CARDIOVASCULAR EFFECTS OF POSITIVE PRESSURE BREATHING

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April 7, 1983

Background and Historical Perspective

Positive pressure ventilation has been used for a variety of clinical purposes for over 100 years. Reviews of early literature can be found in papers by Barach (8,9), Stokke (152), and Sugerman (153). Norton (120) in 1897 may have been the first to describe the use of positive pressure ventilation through an endotracheal tube in a patient with non-cardiac pulmonary edema. He successfully treated a 34 y/o man who had been overcome with chlorine gas and was cyanotic, dyspneic, and coughing pink frothy sputum. Subsequently during the early 20th century experimental studies regarding treatment of patients with pulmonary edema using positive pressure ventilation were initiated by Emerson, Barach, and others (7-9, 59). There were two major differences between the level of understanding of the pathophysiological mechanisms of pulmonary edema that existed then compared to the present day. The Starling relationship governing transmembrane movement of fluid had not been applied to physiological systems; thus; the differentiation between edema caused by elevated hydrostatic pressures and that caused by increased vascular permeability was not made. Secondly, the technology to analyze blood gas tensions had not been developed; and therefore, arterial oxygen tensions were not known and were not considered in evaluating either the effects of pulmonary edema or the effects of positive pressure ventilation. Clinical improvement associated with positive pressure ventilation was documented, and the salutary effects of positive pressure ventilation were attributed to increased intrathoracic pressure which was thought to "unload" the heart and reduce pulmonary venous congestion. Thus, the idea that positive pressure ventilation reduced left ventricular afterload is certainly not a new concept.

The advent of high altitude aviation during the World Wars posed a problem of how to supply adequate alveolar oxygen tension in order to saturate the blood. Alveolar oxygen tension at 35,000 ft breathing atmospheric air would be less than 20 mmHg which would desaturate arterial blood to < 40%. Pressurizing aircraft cabins to maintain adequate alveolar oxygen tension presented insurmountable problems to aircraft designers of that era, and the approach to increasing alveolar oxygen tension was to increase alveolar pressures by means of a face mask (7). It was soon appreciated by aerospace physiologists that increasing alveolar pressure to approximately 50-100 mmHg resulted in the loss of consciousness within seconds (17). This phenomenon prompted an extensive evaluation of the cardiovascular effects of positive pressure ventilation that lasted through the 1940's (22,26,63,94,108).

These studies culminated in a report by the Nobel laureates Cournand, Richards, and Wërko (42) in which the effects of positive pressure ventilation with 5 cmH_2O PEEP on right heart filling pressures and pleural pressure were measured. In this classic paper (by far Cournand's most often cited publication) they conclude that positive pressure ventilation restricted the filling of the right ventricle because the elevated intrathoracic pressures restricted venous flow into the thorax. They concluded that doing so was the cause for the reduction in cardiac output.

Until 1975, much of what was known about the cardiovascular effects of positive pressure breathing was generated from this aerospace research. It had been demonstrated in animals and human subjects that positive pressure ventilation especially with positive end-expiratory pressure decreased cardiac

output, blood pressure, and often heart rate (22,63,94,95,107,108,114,118, 137). If cardiovascular collapse or syncope did not occur within a few seconds, compensatory mechanisms occurred which restored cardiac output, blood pressure, and heart rate although never to their previous levels. These deleterious cardiovascular effects of positive end-expiratory pressure caused its use in the treatment of pulmonary edema to be practically abandoned throughout the late 1940's through the 1960's.

In 1967 Ashbaugh and associates published a report that stimulated the widespread clinical use of positive pressure ventilation with positive end-expiratory pressure (5). They studied patients with respiratory insufficiency characterized by tachypnea, hypoxemia, and diffuse bilateral infiltrates on chest radiographs. The pulmonary injuries among their patients were caused by a variety of causes, but the clinical and physiological characteristics were similar and not unlike those of the infant respiratory distress syndrome. Because of these similarities, they proposed that management of these pulmonary injuries would be enhanced by directing therapy toward the altered physiology irrespective of the cause and they called this syndrome of pulmonary injury the adult respiratory distress syndrome (ARDS). In this report they also described improvement of arterial hypoxemia with positive end-expiratory pressur (5). Thus, the concept of the adult respiratory distress syndrome and the use of positive end-expiratory pressure to manage the associated hypoxemia emerged together.

Adult Respiratory Distress Syndrome

At postmortem examination lungs from patients with ARDS demonstrate alveolar and interstitial edema, atelectasis, alveolar epithelial injury and sloughing of epithelial cells into the air spaces, and hyaline membranes along alveolar ducts. Similar pathologic descriptions of lung injury are associated with diseases as varied as viral pneumonia, endotoxemia, gastric acid aspiration, near drowning, extensive trauma, fat emboli, post cardiopulmonary bypass perfusion, hemorrhagic and septic shock, pancreatitis, and many more (5,61).

Radiographic features of adult respiratory distress syndrome include the presence of diffuse, bilateral infiltrates which represent alveolar and interstitial edema and small lung volumes which represent atelectasis (92,115,154).

ARDS has been characterized physiologically by a reduction in functional residual capacity (FRC), a reduction in dynamic compliance of the lung and respiratory system, and enhanced hysteresis of static lung pressure-volume curves (5,61,81,96,99). These alterations in lung mechanics indicate that high inflation pressures will be required to ventilate the lungs and that alveolae will tend to collapse during expiration.

Hypoxemia is the primary derangement in gas exchange (5,61,81,99). Carbon dioxide retention occurs infrequently usually late in the course of the illness and may be associated with a collapse of small airways caused by high alveolar pressures. This compliaction of positive pressure ventilation has

been recognized in infants and is called bronchopulmonary dysplasia (13). It is being recognized increasingly in adults, also (147,37). Characteristically, the hypoxemia of ARDS is severe and improves little with increasing concentrations of inspired oxygen (5,17,35,61,74,81,99,162). This inability to substantially improve arterial oxygenation in spite of raising inspired oxygen concentrations to high levels is caused by $\dot{V}/Q$ mismatching with perfusion of large regions of lung that are not ventilated at all. This extreme mismatching of ventilation with respect to perfusion is also called intrapulmonary shunting or venous admixture. In an effort to provide adequate arterial oxygen concentrations, many patients eventually received high concentrations of inspired oxygen which further injures the lungs and worsens gas exchange.

It is obvious then that the discovery that ventilation with positive end-expiratory pressure would raise arterial oxygen tension in many of these patients with ARDS was greeted with enthusiasm. Studies which followed the initial report of Ashbaugh and his associates demonstrated that the increase in arterial oxygen tension with positive end-expiratory pressure was a consequence of reducing atelectasis thereby increasing FRC. Positive end-expiratory pressure held open alveolae that otherwise would not reexpand with subsequent inflation at lower alveolar pressures. This opening of alveolae reduced intrapulmonary shunting and venous admixture and raised the arterial oxygen tension without having to raise the inspired oxygen concentration.

Positive Pressure Ventilation

There are basically two methods whereby expiratory lung volume is enlarged by raising airway pressure. One method is to deliver the desired tidal volume with positive airway pressure and terminate expiration at a designated pressure, thereby increasing end-expiratory pressure and lung volume. This ventilatory maneuver is called positive end-expiratory pressure, abbreviated PEEP (5,61). It is necessary that the respiratory muscles be relaxed for this form of ventilation to accomplish an increase in end-expiratory lung volumes. Consequently, muscle relaxants and sedatives are often administered to ventilate patients with PEEP.

The other ventilatory maneuver to increase end-expiratory lung volume is to allow the patient to breathe spontaneously through a tube in which a specified pressure above atmospheric is maintained. This is called continuous positive airway pressure or CPAP (45,74). CPAP is used more frequently in infants with respiratory distress than in adults. The effect of this ventilatory maneuver on resting lung volume is variable because the patient can use his expiratory muscles to expire to any desired lung volume. Only if expiration is relaxed and passive will end-expiratory lung volume be determined by the pressure maintained in the airway.

The elevated pressure at the end of expiration is intended to prevent the lung from emptying to its natural resting volume. A combination of these two methods, PEEP and CPAP, for increasing end-expiratory volume is used, also.

In the combined maneuver, tidal volumes are delivered regularly by positive pressure and positive end-expiratory pressure is maintained at a set level. In addition patients are able to breathe spontaneously through the system with a continuously positive airway pressure set at the level of PEEP. This ventilatory maneuver has been termed intermittent mandatory ventilation (IMV) + PEEP (38,51,52).

