A potential method of correcting intracavitary left ventricular filling pressures for the effects of positive end-expiratory airway pressure

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ABSTRACT Based on the observation that positive end-expiratory airway pressure (PEEP) causes comparable increments in intrapericardial and right-sided intracardiac pressures, we hypothesized that intracavitary left ventricular filling pressures measured in the presence of PEEP can be corrected for increased intrathoracic pressure by subtracting the effects of PEEP on intracavitary right ventricular filling pressures. Ventricular function curves (aortic blood flow vs intracavitary left ventricular end-diastolic pressure [LVEDP]) were generated with and without 15 cm of water of PEEP in eight dogs. All curves were shifted to the right by PEEP (i.e., intracavitary LVEDP was higher for any submaximal level of aortic blood flow). However, when pressures measured in the presence of PEEP were “corrected” by subtracting the corresponding increment in intracavitary right ventricular end-diastolic pressure caused by PEEP at each level of ventricular filling, control and corrected PEEP data points appeared to fall on the same curve in five dogs, and differed only slightly in three dogs. Mean control and corrected PEEP curves derived by averaging polynomial regression coefficients for each condition differed significantly from uncorrected PEEP curves (p < .05), but not from each other. Analogous curves based on mean left atrial pressure were corrected equally well by subtracting the effects of PEEP on mean right atrial pressure. We conclude that the increments in intracavitary right heart filling pressures caused by PEEP can be used to correct intracavitary left heart filling pressures for the effects of PEEP on intrathoracic pressure.


POSITIVE end-expiratory airway pressure (PEEP) complicates hemodynamic monitoring in critically ill patients by increasing intrathoracic pressure. This effect alters the usual relationship between intravascular filling pressures and cardiac output, and invalidates standard guidelines1,2 for optimizing left ventricular preload in patients in low-output states. This is because left ventricular filling and stroke volume are functions of transmural, rather than intracavitary left ventricular end-diastolic pressure (LVEDP).3 As a result, the increment in pressure around the left ventricle caused by PEEP effectively shifts ventricular function curves based on intracavitary pressures to the right (i.e., ventricular volume and cardiac output are lower for any measured pressure).4 To remain useful as indexes of left ventricular preload in this setting, intracavitary filling pressures must be corrected for the effects of PEEP on intrathoracic pressure.

We recently found that PEEP causes changes in intracavitary right ventricular end-diastolic pressure (RVEDP) that are similar to changes in mean intrapericardial pressure over a wide range of ventricular filling conditions.5 Based on this observation, and the knowledge that right ventricular pressure constitutes part of the effective pressure around the left ventricle,3 we hypothesized that intracavitary left ventricular filling pressures measured in the presence of PEEP can be corrected for increased intrathoracic pressure by subtracting the effects of PEEP on right-sided intracardiac pressures. To test this hypothesis, we generated ventricular function curves with and without 15 cm of water of PEEP in anesthetized dogs. Curves based on intracavitary LVEDP and mean left atrial pressure were “corrected” by subtracting the effects of PEEP on intracavitary RVEDP and mean right atrial pressure, respectively, at each level of ventricular filling.
Methods

Studies were performed in eight mongrel dogs weighing 22.3 to 32.0 kg. A preliminary left lateral thoracotomy was performed to allow instrumentation. At the time of surgery, a small (approximately 5 cm) incision was made in the superior, left lateral portion of the pericardium, through which an electromagnetic flow probe was placed around the proximal portion of the ascending aorta. In addition, a fluid-filled catheter was placed in the left atrium through the atrial appendage, and a balloon-type pressure manometer was positioned over the lateral surface of the left ventricle within the pericardial space. Each balloon was hand-constructed according to previously described methods,5 6 and consisted of condom rubber cemented to both sides of a thin ring of silicone rubber sheeting with an inner chamber containing a silicone rubber tube with multiple sideholes. These balloon manometers were specifically designed for the measurement of pressure between two contiguous surfaces.7 The pressure-volume characteristics of each balloon were determined before its insertion, and the internal volume necessary to maintain zero pressure was recorded. In addition, a linear pressure response over the range of pressures encountered in each study was confirmed for each balloon in vitro. The balloon rim was attached to the parietal pericardium at one or two points to prevent migration, after which the pericardial incision was closed, and the flow probe electrodes, left atrial catheter, and balloon connecting tubing were exteriorized through small incisions in the lateral chest wall. The chest then was closed in layers, and the dogs were allowed to recover for several days.

