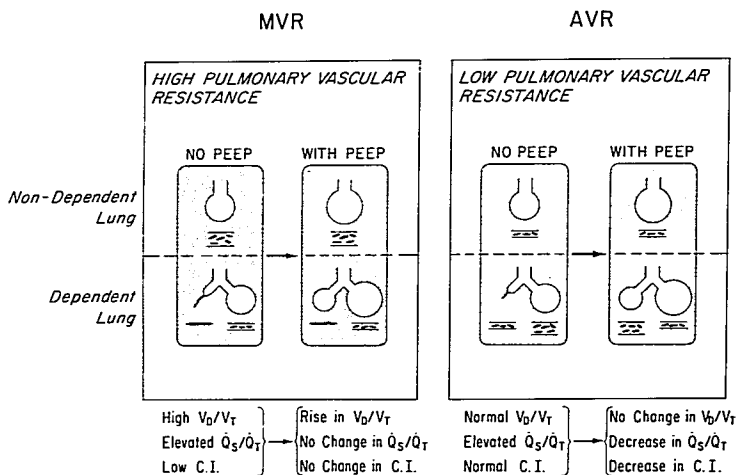


FIG. 4. Schematic diagram indicating the different responses to be expected when PEEP (10 cm H<sub>2</sub>O) is added to the ventilatory pattern in patients with high (MVR) and those with normal (AVR) pulmonary vascular resistances. Long-standing mitral valve disease is associated with a significant increase in flow to the nondependent portions of the lung (note width of blood vessels in drawing). Acute left-sided heart failure influences predominantly the dependent part of the lung. Addition of PEEP to the ventilatory pattern improves ventilation of the dependent lung and has a striking effect on pulmonary blood flow in patients following AVR. In the presence of pulmonary vascular disease increased ventilation of the dependent lung has a lesser effect on cardiac index but increases physiologic deadspace ( $V_D/V_T$ ).

TABLE 3. Effects of Mechanical Ventilation with and without PEEP on Regional Pulmonary Oxygenation Following Mitral Valve Replacement in a Patient\* with Severe Pulmonary Vascular Disease†

	Preoperative Catheterization: PA 160/90 torr; P <sub>AP</sub> 105 torr; PVR 78 units; CI 0.7 l/min/m <sup>2</sup>								
	Supine						Right Lung Down		
	Without PEEP			8 cm H <sub>2</sub> O PEEP			8 cm H <sub>2</sub> O PEEP		
F <sub>IO<sub>2</sub></sub> = 1.0; V <sub>T</sub> = 900 ml	P <sub>O<sub>2</sub></sub> (torr)	P <sub>CO<sub>2</sub></sub> (torr)	pH	P <sub>O<sub>2</sub></sub> (torr)	P <sub>CO<sub>2</sub></sub> (torr)	pH	P <sub>O<sub>2</sub></sub> (torr)	P <sub>CO<sub>2</sub></sub> (torr)	pH
Right upper pulmonary vein	309	25	7.63	427	30	7.57	†	†	†
Right lower pulmonary vein	34	31	7.57	70	35	7.51	398	38	7.51
Radial artery	242	25	7.62	371	30	7.56	620	31	7.57

\* The patient was a 59-year-old woman who weighed 61 kg.

† Preoperative pulmonary arterial pressure was at systemic levels. Catheters were inserted into the right upper (RUPV) and right lower (RLPV) pulmonary veins at operation when the left atrium was open. Congestive heart failure was a prominent problem postoperatively, but the chest x-ray did not reveal right lower lobe collapse. Note the minimal contribution of blood from RLPV (P<sub>O<sub>2</sub></sub> = 34 torr) compared with RUPV (P<sub>O<sub>2</sub></sub> = 309 torr) to arterial oxygenation with the patient supine, ventilated without PEEP. Addition of 8 cm H<sub>2</sub>O PEEP substantially improved ventilation in the lower lobe, where P<sub>O<sub>2</sub></sub> rose from 34 to 70 torr. An impressive improvement of ventilation in the right lower lobe occurred when the patient was turned to the right lateral decubitus position (i.e., both right upper and lower lobes dependent). Unfortunately, turning the patient resulted in displacement of the RUPV catheters, and samples could not be obtained. Cardiac index at the time of this study was 3.4 l/min/m<sup>2</sup>. The patient survived.