The physiological mechanisms by which these methods increase end-expiratory lung volume and raise arterial oxygen tension or by which they cause cardiovascular depression are not very different. The primary differences between these maneuvers are the level of sedation and muscle relaxation required to control ventilation, and the extent to which the desired increase in lung volume is actually achieved. Desired ventilation with CPAP or with IMV + PEEP can be achieved without as much sedation as is often necessary with controlled positive pressure ventilation and PEEP. Most sedatives have the potential to depress cardiovascular function. Additionally, with IMV and CPAP the respiratory muscles can prevent the lung from being dangerously over expanded. However, continued ventilation with PEEP is usually more successful in recruiting collapsed alveolae and in raising Pa_{O_2}, and the work of breathing is less (70).

Effects of PEEP on Gas Exchange

The physiologic alterations that result in arterial hypoxemia that are characteristic of ARDS are venous admixture or intrapulmonary shunting of blood, atelectasis, and a reduction in resting lung volume, and reduced dynamic compliance. Intrapulmonary shunting of blood can be quantitated as the ratio of blood flow shunted through nonventilated regions of lung, $\dot{Q}_s$, to the total blood flow through the lungs, $\dot{Q}_t$. This ratio, $\dot{Q}_s/\dot{Q}_t$, is normally less than 5% but in ARDS may increase to as high as 50%. Sometimes it is useful to quantitate the degree of venous admixture or intrapulmonary shunting ($\dot{Q}_s/\dot{Q}_t$). This can be done by having the patient inspire 100% O_2 for a sufficient time to rinse out the N_2 in the lung. $\dot{Q}_s/\dot{Q}_t$ can be determined clinically as follows:

$$\frac{\dot{Q}_s}{\dot{Q}_t} = \frac{Ca_{O_2} - Cc'_{O_2}}{Cv_{O_2} - Cc'_{O_2}}$$

Ca_{O_2}, Cc'_{O_2}, and Cv_{O_2} are the oxygen content of arterial, capillary and mixed venous blood. Blood oxygen content (in ml O_2/100 ml blood) = P_{O_2} x 0.003 + [Hgb x 1.34]% saturation. 1.34 is the volume of oxygen carried by one gram of hemoglobin.

The arterial oxygen tension increases as a direct function of the level of airway pressure as shown in Figure 1 (74). The extent to which any level of PEEP raises the arterial oxygen tension is variable among patients. Thus the improvement may be striking with only 5 cmH_2O PEEP or there may be very little augmentation of Pa_{O_2} with even 15 cmH_2O PEEP or higher. Similarly the shunt, $\dot{Q}_s/\dot{Q}_t$, is reduced as the level of PEEP is raised although this is not universal, and blood flow from the least involved regions of lung may be redistributed to the nonventilated areas especially if the latter are not recruited by PEEP (47,53,68,93,100,117,119). Thus, it is possible that the $\dot{Q}_s/\dot{Q}_t$ will increase and that Pa_{O_2} will fall.

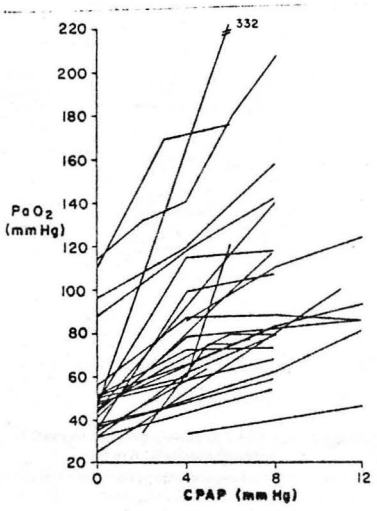
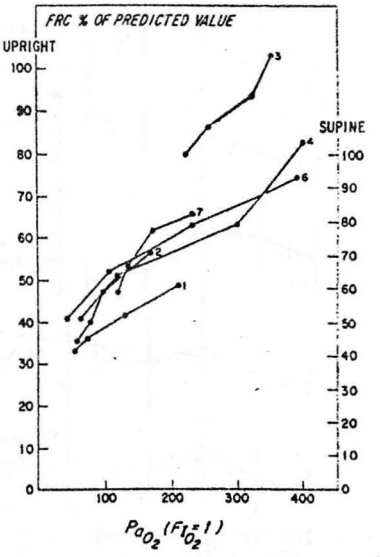


Figure 1 Gregory (74)

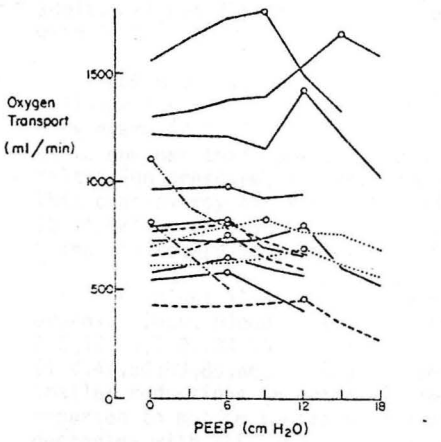


Correlation between FRC and the Pa_{O_2} ($FI_{O_2} = 1.0$) at four different levels of end-expiratory pressure. Each lowest point represents the relationship during IPPV, the next at 5 cm PEEP, etc. Note that patient No. 3 had bronchiectasis. Values for the predicted FRC are from Bates, Macklem, and Christie (10).

Figure 2 Falke (61)

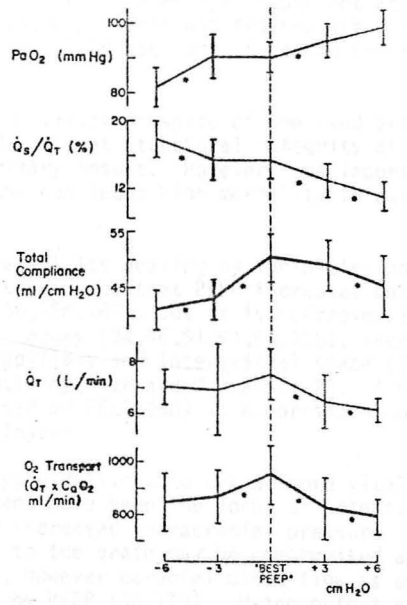
The effects of PEEP on oxygen delivery and recruitment of lung is summarized in a study by Falke et al, Figure 2 (61). In 10 patients treated with PEEP, the increase in resting lung volume was associated with increased arterial oxygen tension. In those in whom increasing PEEP causes very little increase in FRC the concomittant improvement in arterial oxygen tension was also small (3,36).

PEEP also may increase dynamic compliance of the respiratory system (11,100) so that less pressure is required to expand the lungs a given volume. This increase in dynamic compliance was formerly thought to be a useful tool to select an ideal level of PEEP with which to ventilate to a patient (155). In general, it is true that recruitment of atelectatic lung usually accompanies an increase in dynamic compliance, $\dot{Q}_S/\dot{Q}t$, and an improvement in arterial oxygen tension, but these associations may be fortuitous. Presently, our assessment of these parameters requires direct measurement of the variables that are in question. The study by Suter et al. (155) demonstrated well that the level of PEEP was directly proportional to an increase in Pa_{O_2}, lung compliance, lung volume, and oxygen delivery up to a point where the fall in cardiac output outweighed these salutary effects, Figure 3.



Effect of Varying Levels of PEEP on Oxygen Transport in All Patients Studied.

The point of maximum oxygen transport is indicated (o). Differing lines are used merely to distinguish individual patients.



3. Mean Values ± S.E. of Arterial Oxygen Tension (PaO_2), Intrapulmonary Shunt ($\dot{Q}_S/\dot{Q}_T$), Total Static Compliance, and Oxygen Transport, Measured at the Level of PEEP Resulting in Maximum Oxygen Transport ("Best PEEP"), Compared to Values Obtained at 3 and 6 Cm of Water of PEEP below (−3, −6) and above (+3, +6) That Level.

*Significant changes ($p < 0.05$) at each 3-cm-of-water increment of PEEP.

Figure 3 Suter (155)

Fourteen years have lapsed since the discovery that positive end-expiratory pressure would increase arterial oxygen tension in the presence of hypoxemia associated with pulmonary edema. Yet, it has become apparent that many patients with the adult respiratory distress syndrome still die of pulmonary insufficiency and hypoxemia in spite of therapy with positive end-expiratory pressure. A retrospective study by Springer and Stevens demonstrated survival was not increased in patients with ARDS by ventilation with positive end-expiratory pressure (149). Positive pressure breathing with PEEP and other supportive measures only prolonged the hospital course before death. Actually, survival

was better in patients with ARDS who did not receive PEEP although not at a statistically high level. Incidentally these patients not treated with PEEP were done so because they were in shock, and PEEP was contradictated under those circumstances.