On the day of study, the dogs were anesthetized with intravenous morphine (2 mg/kg) and α-chloralose (100 mg/kg), intubated, and mechanically ventilated with 100% oxygen. Fluid-filled catheters were introduced through a femoral artery and femoral and external jugular veins and positioned in the left atrium, right ventricle, and right atrium, respectively. Catheter positions were confirmed by fluoroscopy and appropriate pressure recordings in all cases. In addition, a transvenous pacing wire and a large-bore catheter for fluid administration were introduced through separate veins and positioned in the right atrium and inferior vena cava, respectively. Propranolol (1 mg/kg) was administered intravenously, after which atrial pacing was instituted at a rate of approximately 10 to 20 beats/min above each animal’s intrinsic heart rate. This was done in an attempt to prevent spontaneous or volume-related changes in cardiac sympathetic stimulation and heart rate that might influence the shape of the ventricular function curves generated during each study. Four dogs were given 0.4 mg iv atropine to eliminate Mobitz I atrioventricular block. The right and left atrial and ventricular catheters were connected to Gould P23Db pressure transducers with zero reference set at the midhearts level (determined by fluoroscopy). The intrapericardial balloon was connected to a fifth Gould transducer set at the same level and then filled with the volume of air previously shown to maintain zero pressure in the absence of deformation in vitro. The ascending aortic flow probe was connected to a Zepeda SWF-4 square-wave electromagnetic flowmeter and pressures and aortic flow signals were recorded along with a limb-lead electrocardiogram on a Beckman R611 eight-channel recorder. Measurements were made with respiration suspended for several seconds at end-expiration, at a time when pressures and aortic blood flow were stable. Pressures were checked frequently throughout each study for baseline drift, and the end-diastolic flow signal recorded under each set of study conditions was assumed to represent zero flow. Flow probe calibrations were performed in vitro.

To compare the effects of PEEP on intrapericardial and intracardiac pressures, intrapericardial and right and left atrial and ventricular pressures were recorded as airway pressure was increased from 0 to 20 cm of water in 2 cm of water increments by placing the expiratory hose of the ventilator under water. Paired ventricular function curves were then generated by recording pressures and aortic flow signals both with and without 15 cm of water of PEEP under baseline filling conditions, and again after each increment in blood volume as volume was expanded by administering 10% dextran in 100 ml aliquots. This procedure was continued until ascending aortic blood flow (a close approximation of cardiac output) appeared to reach a plateau. Intrapericardial and intracardiac pressures were then recorded again as airway pressure was increased from 0 to 20 cm of water in 2 cm of water increments to determine whether the relative effects of PEEP on intrapericardial and right and left atrial and ventricular pressures were altered by volume loading. At the end of each study, the dog was killed by administration of intravenous potassium chloride, and the ascending aortic blood flow signal was recorded under conditions of circulatory arrest. This signal closely approximated the end-diastolic reference points recorded immediately before the animal was killed in each case.

Ventricular function curves were generated from measurements made with and without 15 cm of water of PEEP by separately plotting ascending aortic blood flow as a function of either intracavitory LVEDP or mean left atrial pressure. Left-sided intracardiac pressures measured in the presence of PEEP were “corrected” by subtracting the increment in the analogous right heart pressure caused by PEEP at each respective level of ventricular filling. Intracavitary LVEDP was corrected by subtracting the increment in intracavitary RVEDP, and mean left atrial pressure was corrected by subtracting the increment in mean right atrial pressure.

Data from each control and uncorrected and corrected PEEP curve were fit to second-order polynomial equations by standard regression techniques. Ascending aortic blood flow (Q A) was considered a function of left ventricular filling pressure (P) according to the relationship

\[ Q_A = a + b_1 P + b_2 P^2 \]

where a is the value of Q A at zero pressure, b1, and b2 are regression coefficients that describe the shape of the Q A vs P curve, and P is either intracavitary LVEDP or mean left atrial pressure. This model was chosen when higher order polynomial regressions demonstrated that mean coefficients corresponding to third- and fourth-order terms did not differ significantly from zero.8 Mean curves for each condition were derived by averaging regression coefficients.

The differences between control, uncorrected, and corrected PEEP curves were tested statistically by multivariate analysis of regression coefficients using the Bonferroni inequality for multiple simultaneous comparisons.8

Results

The effects of incremental increases in end-expiratory airway pressure on intrapericardial and right- and left-sided intracardiac filling pressures are compared in figures 1 and 2. PEEP caused increments in intracavitary RVEDP and mean right atrial pressure that were nearly identical to changes in intrapericardial pressure under baseline filling conditions, and that were similar to (although slightly less than) changes in intrapericardial pressure after volume loading. PEEP caused changes in intracavitary LVEDP and mean left atrial pressure that were similar to (although slightly
less than) the increments in intrapericardial pressure under baseline filling conditions, but which bore no relationship in either magnitude or direction to the changes in intrapericardial pressure after volume loading.