‡ Catheter inadvertently moved out of position; blood sample unavailable.

vasculature (i.e., MVR group). Mechanical ventilation with PEEP intended to increase FRC and improve oxygenation will have a predominant effect on the lower lobes and increase ventilation to regions with the greatest blood flow when pulmonary vascular disease is absent (i.e., AVR patients). The results are improved oxygenation and a decrease in cardiac output. Similarly, in the presence of pulmonary vascular disease (i.e., MVR patients), added PEEP will increase ventilation to the same portions of the lung (i.e., lower lobes), but in areas which receive significantly less blood flow. Consequently, cardiac output will be affected little, if at all, oxygenation will improve minimally (unless intra-alveolar edema is extensive), and V<sub>D</sub>/V<sub>T</sub> will increase because the V/Q abnormality is intensified. These responses, typical for the MVR patients, are summarized in figure 4.

Support for our hypothesis was provided by a recent opportunity to study regional differences in oxygenation during mechanical ventilation with and without added PEEP following MVR in a patient with severe pulmonary hypertension (see table 3). Catheters were inserted under direct division

into the right upper and lower pulmonary veins at the time of left atriotomy and samples obtained from these lung regions postoperatively. Prior to operation the patient arrived in the operating room with severe pulmonary edema, with a large alveolar-arterial P<sub>O<sub>2</sub></sub> gradient and a cardiac index reported at catheterization to be 0.7 l/min/m<sup>2</sup>. Postoperatively, the chest x-ray revealed moderately severe congestive changes. Samples of blood from the right upper (RUPV) and right lower (RLPV) pulmonary veins were strikingly different. More important, closeness of the arterial blood P<sub>O<sub>2</sub></sub> to that obtained from the RUPV indicated that blood flow was predominately to the upper lobe. Addition of 8 cm H<sub>2</sub>O PEEP increased ventilation to the lung base with an appropriate rise in Pa<sub>O<sub>2</sub></sub>. The response was more marked than in the patients we have studied, and we believe that the improvement reflected the severity of pulmonary edema. Nevertheless, the cardiac index demonstrated no significant change when PEEP was added (from 3.4 to 3.2 l/min/m<sup>2</sup>). Samples of blood obtained with the patient's right side dependent indicated significant im-



provement of ventilation to both right upper and lower lung. Unfortunately, the catheter in the right upper pulmonary vein was displaced and samples could not be obtained. Approximations made on the basis of arterial and lower pulmonary vein  $P_{O_2}$ 's suggested that blood flow to the apices of the lungs was sevenfold higher than that at the bases.

Whether addition of PEEP to the pattern of ventilation is of value has frequently been decided on the basis of a change in  $Pa_{O_2}$ . When perfusion of the lower lobes is reduced (as in the MVR patients), improved ventilation of this region may not be reflected by a striking rise in  $Pa_{O_2}$ . An example is shown in table 4. The patient had a catheter inserted intraoperatively into the left lower pulmonary vein (LLPV). Persistent "low output" postoperatively with congestive heart failure necessitated hemodynamic support with an intra-aortic balloon and mechanical ventilation. Since a sample from the LLPV revealed essentially no ventilation of the lower lung ( $P_{O_2}$  of blood from LLPV = 38 torr, compared with  $P_{O_2}$  87 torr in blood from the radial artery), the tidal volume was increased. This was followed by increases in arterial and LLPV  $P_{O_2}$ . Subsequent addition of PEEP had

little influence on  $Pa_{O_2}$ , since blood flow to the lower lobe was markedly diminished, although ventilation of the same lobe was improved further, as demonstrated by an increase of  $P_{O_2}$  (LLPV) from 95 to 176 torr.