One explanation for continued high mortality in spite of improved arterial oxygen tension in patients with ARDS is that structural integrity of the lung cannot be restored following the primary insult. However, two important additional possibilities are raised by the continued high mortality in patients with ARDS.

PEEP might injure lung tissue or prevent its healing by inhibiting normal cellular function. There is considerable evidence that PEEP increases pulmonary edema (2,21,23,24,48,54,73,84,106,136,158,167), but it is controversial as to whether this represents additional injury (34,46,51,91,98,158), increased filtration pressure, or recruitment of capillary and interstitial space (2,73). This controversy has been reviewed recently by Rizk and Murray (132). A near obliteration of bronchial blood flow caused by PEEP (80) is a worrisome consequence in regard to enhancement of lung injury.

PEEP might also adversely affect oxygen delivery to one or more vital organs. Thus, blood flow to various organs have been the focus of attention (15,18,20,110,134,160). Because of PEEP increased intracranial pressure (1,4,41,50,69,85,86,105,145), blood flow to the brain may be compromised at much smaller reductions in arterial pressures; however cerebral blood flow is usually reported to not be substantially reduced by PEEP (50,110). Urine output also decreases with PEEP (90,128), but whether this is caused by the decreased renal blood flow (110, 134) or by the secretion of ADH which may be elevated to inappropriately high levels during PEEP (10,83) is not known.

While the studies that will be discussed have emphasized the deleterious effects of PEEP, by no means are these adverse responses always the prevailing issue. In fact there have been several studies indicating that PEEP may actually have prophylactic value in preventing ARDS (6,168). This is particularly so in the post-operative and post-trauma setting in which the patients are under observation before and during the development of ARDS.

Cardiovascular Effects of Positive End-Expiratory Pressure

Continued high mortality in patients with ARDS treated by PEEP prompted a reexamination of the adverse cardiovascular effects of PEEP beginning about 1975, although it should be pointed out that even Asbaugh's original studies indicated that a fall in cardiac output occurred with PEEP which parallelled the increase in arterial oxygen tension.

The primary cardiovascular effects of PEEP are a decrease in cardiac output, heart rate and blood pressure as illustrated in Figure 4 (29). These changes are proportional to the level of end-expiratory pressure with cardiac output falling approximately 50% and blood pressure falling approximately 20% during 15 cmH_2O PEEP. Heart rate does not change significantly, falling less than 5%. These findings have been observed by many investigators in animals both with normal lungs and with pulmonary edema (27,64,76-78,87,94,102,111,119,125, 127,129,130,135,137-140,143,144,148,150,152,153,162,173) and in normal human subjects (16,28,42,60,70,95,96,99,116,123,126,130,131,155-157,159).

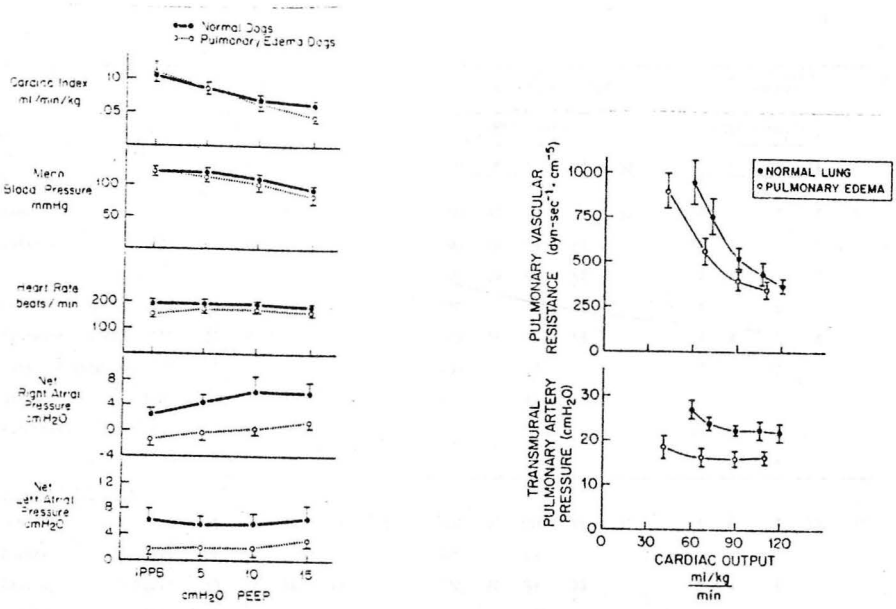


Figure 4 Cassidy (29)

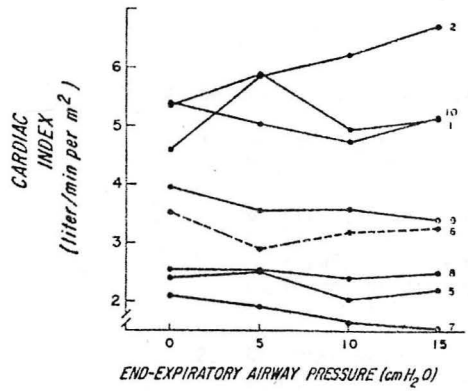
The effects of PEEP on pulmonary arterial pressure are the most misrepresented of all the cardiovascular responses. The data in Figure 4 show why. It is true that PEEP increases pulmonary vascular resistance (PVR). This is both because PEEP enlarges the lung which increases PVR and because PEEP increases alveolar pressure which also increases PVR. The pulmonary artery pressure would have risen if flow through the pulmonary capillaries (cardiac output, C.O.) remained constant, but it did not. Cardiac output fell with PEEP, and a reduction in flow through the system would have lowered pulmonary arterial pressure. The only way to know the relative influence of the increase in PVR and the decrease in C.O. on pulmonary arterial pressure during PEEP is to actually measure pulmonary arterial pressure during PEEP. As also illustrated in Figure 4, pulmonary arterial pressure did not rise to any substantial degree as the level of PEEP was raised. Table 1 shows the results of several other studies in which cardiac output and pulmonary arterial pressures were measured during ventilation with PEEP. In none of them did PEEP cause an elevation of pulmonary arterial pressure to a level that would be expected to reduce right ventricular stroke volume, even in the one study in patients (88). It is of interest to note that pulmonary hypertension did not exist in the animal models of ARDS nor in the ARDS patients. Thus, it would seem that the reported increase in RV afterload has been exaggerated.

Table I

		PAP (mmHg)					Cardiac Output (% Δ from 0 PEEP)					LAP or LVEDP (mmHg)				
		PEEP (cmH_2O)					PEEP (cmH_2O)					PEEP (cmH_2O)				
		0	5	10	15	20	0	5	10	15	20	0	5	10	15	20
Dogs Normal Lungs																
Rankin	(138)	15	17	22	29		100	93	78	63	52	6	6	7	7	8
Cassidy	(32)	16	14	13	15		100	88	79	63		10	8	7	7	
	(27)	16	17	20	23		100	89	65	58		4	5	7	7	
Fewell	(67)	16		19			100		75			4		6		
Schreuder (pigs)	(151)	22	20	19	22		100	85	72	55		4	4	6	8	
Quist (diastolic)	(137)	7		13			100		57			7		12		
Uzawa	(170)	15		19			100		45							
Robotham	(143)											6		7		
												17		16		
Dogs Edematous Lungs																
Scharf	(48)	15	16	17	19	15	100	91	70	49	41	5	6	7	10	10
Cheney	(35)	22		29			100		68							
Cassidy	(27)	13	14	16	19		100	80	59	39		2	4	5	7	
Prewitt	(33)	18		21			100		77					N.C.		
Patients																
Jardin	(96)	20		21			100		84			5		7		

PAP = pulmonary artery pressure; LAP = left atrial pressure; LVEDP left ventricular end-diastolic pressure

On the contrary the cardiovascular responses to ventilation with PEEP in patients with ARDS are variable. Adding or increasing PEEP in patients may increase, decrease, or not alter the cardiac output (39,45,57,58,88,89, 97,101,149) as shown in the study by Falke, Figure 5 (61). The presumed mechanism of an increase in cardiac output in some patients with ARDS is that PEEP may sufficiently increase arterial oxygen content to reverse tissue hypoxemia, especially of the myocardium, to a sufficient degree as to restore vascular integrity and cardiac function. Alternatively, it is recognized that it is not possible to control all the other variables that would alter cardiovascular function in these critically ill patients. Thus, the concurrent administration of intravenous fluids, diuretics, inotropic and vasopressor agents would modify the cardiovascular response to changing the level of PEEP. There have been several recent reviews of the subject (17,124,166,169,172) which deal with the variability of the responses to PEEP in more depth.