Ventricular function curves based on intracavity left heart filling pressures were shifted to the right by PEEP (i.e., pressures were higher for any submaximal level of ascending aortic blood flow) in all eight dogs. This was true whether curves were based on intracavi-

FIGURE 1. Relative effects of PEEP on intrapericardial and intracavity RVEDP and LVEDP before (A) and after (B) volume loading. Data points represent average changes from baseline values in eight dogs as end-expiratory airway pressure was increased from 0 to 20 cm of water in 2 cm of water increments. The solid line represents the line of identity. Intracavity LVEDP in the absence of PEEP averaged 0.6 ± 0.4 and 19.1 ± 1.6 mm Hg before and after volume loading, respectively.

FIGURE 2. Relative effects of PEEP on intrapericardial and intracavity mean right (RAP) and left (LAP) atrial pressures before (A) and after (B) volume loading. Data points represent average changes from baseline values in eight dogs as end-expiratory airway pressure was increased from 0 to 20 cm of water in 2 cm of water increments. The solid line represents the line of identity. Mean LAP in the absence of PEEP averaged 0.6 ± 0.5 and 20.3 ± 1.6 mm Hg before and after volume loading, respectively.
tary LVEDP or mean left atrial pressure. Correction by subtracting the increment in intracavity RVEDP or mean right atrial pressure caused by PEEP from the corresponding left-sided intracardiac pressure shifted these curves back toward control in each case (two examples are shown in figure 3). In five dogs, control and corrected PEEP data points appeared to fall on the same curve; the corrected PEEP curves fell slightly to the right of the control curves in two dogs and slightly to the left of the control curves in one dog. Individual control, uncorrected, and corrected PEEP curves were well described by second-order polynomial equations \((r = .84 \text{ to } .99)\). Mean regression coefficients for control and corrected PEEP curves differed significantly from coefficients for uncorrected PEEP curves \((p < .05)\), but not from each other (table 1 and figure 4). This was true whether curves were based on intracavity LVEDP or mean left atrial pressure. For the purpose of comparison, a second set of corrected curves was generated by subtracting the corresponding increment in intrapericardial pressure from each intracavity LVEDP and mean left atrial pressure measured in the presence of PEEP. Curves corrected in this manner were also well described by second-order polynomial equations \((r = .93 \text{ to } .99)\), and did not differ significantly from either control curves or curves corrected by subtracting the effects of PEEP on intracavity right heart filling pressures (figure 5).

**Discussion**

Intracavity LVEDP and its correlates, mean left atrial and pulmonary arterial wedge pressures, are useful indexes of left ventricular preload when measured in the presence of atmospheric airway pressure.\(^1,2\) This has proven to be the case\(^1,2,9-12\) even though the relationship between these pressures and ventricular filling in any individual patient is influenced to an unknown extent by the compliance of the cardiac chambers and the effective pressure acting on the outer surfaces of the left ventricle. However, standard guidelines for interpreting these pressures are based on studies performed in the presence of atmospheric airway pressure,\(^1,2\) and are not valid in the presence of PEEP, when the usual relationship between intracavity pressure and volume is altered by an increase in intrathoracic pressure. Accurate interpretation of intravascular filling pressures must take into account any baseline change in pressure around the left ventricle.

Changes in left-sided intracardiac pressures are not indicative of the effects of PEEP on this external pressure for several reasons. First, although PEEP consistently increases intrathoracic pressure, it decreases left ventricular volume and, under most circumstances, transmural LVEDP.\(^5,14,15\) Since, by definition, changes in intracavity LVEDP must equal the sum of changes in transmural and external pressures \((\Delta \text{LVEDP}_{\text{intracavity}} = \Delta \text{LVEDP}_{\text{transmural}} + \Delta \text{external pressure})\), net changes in intracavity pressure are determined by the combined (and opposite) effects of PEEP on intrathoracic pressure and ventricular volume. Furthermore, the magnitude and direction of these changes depend not only on the level of PEEP, but also

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**FIGURE 3.** Individual ventricular function curves based on intracavity LVEDP (A) and mean left atrial pressure (B) obtained in two separate studies. Each intracavity left heart pressure measured in the presence of PEEP was corrected by subtracting the corresponding increment in right heart pressure (RVEDP or mean right atrial pressure) caused by PEEP at each level of ventricular filling. Control and corrected PEEP data points appear to fall on the same curve in both A and B.
TABLE 1
Polynomial regression coefficients (mean ± SEM)