It is worthwhile to emphasize that all patients were studied while they were semirecumbent. According to Ueda *et al.*<sup>17</sup> and Hughes *et al.*,<sup>18</sup> no difference in the distribution of perfusion was found when patients with mitral valve disease were studied upright and supine. Thus, it is unlikely that our findings in patients with high pulmonary vascular resistance are peculiar to the position in which they were studied.

A final factor to consider is the state of ventricular contractility and the response of cardiac output to changes in airway pressure. Qvist *et al.*<sup>19</sup> found that mechanical ventilation with PEEP in the experimental animal was associated with a diminution of cardiac output secondary to reduced preload, correctable by additional blood transfusion and a state of moderate hypervolemia.

If ventricular function is compromised, the hypervolemic state is tolerated so long as the added airway pressure (*i.e.*, PEEP) provides a continuous impedance to thoracic inflow.

TABLE 4. Data from a 65-year-old Man (Weight 75 kg) Who Had Received Two Coronary Artery Bypass Grafts\*

	$F_{iO_2}$	$P_{O_2}$ (torr)	$P_{CO_2}$ (torr)	pH	$V_T$ (ml)	PEEP (cm H <sub>2</sub> O)
8 minutes						
Radial artery	1.0	87	40	7.44	1,000	5
Left lower pulmonary vein		38	47	7.40		
15 minutes						
Radial artery	1.0	271	28	7.54	1,400	0
Left lower pulmonary vein		95	42	7.40		
45 minutes						
Radial artery	1.0	273	27	7.49	1,400	5
Left lower pulmonary vein		176	33	7.43		
24 hours						
Radial artery	1.0	248	30	7.58	1,400	5
Left lower pulmonary vein		182	34	7.53		

\* The patient needed mechanical ventilation postoperatively because of severe congestive failure. The left atrial catheter (inserted at the time of operation) had been threaded into the left lower pulmonary vein (LLPV). Initial blood gases, with the patient receiving a tidal volume of 15 mg/kg and 5 cm H<sub>2</sub>O PEEP, revealed a radial arterial blood  $P_{O_2}$  of 87 torr, while the  $P_{O_2}$  of blood from LLPV was 38 torr. Increasing the tidal volume to 20 ml/kg improved arterial  $P_{O_2}$ . Addition of 5 cm H<sub>2</sub>O PEEP resulted in further improvement of ventilation of the left lower lobe, although this was not reflected by the arterial  $P_{O_2}$ , probably because blood flow to the lower lobe was minimal.

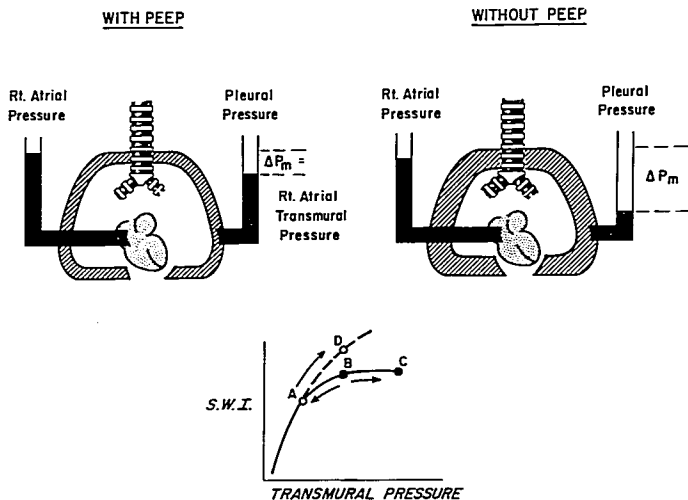


FIG. 5. Effect of change in airway pressure (i.e., mechanical ventilation with or without PEEP) on blood flow. Right and left ventricular preload are determined by transmural atrial pressures, in turn the algebraic sum of atrial and pleural pressures measured relative to atmospheric. If addition of PEEP to the ventilatory pattern increases functional residual capacity, then pleural pressure will rise more than left or right atrial pressure and the transmural pressure (preload) will decrease. The magnitude of the associated decrease in cardiac output will depend on ventricular function as defined by the Frank-Starling curve shown below. If the patient is in failure (point C), a decrease in transmural pressure (from C to B) will result in virtually no change in stroke work index (SWI). If ventricular function is normal (point D), addition of PEEP will decrease transmural pressure and SWI (from D to A). Decreases of FRC and pleural pressure follow removal of PEEP, as shown by an increase in the width of the crosshatched area. In a hypovolemic patient the fall in right atrial pressure (relative to atmospheric) will be offset by redistribution of blood volume into the thorax and result in a rise in transmural pressure ( $\Delta P_m$ ).