Cardiac index recorded at four different levels of end-expiratory pressure, each used for a period of 30 to 35 min. Patient number is entered at right (see Table I). Patient No. 6 received metaraminol 8 μg/min and isoproterenol 8 μg/min as i.v. infusion during IPPV. The infusion rate for metaraminol was increased to 75 μg/min, 150 μg/min, and 204 μg/min during ventilation with PEEP at 5, 10, and 15 cm H_2O, respectively.

Figure 5 Falke (61)

Mechanisms by which Positive Pressure Ventilation Reduces Cardiac Output

Since the fall in cardiac output is a major limiting factor in utilizing PEEP to treat hypoxemia in patients with ARDS, a major effort has been expended to determine the mechanisms by which PEEP causes the fall in cardiac output. A useful approach to evaluating potential mechanisms for reducing cardiac output has been to assess the individual components of right and left ventricular stroke volume: preload; afterload; and contractile state.

A. Determinants of right ventricular stroke volume.

1. A reduction in right ventricular preload is often proposed as the mechanism that initiates the reduction in stroke volume caused by PEEP. This reduction in RV preload is caused by the increased pleural or extrapulmonary intrathoracic pressures. Also, a reduction in mean systemic capillary driving pressure caused by peripheral vasodilation would decrease RV preload.

2. An alternative mechanism that has been proposed to cause or contribute to the reduced stroke volume caused by PEEP is an elevation in right ventricular afterload associated with an increased pulmonary vascular resistance (PVR). This increase in PVR is produced both by the elevation in alveolar pressures and the enlargement of lung volume.

3. A decrease in right ventricular contractility caused by PEEP could be a potential cause for or contributory factor to the reduced stroke volume although there are no compelling data for such a mechanism.

B. Determinants of left ventricular stroke volume.

1. It is proposed that left ventricular preload is reduced by PEEP for potentially three different reasons.

   a. First, because right ventricular output is reduced;
   b. Second, because the septum is shifted leftward to further compromise LV size; and
   c. Third, by direct compression of the left ventricle by the left lung.

2. An afterload mechanism is not a conceivable mechanism to account for the PEEP-induced fall in LV stroke volume. This is both because PEEP causes systemic arterial blood pressure to fall, not increase, and because the increased intrathoracic pressure would enhance, not hinder, the emptying of the ventricle.

3. A reduction in LV contractility has been proposed as contributing to the lowered LV stroke during PEEP. The mechanisms that are suggested to be responsible for the reduction in LV contractility are:

   a. release of a myocardial depressing humoral substance from the lung.
   b. reflex inhibition of LV contractility initiated by lung expansion;
   c. inappropriately reduced myocardial blood flow;

Thus, of the six determinants of stroke volume, only one, LV afterload, can be excluded on theoretical grounds as a potential source for the reduction in cardiac output during PEEP. It should be possible however to determine the presence or absence of abnormalities in the other 5 determinants by simply measuring preload, afterload and contractility before and after adding PEEP. In the last 5-8 years there are over 1000 papers written on this subject which belies their simplicity. The results have been somewhat contradictory, but more often it is the interpretations of the data that are in conflict It will be the major emphasis of this presentation to summarize the data regarding the effects of PEEP on intrathoracic pressures and left and right ventricular preload, afterload. and contractility.

Determining the effects of PEEP on preload, afterload and contractility is more difficult than it is for other interventions such as testing the effects of various drugs, ischemia, intravascular volume expansion, hemorrhage, etc. This is because the pressure surrounding the heart is not considered to change during the latter interventions. The extent to which the heart deforms when it is relaxed is determined by the net forces acting on it both from the outside as well as inside the ventricular chamber. If the extracardiac pressure does not change, the intracardiac pressure can be referenced to atmosphere at a fixed level (usually approximating the vertical location of the left atrium) to monitor changes in intracardiac pressures that follow with the respective intervention. The possibility always exists of course that absolute pressures will misrepresent transmural ventricular pressures by whatever the difference is between extracardiac and atmospheric pressures. During the inspiratory phase of positive pressure ventilation and when the level of PEEP is being changed, the intrathoracic pressure in general and more specifically that pressure surrounding the heart would increase. Therefore, to estimate changes in preload and afterload from intracardiac pressures (end-diastolic pressure, and peak systolic pressure), during PEEP these pressures must be referenced to pressure surrounding the heart rather than to atmospheric pressure. This is an important concept to understand when attempting evaluation of the effects of any respiratory phenomenon on cardiac mechanics.

The Concept of "Pleural Pressure"

Since the inside surface of the chest wall, the lungs and the heart are lined with a separate epithelial lining, a potential space is created allowing the structures to glide over each other. This potential is realized when either fluid or air enter the space and the space becomes real rather than a virtual space. It is thought that if appropriate provisions were made to avoid introducing artifacts, catheters or other pressure monitoring devices could be placed between these surfaces to record changes in distensibility of the structures encompassing the space. The pressure thus measured has been called the pleural pressure. There is a gravity-dependant gradient in pleural pressure so that the pressure measured near the diaphragm is more positive (or less negative) than that measured near the apex in an upright individual. Regardless of this verticle pressure gradient, a change in lung volume is thought to produce a change in pleural pressure that is appropriate for the distensibility of the opposing structures irrespective of the site at which it is measured (72). Such reasoning has been verified by comparing lateral pleural and intraesophageal pressures while altering lung volume to estimate lung and chest wall compliance. This reasoning was carried over to equate intraesophageal and mediastinal pleural pressures which are more closely associated with the heart surface.

The pressure surrounding the heart would be the pressure in the pericardial space. Outside the pericardium would be the mediastinal pleural space or the anterior and posterior mediastinum. Since the pericardium is only outwardly restricting, not inwardly limiting, it is thought that increases in the pleural pressure would be fully transmitted to pericardial space (22).

The reverse would not be true, however. That is an increase in pericardial pressure whether caused by a dilating heart or by a pericardial effusion is not believed to be transmitted outwardly to the pleural space, and a change in pleural pressure in a negative direction may not be fully transmitted across the pericardium to influence ventricular deformity. For the present it will be considered that there is one "pleural pressure", changes in this "pleural pressure" are the same no matter where they are measured, and the pressure surrounding the heart is the "pleural pressure".

It would be appropriate at this point to make some general comments regarding pleural pressure, ARDS, and PEEP. In ARDS with atelectasis and edema, one would expect pleural pressure to be more negative (40). Alternatively, extensive abdominal surgery, obesity and trauma to the thorax would markedly limit outward expansion of the chest wall. This reduction in outwardly directed chest wall recoil would tend to increase pleural pressure or make it less negative (60). Thus, the pleural pressure even at FRC is likely to be quite variable in circumstances associated with ARDS when one likely would consider using positive pressure ventilation and PEEP. It is often said that ARDS might protect the individual from as great an increase in pleural pressure caused by PEEP. On the other hand chest wall injury, including abdominal surgery, might increase the pleural pressure and increase the extent to which PEEP would raise pleural pressures enhancing the effects of PEEP. Thus, the adverse cardiovascular responses to PEEP in patients with ARDS, if these responses are related to pleural pressure, could be expected to be enhanced or to be mitigated depending on the circumstances.

The factors that determine pleural pressure during positive pressure ventilation are quite different from those that determine pleural pressure during spontaneous ventilation. The effect of spontaneous breathing and positive pressure breathing on pleural and right atrial pressures are illustrated in the polygraphic recordings below.

Spontaneous Breathing (Figure 6). At resting lung volume (also called functional residual capacity, FRC) the pleural pressure represents the outward recoil of the chest wall and the inward recoil of the lungs. The volume at FRC will be that which results when the recoil pressures are balanced. During inspiration the respiratory muscles contract enlarging the thorax, and the pleural pressure falls reflecting the force needed to overcome airways resistance to move air into the alveolae and to overcome lung recoil.

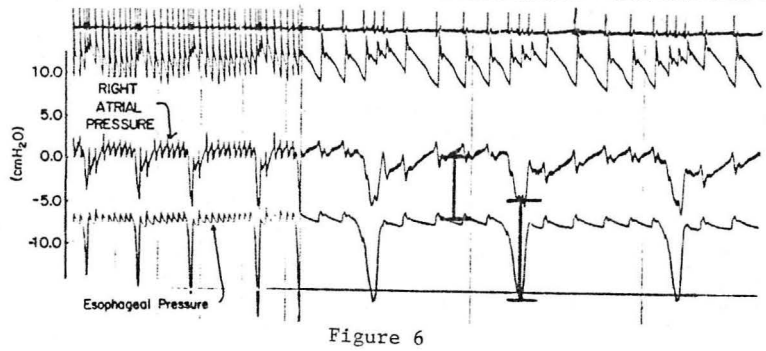


Figure 6

At end inspiration when airflow has ceased, pleural pressure reflects the force necessary to expand the lung to that designated volume determined by respiratory muscle action. Note that right atrial pressure also falls during spontaneously generated lung expansion. Because right atrial pressure does not fall as much as the pleural pressure does, the difference between the atrial and pleural pressures, often called transmural or net right atrial pressure, actually increases. This explains in pressure terms the enhanced right heart filling during spontaneous inspiration; whereas, the right atrial pressure, per se, if considered alone would reflect a lowered filling pressure.

Positive pressure breathing (Figure 7). Again at resting lung volume (FRC), pleural pressure is determined by the equal and opposite recoil of the lungs and chest wall. Pleural pressures rises with each positive pressure lung inflation. Right atrial pressure rises also, but not as great an extent as does the pleural pressure; therefore, transmural right atrial pressure actually falls during positive pressure inspiration explaining the reduced filling of the right heart during positive pressure lung inflation.

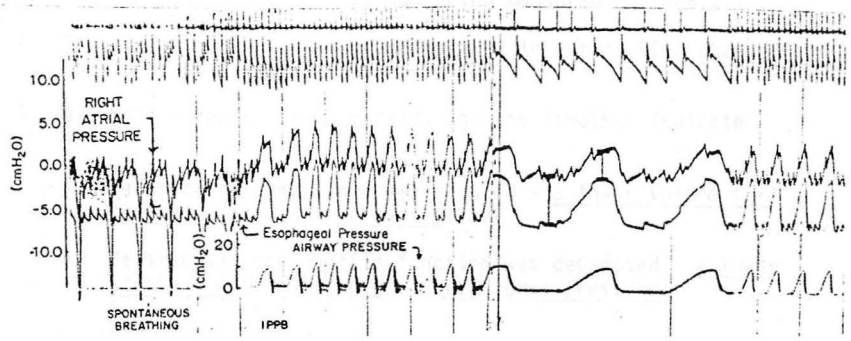


Figure 7

The primary difference between positive pressure ventilation and spontaneous ventilation with respect to pleural pressure is that the chest wall remains relaxed during lung expansion with positive airway pressures; whereas, during spontaneous inspiration the thorax is actively deformed by the muscles of respiration. In mechanical terms it is said that the lungs and chest wall expand in series during positive pressure ventilation. Under these circumstances the change in pleural pressure with positive pressure inflation reflects only the recoil of the chest wall. The recoil of the lung is represented by the difference between pleural and airway pressure; i.e. transpulmonary pressure. The airway pressure reflects the added recoil of both the lungs and chest wall.

Therein lies the important difference regarding cardiac mechanics between spontaneous breathing and positive pressure ventilation. During a spontaneous inspiration the change in pleural pressure for a given change in lung volume is a measure of lung compliance. During positive pressure ventilation the pleural pressure change is a measure of chest wall compliance. Remember the abdomen is a component of the chest wall.

Based on these often observed findings, it was hypothesized that consequent to PEEP, mean cardiac filling pressures (right atrial or end-diastolic and left atrial or end-diastolic) measured in the steady state should be increased, but not as much as pleural pressure would increase; therefore, transmural pressures at end diastole, or transmural mean atrial pressures, would fall reflecting the reduction in end-diastolic volumes.

The results of such experiments in which left and right atrial pressures and pleural pressure were measured as the level of PEEP was increased were shown in Figure 4 contrary to what was expected, atrial pressure increased more than, not less than, pleural pressure. Thus, transmural filling pressures actually increased rather than decreased as cardiac output fell. Similiar findings were reported from several laboratories (cited above), but the interpretations varied widely as outlined below:

1. The "pleural pressure" was not being measured correctly.

2. The atrial pressure measurements were in error (PEEP changed the level of the heart).

3. All measurements were accurate, and the findings indicate that:

   a. Ventricular compliance was reduced - a lower volume for the same transmural pressure; or

   b. Ventricular contractile function was depressed - a lower stroke volume for the same transmural pressure.

Subsequently, studies were initiated at several centers to clarify these issues. The studies can be grouped into five categories according to experimental design.

I. Experiments that replaced the heart or its chambers with balloons and measured the effect of PEEP on intraballoon pressure (103,104,165).

II. Experiments that measured the effects of PEEP on extracardiac pressure at multiple sites over the heart surface (43,67,112).

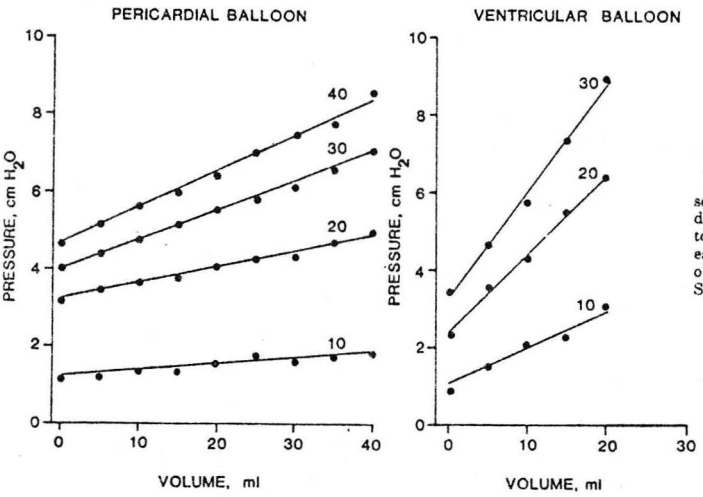
III. Experiments that measured the effects of PEEP on end-diastolic and end-systolic left and right ventricular volumes directly (32,33,64,65,142,164,171).

IV. Experiments that measured the effects of PEEP on cavitary dimensions and addressed the issue of potential shifts in the position of the septum (32,33,79,89,130,141,142,148,163).

V. Experiments that examined the effects of PEEP or ventricular contractility (33,44,49,75,109,170,173).

The results of those studies have been very enlightening although in any one particular study it was often difficult to place the findings in perspective (31). This has led to some confusion as to exactly how positive pressure ventilation with PEEP alters cardiovascular function.

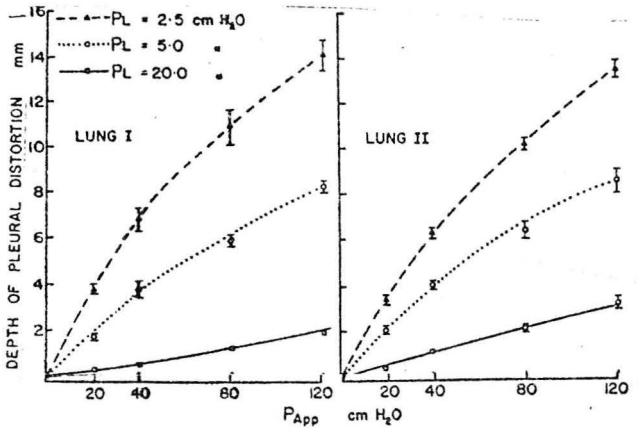
I. The compressive effect of PEEP on the heart was studied by Lloyd (104) and Robotham (165) by replacing the heart with a balloon in freshly killed dogs and measuring balloon pressure at different volumes during ventilation with various levels of PEEP. As illustrated in Figure 8 each level of PEEP



Pressure-volume curves obtained at several end-expiratory pressures with pericardial and left ventricular balloons. End-expiratory pressure (in cmH_2O) is given at right of each curve. Each *data point* is avg of two observations in each of 6 dogs. Exact values and SE's are listed in Table 1.