When PEEP, or the impedance, is removed, redistribution of blood volume occurs and the patient may manifest the consequences of a substantial autotransfusion (increased preload). If the right ventricle is competent, the increase in preload will result in an increase in stroke volume. On the other hand, if the right ventricle is failing prior to reduction of airway pressure, the response will be substantially different. For example, Beach *et al.*,<sup>20</sup> recently found that a shift from mechanical to spontaneous ventilation in a group of 18 patients with a mean cardiac index of 1.82 l/min/m<sup>2</sup> resulted in a further paradoxical decrease in cardiac index. Figure 5 and a review of the data published by Qvist *et al.*<sup>19</sup>

explain how these changes are possible in the face of diminished myocardial contractility. The effective preload for right and left ventricle is the algebraic sum of right atrial and pleural (or esophageal) pressures, both measured relative to atmospheric, and is defined as the atrial transmural pressure. The difference between the two will be small when patients are ventilated mechanically with PEEP and substantially higher when PEEP is removed, if and only if removal of PEEP is associated with a reduction in FRC (i.e., partial collapse of lung) and a decrease of intrapleural pressure. If the right ventricle is on the flat portion of its function curve (i.e., plot of stroke work index vs. transmural

pressure), then removal of PEEP and the increased venous return or preload will have little or no effect on flow. Conversely, a well-functioning ventricle operating on the steep portion of its function curve will respond with an increase in flow. If we now combine the presence of right ventricular failure with high pulmonary vascular resistance, the volume of blood added to the pulmonary circuit represents an increased right ventricular afterload and the mechanism for a decrease in cardiac output with a decrease in airway pressure becomes apparent. Support for the effect of right ventricular afterload is provided by Qvist *et al.*,<sup>19</sup> who have shown that a marked rise in transmural pulmonary arterial diastolic pressure (indicative of redistribution of blood) will appear only if PEEP is removed in an animal previously made hypervolemic. We suggest that this mechanism explains why removal of PEEP (reduction in airway pressure) was not associated with a change in CI in the MVR patients, a consideration strengthened by the fact that right ventricular afterload, or impedance<sup>21</sup> (a composite of pulmonary arterial pressure, PVR index, and stroke volume) is higher in the patient with long-standing mitral valve disease.

Based on these findings, certain predictions are possible during treatment of patients who have acute respiratory failure. First, if the PVR index is high, right ventricular performance is likely to be impaired. Second, if mechanical ventilation with PEEP is necessary, a significant decrease in cardiac output is likely to accompany improvement in oxygenation. In the latter case, increased alveolar pressure to perfused but previously nonventilated areas will produce a more prominent increase in the PVR index. Third, addition of PEEP to the ventilatory pattern is likely to improve lung volume by overdistending open terminal air units, as shown in Falke *et al.*<sup>22</sup> or by opening up units initially closed but hypoperfused. Fourth, the directional change in cardiac output will depend on the patient's blood volume, the state of myocardial contractility, and the effect of the altered ventilatory pattern on right and left ventricular pre- and afterload. Fifth, if airway pressure is reduced or if weaning from the

ventilator is attempted in the presence of right ventricular failure combined with a state of hypervolemia, the extent of right ventricular failure may be accentuated and a paradoxical decrease in cardiac output will be in evidence. Conversely, it should come as no surprise that, given these circumstances, myocardial performance and cardiac output will improve as airway pressure is elevated, or that a patient in respiratory failure will manifest hemodynamic improvement when mechanical replaces spontaneous ventilation.

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