Figure 8 Lloyd (104)

raised the balloon pressure, but not by a fixed amount. The pressure to fill the balloon a specified volume increased incrementally as the level of PEEP was raised. This means that this hollow space in which the heart usually rests has a compliance which decreases as the level of PEEP increases. Lloyd coined the term "cardiac fossa" to describe this hollow space. In essence Lloyd and Robotham were saying that the lung becomes stiff when pressure is applied to the airway. A clue to the fact that the lung would become less deformable as it enlarged under positive airway pressure originated from a study by Robertson et al. (133). They measured the extent to which a probe would indent the surface of the lung, Figure 9. The same force was used with the lung at FRC and with the lung inflated to 20 cmH_2O pressure. Near FRC the probe would depress the lung surface 13-14 mm, but the same force applied to the lung expanded with 20 cmH_2O pressure was not able to depress the lung surface more than 1-2 mm.



Distortions produced in pleural surface by various localized pressures are shown at three different transpulmonary pressures for two of six lobes. Absolute differences and change in slope show that marked resistance to distortion is produced by lung inflation. Symbols at each point indicate mean and standard error of four separate measurements.

Figure 9 Robertson (133)

Similar studies were performed in dogs in which the heart and pericardium, remained intact anatomically and a balloon was placed in the LV cavity, Figure 8. As the level of PEEP was raised from 0-15 cmH_2O, the pressure required to fill the LV to a volume of 20 ml is increased from 3 to 9 cmH_2O. This represents a reduction in the compliance of the LV system that was much greater than the reduction in compliance of the cardiac fossa, per se.

The heart is in the same position that their probe was in (Figure 10). If the left ventricle is to expand outwardly to fill, it must depress the lung surface to a corresponding degree. During PEEP far greater intracavitary pressure is required to do so. This would not be a compliance change in the LV myo-

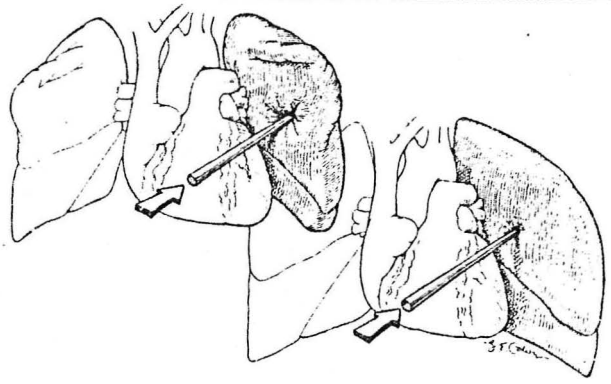
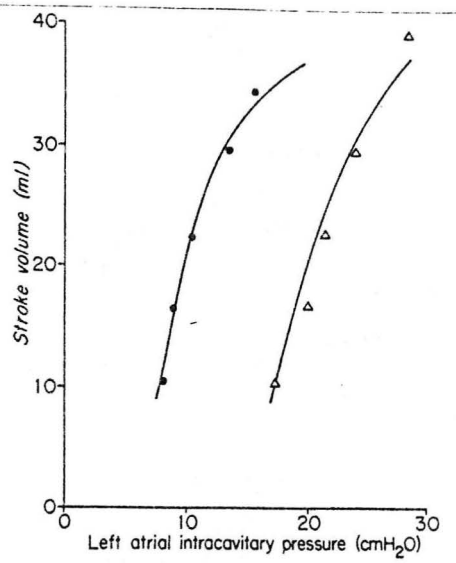


Figure 10

cardium, but rather a change in the compliance of the LV system. This would be a compliance that measured the pressure required to distend the LV walls and septum and the pericardium outwardly and to lift away the lungs or other surrounding structures. Stated in mechanical terms the heart, lungs, and chest wall are in series in regard to filling the ventricular chambers in much the same way that the lungs and chest wall are in series in regard to filling the lungs with positive airway pressure. The presence of the pericardium seemed not to alter the distensibility of the LV system at the various levels of PEEP except when the LV was overdistended volume-wise (165).

Recall now the initial problem with the transmural pressures which showed that atrial or end-diastolic pressures increased more than did the pleural pressure as it was estimated from intraesophageal pressure. If these measurements were correct they would indicate that cardiac filling volumes were increased rather than decreased as was expected. The Frank-Starling curves constructed by Marini (Figure 11) illustrate the increase in intracavitary pressures needed to generate various levels of stroke volume. When 15 cmH_2O PEEP was added. A LAP of 25 cmH_2O (19 mmHg) is needed to generate a stroke volume of 30 ml.



An example of curves constructed from left ventricular function data obtained from a single closed-chest animal before (●) and after (△) 15 cmH_2O PEEP was applied to airway. Curves represent least-squares parabolic equation fit to data. At 0 cmH_2O PEEP, SV = $-0.27\ (LAP)^2 + 9.33\ (LAP) - 46.26$. At 15 cmH_2O PEEP, SV = $-0.13\ (LAP)^2 + 8.41\ (LAP) - 96.83$. LAP, left atrial pressure.

Figure 11 Marini (112)

Table 2

Intrathoracic pressure increments after a 15-cmH_2O increase in end-expiratory airway pressure (closed chest)

	Pressure increment, cmH_2O		
	Esophageal	Left mediastinal	Right mediastinal
Venous diversion	5.2 ± 0.7	9.2 ± 0.8*	13.0 ± 0.9*
No diversion	6.5 ± 0.5	9.1 ± 0.7*	9.2 ± 0.4*

Values are means ± SE, with data obtained from 4 dogs. Cardiac output was constant at 2.5 l/min. *Significant difference from esophageal value, $P < 0.01$.

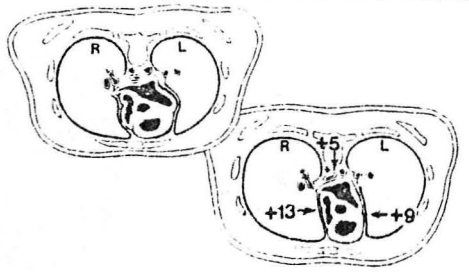


Figure 12

II. Marini et al. (112,113) and Fewell et al. (67), using pressure monitoring devices that were modified so as not to produce artifacts, have measured the pressures overlying the heart at various points before and during ventilation with PEEP. The important findings from these studies (Table 2) are that the pressures overlying the lateral surfaces of the heart increase to a much greater extent with PEEP than do the posterior mediastinal pressures. The posterior mediastinal pressure would most closely correspond to the intra-esophageal pressure. This was the first compelling evidence that the concept of a pleural pressure that was uniform throughout the entire pleural space would be invalid for understanding cardiac mechanics during changes in lung volume or respiratory mechanics.

It is clear that a single intraesophageal pressure measurement would not have sufficed to measure the net forces acting on the external heart surface to deform the myocardium. Some interest was generated in an attempt to locate a single site which would represent the sum of those external forces. A more important impact of these studies, however, was to reveal that not only is pleural pressure not uniformly distributed throughout the pleural space, but changes in pleural pressure brought about by various levels of positive pressure ventilation are not uniformly distributed throughout the pleural space especially in regions surrounding the heart. The effect that this uneven distribution of force generated by the lung would have on the heart is illustrated in Figure 12. Thus, if lateral pressures rise to a greater extent than do anterior and posterior pressures, it is because the forces acting in the lateral direction are greater. From these results of uneven distribution of compressive force generated by the lung, we would project that the heart would be deformed and reshaped to become more oblong in the anterior to posterior direction in cross section.

III. To determine whether or not such deformation of the heart takes place as a consequence of ventilation with PEEP, the LV dimensions have been studied (32,33). Beads were placed in the left ventricular wall of dogs near the endocardium in positions that would define three mutually perpendicular LV dimensions: anterior-to-posterior; septum-to-lateral; and apex-to-base. After sufficient time to heal from this surgery, biplane cinefluorography recordings could be made at 60 frames/sec to record the 3-dimensional position of these beads that define the position of the ventricular walls (Figure 13). The effects of adding PEEP on LV dimensions at end diastole and end systole are illustrated in Figure 14a which shows that all LV end-diastolic dimensions decreased, but the septal-to-lateral dimension decreased the most falling to a width that at end diastole was narrower than it was at the end of systole. The extent that

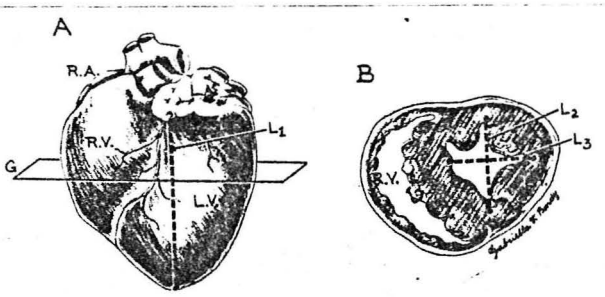


Figure 13 Cassidy (32). LV bead placement. L_1, apex to base; L_2, anterior to posterior; and L_3, septal to lateral.

this width could narrow on contraction was reduced by 80%. Thus, whatever was causing this narrowing was greatly compromising stroke volume. Was this caused by the septum shifting into the LV or by the lateral LV wall being forced inward? To answer this, a geometric plane was defined through the anterior, posterior and apical beads, and the relative shifts in the septum and lateral LV wall to the center of the LV were determined. The septum at end diastole shifted toward the center of the LV only to the same degree as did the anterior, posterior, and apical portions of the LV wall. It was the lateral wall that was greatly shifted inward at end diastole during 10 cmH_2O PEEP out of proportion to the otherwise concentric reduction in the left ventricle. When LV end-diastolic volume was restored, Figure 14b, this altered LV shape was preserved. Thus, to accomodate for the compression of the lateral LV wall by the stiff nondeforming left lung, the LV volume was restored by expanding in the anterior and posterior directions and by shifting the septum rightward into the right ventricular chamber.

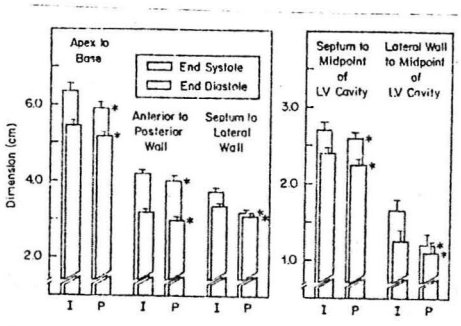


Figure 14a Cassidy (33). LV Dimensional changes following 10 cmH_2O PEEP. I = IPPB. P = PEEP.

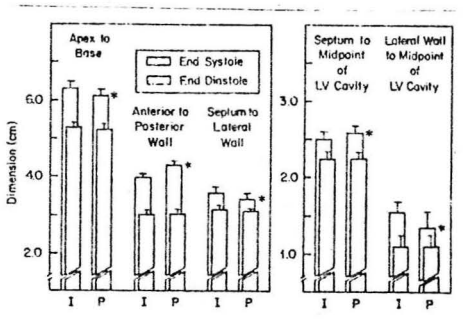


Figure 14b Cassidy (33) LV dimensional changes following 10 cmH_2O PEEP after cardiac output was restored.

These alterations in geometric relationships are pictured in Figure 15. During hemorrhage the LV size in cross section is reduced concentrically; likewise, it is restored concentrically. During PEEP the anterior, septal, and posterior walls move concentrically toward the center of the LV, but the lateral wall is deformed inwardly to a greater extent. Following restoration of left ventricular end-diastolic volume the anterior, septal, and posterior walls expand concentrically leaving the lateral wall deformed.

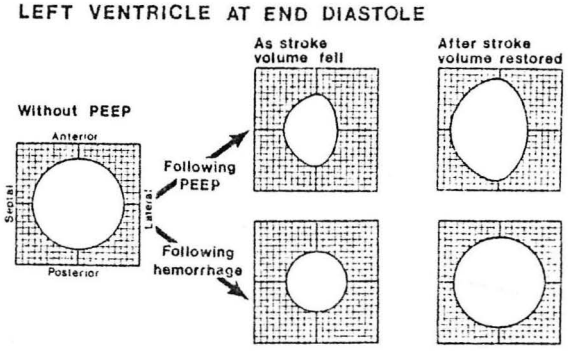


Figure 15

The effect that this compression of the lateral LV wall has on cardiac shape throughout the cardiac cycle has also been examined. Figure 16 illustrates these dimension changes throughout a cardiac cycle for the entire group of animals. All the dimension narrow and widen as expected during systole and diastole without PEEP showing a brief isovolumic phase, ejection and rapid and slow filling phases. During PEEP a departure from this pattern is noted only for the lateral wall and the septal-to-lateral-wall dimension. The lateral wall moves outward during isovolumic contraction widening the septal-to-lateral wall dimension considerably. Then the lateral wall moves inward with narrowing of the septal-to-lateral wall dimensions during ventricular emptying. As soon as the myocardium begins to relax the lateral wall is deformed inwardly which actually narrows the septal-to-lateral wall dimension considerably while the remainder of the heart is expanding. Subsequently, the lateral wall moves slowly outward allowing the heart to expand slowly in the septal-to-lateral direction.

A 2-dimensional horizontal cross-sectional view of these events is illustrated in Figure 17. During PEEP the deformed asymmetric left ventricle undergoes a sphericalization during early systole; then the LV empties concentrically. During early relaxation the deformation is restored rapidly, presumably by the rigid lung juxtaposed along the left lateral heart border. Continued expansion is primarily in the anterior, septal, and lateral directions.

In a study of patients with ARDS in France, Jardin et al. (89) came to opposite conclusions about the relative position of the septum during ventilation with PEEP. Using echocardiography to assess LV geometry, they reported

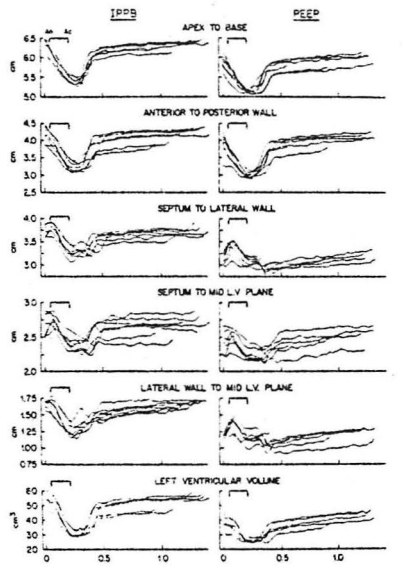


Figure 16 (Cassidy (33)

LV dimensional changes throughout a cardiac cycle (R wave to R wave) during IPPB and during 10 cmH_2O PEEP.

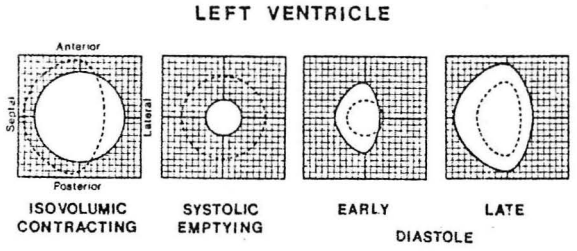


Figure 17. Dotted line represents the beginning of the phase, solid lines the end of the phase.

that PEEP increased the radius of septal curvature and narrowed the LV in the septal to lateral direction. From their findings they concluded that the septum had to be pushed from its normal position of curving into the RV to a station closer to the center of the LV. However, these data in dogs show similiar findings; that is the LV is narrowed and the radius of septal curvature would be increased because of the outward expansion of the anterior and posterior walls. However, in these biplane cinefluorography experiments the closeness of the septum and other parts of the LV to the center of the LV chamber was actually measured. It was not the septum that moved inordinately toward

the center of the LV, but rather it was the lateral wall that did so. The septum will flatten whether it is directly compressed from the RV side or whether the LV cavity is encroached upon from the opposite side, expanding the adjacent sides outward.

IV. As already may be apparant by now the end-diastolic volumes of both ventricles are in fact reduced by ventilation with PEEP (Figure 18), and the fall in volume is proportional to the level of PEEP (32,33,64,65,142,164,171). End-systolic volumes are also reduced even on the right side, but the fall in RV and LV end-systolic volumes are not as great as the fall in end-diastolic volumes so that the stroke volume is reduced. Stroke volume and end-diastolic volume can be restored either by fluid administration (33,122) or by infusion of drugs such as aramine (19) or dopamine (14,82), but only at the cost of the previously described increased capillary hydrostatic pressure.

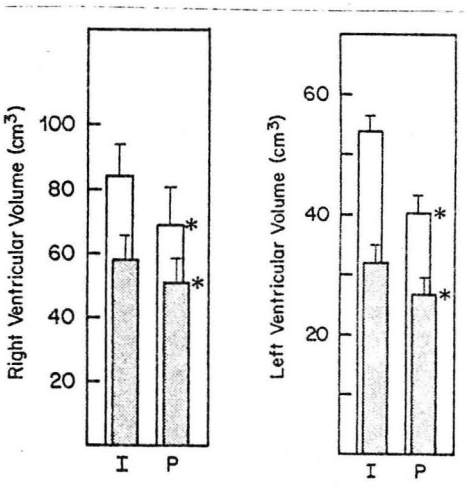


Figure 18. Right and left ventricular volumes during IPPB (I) and during 10 cmH_2O PEEP (P). Open bars, volume at end diastole; shaded bars, end systole.

V. The question as to whether or not left or right ventricular contractility are reduced during PEEP has not been fully resolved. Studies measuring LV contractility have shown that Frank-Starling function curves are not shifted as a consequence of ventilation with PEEP (Figure 19). LV dP/dt, on the other hand has been shown most often to be depressed with PEEP. Problems can be uncovered easily in the studies, both those showing increases in contractility and those showing decreases, and the final word on changes in contractility during PEEP has not been presented (25,33,49,55,75,109,173).

A different approach to determining the effect of PEEP on contractile state has been to look for mechanisms that could be responsible for decreased contratility. To date potential mechanisms that would depress myocardial function would be:

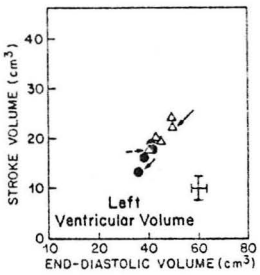


Figure 19 Cassidy (33).
LV stroke volume/end-diastolic volume curves during IPPB (triangles) and during PEEP (circles). No shift in the curve is suggested with PEEP.

1. Release of a myocardial depressing substance (55,75,121,161);

2. Initiation of a reflex evoked by stretching the lung which depresses myocardial contractility (30,62,144,150); and

3. Myocardial ischemia (110,134,160).

1. Manny et al. (109) and Patten et al. (121) have reported that the blood of dogs and patients treated with PEEP contains a substance that was not present before PEEP which will depress cardiac output and LV function. Apparantly this depressor substance can be inhibited if prior treatment with an inhibitor of cycloxygenase is administered (55,56). Data regarding the effects of treatment of patients with cyclooxygenase inhibitors on the cardiovascular response to PEEP are not convincing. PEEP-induced prostaglandin release (55) may enhance the increase in FRC (12) thereby augmenting the cardiovascular depression.

2. Reflex effects of lung expansion are illustrated in Figure 20. Lung expansion has been known for many years to cause reflex hypotension, bradycardia, and apnea (71). Recently, lung expansion has been shown to decrease stroke volume and LV contractility, also (30,6a). These reflexes are mediated through the afferent fibers in the ipsilateral vagus nerves. Selective blockade of neural efferent pathways have shown that the bradycardia is mediated by cholinergic stimulation and withdrawal of β-adrenergic tone. The hypotension is caused both by α-adrenergic mediated peripheral vasodilation and a reduction in stroke volume. The reduction in LV contractility and stroke volume are believed to be caused by a reduction in β-adrenergic tone, but this mechanism has not been proven. These lung inflation reflex responses are profound only transiently, and then they return toward normal. Demonstration that lung expansion reflexes mediate part of the steady state cardiovascular depression during PEEP has been reported by Stinnett et al. (144,150,151). Comparing changes in the cardiovascular responses to PEEP after cutting both vagi is a poor experimental design because baseline neural control of cardiovascular function is altered, but doing so does not appreciably alter the cardiovascular responses to PEEP (166). Adrenergic blockade ameliorates the cardiovascular response to PEEP (62,139), but these data are not convincing as to what role these neural mechanisms might contribute to the cardiovascular effects of PEEP.

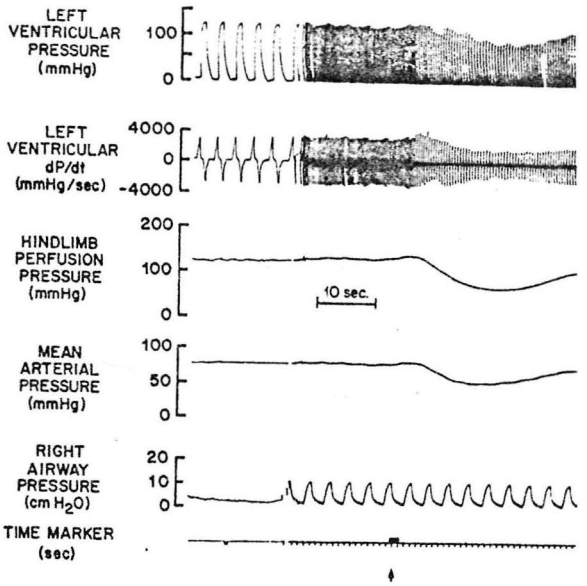


Figure 20. Cardiovascular responses to inflating the vascularly isolated left lung to 30 cmH_2O.

3. Left ventricular blood flow is reduced by PEEP, but the blood flow remains proportional to the cardiac output which also is reduced. Thus, it is believed that the left ventricular blood flow is appropriate for work performed. The right ventricular blood flow is reduced (110-134), but slightly more so than that to the left ventricle. If one considers the heart rate and pulmonary arterial pressure (neither of which are reduced with PEEP) as determining the work the RV has to perform, this reduction in right ventricular blood flow seems inappropriate. On the other hand right ventricular stroke volume is reduced, so if stroke volume is the primary determinant of right ventricular work and blood flow, this reduction may be appropriate. The question remains unresolved for the present.

Summary of altered cardiac mechanics caused by ventilation with PEEP

1. During ventilation with PEEP the lung is expanded beyond normal. This greater expansion encroaches on the space that is occupied by the heart.

2. This expansion of the lung coupled with positive alveolar pressure renders the lung less deformable (less compliant). Much higher cardiac filling pressures are required, therefore, to expand the ventricles to their previous size.

3. The distribution of the compressive forces is not uniform, and there seems to be no way at the present to measure or predict the net compressive force of the lungs which is clearly underestimated by measurement of posterior mediastinal (or intraesophageal) pressure.

4. This encroachment on the heart by the rigid, stiff lungs is experienced by the left ventricle as much or more so than by the right ventricle, perhaps because the left ventricle is situated in the left hemithorax next to the lung; whereas, the right ventricle is positioned in the anterior mediastinum.

5. Adequate filling of the left ventricle (to the end-diastolic volume that would have given a normal cardiac output without the addition of PEEP) could be accomplished only at the expense of an increase in the absolute level of LVEDP (LVEDP referenced to atmosphere at the level of the heart). The exact amount of the increase in absolute LVEDP would be equivalent to the summation of external pressures surrounding the heart. This increase in absolute LVEDP will be of course transmitted to the pulmonary capillary bed. So that reexpanding the left ventricle can be accomplished only at the price of large elevations in pulmonary capillary hydrostatic pressure.

6. Right ventricular filling is also restricted although apparantly the decrease in right ventricular size is concentric, perhaps because the right ventricle is in a somewhat protected location in the anterior mediastinum.

7. The septum does not shift leftward as a consequence of PEEP even after sufficient volume expansion to restore cardiac output and stroke volume. The best evidence that the compressive force of the lungs is felt more by the LV than by the RV is that after volume expansion, the septum shifts rightward implying the compliance of the "LV system" is reduced more than that of the "RV system".

8. Whether or not there are additional factors that depress myocardial function or cause a decrease the peripheral driving pressure to RV filling are still unresolved issues. Some evidence has been presented that indicate that lung inflation reflexes, and release of humoral substances might enhance the magnitude of the overall reduction in cardiac output caused by PEEP. Myocardial ischemia probably does not contribute to the depressed cardiac output, but it has not been definitely excluded.

Conclusions

These recent data modify our previous concepts as to the mechanisms responsible for the reduction in cardiac output by positive pressure ventilation with PEEP. It has long been known that PEEP increases lung expansion and raises pleural pressure, and it was concluded that the increase in pleural pressure restricting venous return was the sole cause of the reduced cardiac output. It was not recognized until recently that the increased stiffness of the expanded lung expanded with positive airway pressure reduced the compliance of the cardiac fossa and reduced the effective compliance for filling the heart. The net result is compression of the heart, particularly that portion of the left ventircle exposed to the left lung. In order to restore normal filling an end-diastolic pressure nearly 3 times higher than the average increase in pleural pressure caused by PEEP is required. This can be done only at the expense of correspondingly raising pulmonary capillary blood pressure. The reduced compliance of the cardiac fossa during PEEP produces a complex problem in management of the low cardiac output associated with PEEP because the pulmonary capillary blood pressure required to restore normal left ventricular filling with a normal cardiac output may aggravate pulmonary edema and further impair gas exchange.

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