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<tr>
<td></td>
<td>a</td>
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<tr>
<td>PEEP</td>
<td>-856 ± 564</td>
<td>559 ± 88</td>
<td>-14.621 ± 3.027</td>
</tr>
<tr>
<td>Corrected PEEP</td>
<td>1743 ± 185</td>
<td>336 ± 42</td>
<td>-10.076 ± 1.604</td>
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Regression coefficients are for the model: ascending aortic blood flow = a + b₁P + b₂P², where P = either intracavitary LVEDP or mean left atrial pressure. Data for corrected PEEP curves were derived by subtracting the effects of PEEP on intracavitary right heart filling pressures (see text for explanation). Control and corrected PEEP coefficients differed significantly (p < .05) from uncorrected PEEP coefficients, but not from each other. This was true whether curves were based on intracavitary LVEDP (A) or mean left atrial pressure (B).

on the ventricular filling conditions under which PEEP is applied. When baseline ventricular volume is small, PEEP causes pressure around the left ventricle to rise more than transmural pressure falls, and left-sided intracardiac pressures increase. However, with larger initial volumes, comparable reductions in filling due to PEEP cause greater decrements in transmural LVEDP, due to the nonlinear relationship between left ventricular transmural pressure and volume. As a result, transmural pressure falls as much or more than external pressure rises, and intracavitary pressure either remains the same or decreases. This influence of baseline filling conditions on the response of left-sided intracardiac pressures to PEEP is illustrated in figures 1 and 2. When PEEP was applied in the presence of relatively low initial intravascular pressures, both intracavitary LVEDP and mean left atrial pressure increased (although slightly less than intrapericardial pressure). However, after volume loading, changes in left-sided intracardiac pressures bore no consistent relationship to changes in intrapericardial pressure, and often differed in both magnitude and direction.

In contrast, the effects of PEEP on right-sided intracardiac pressures closely approximate changes in intrapericardial pressure regardless of the filling conditions under which PEEP is applied. This is partly because PEEP has opposing effects on right ventricular volume. By increasing intrathoracic pressure, PEEP decreases the driving force for blood return to the thorax, and reduces diastolic right ventricular filling; but, by increasing pulmonary vascular resistance, PEEP increases the systolic load faced by the right ventricle and impedes right ventricular ejection. We have found that PEEP typically increases right-sided intracardiac pressures as much (figures 1 and 2) or slightly more than intrapericardial pressure when baseline filling pressures are low, and by the same amount or slightly less than intrapericardial pressure after volume loading. This suggests that right ventricular volume potentially can either increase or decrease in response to PEEP, depending on the filling conditions present when PEEP is applied. It also suggests that volume loading, by decreasing the effects of PEEP on pulmonary vascular resistance, can shift the balance between the effects of PEEP on right ventricular volume toward decreased filling. However, because the right ventricle is a thin-walled, compliant structure, volume changes that do occur have only minor effects on transmural RVEDP. Since changes in intracavitary pressure must equal the sum of changes in transmural and external pressures for the right as well as the left ventricle, a relatively unchanged transmural pressure predicts that intrapericardial and right-sided intracardiac pressures will increase by similar amounts (ΔRVEDPintracavity = ΔRVEDPtransmural + Δ external pressure).

In the present study, correction for the effects of PEEP on right-sided intracardiac pressures accurately restored the baseline relationships between intracavitary left ventricular filling pressures and ascending aortic blood flow. This was true whether performance curves were based on intracavitary LVEDP and corrected by subtracting the increment in intracavitary RVEDP, or on mean left atrial pressure and corrected by subtracting the increment in mean right atrial pressure caused by PEEP at each level of ventricular filling (figures 3 and 4). Curves corrected in this manner did not differ significantly from curves corrected by subtracting the effects of PEEP on intrapericardial pressure (figure 5). We believe that the accuracy of this correction is partly due to the fact that intracavitary RVEDP is part of the effective pressure around the left ventricle, acting across the interventricular septum. This compensates intrinsically for any differences between the effects of PEEP on intrapericardial and right-sided intracardiac pressures. The correlation between
control and corrected PEEP curves at high filling pressures also may have been aided by the shape of the normal function curve (i.e., slight undercorrection for a change in external pressure would not be appreciable when operating on a relatively flat portion of the curve). However, from a practical standpoint, it is important only that corrected pressures ultimately have the same relationship to ventricular performance as pressures measured in the absence of PEEP.

Although these findings suggest that the rightward displacement of ventricular function curves caused by PEEP results primarily (if not entirely) from an in-
crease in external pressure, we did not attempt to assess changes in other determinants of ventricular performance. As a result, we can only assume that the effects of PEEP on variables other than transmural pressure$^{6,18-20}$ either offset each other, or were relatively unimportant under the present study conditions. In practice, upward or downward displacement of the relationship between ventricular filling and stroke volume due to a change in either afterload or inotropic state$^{20}$ would not negate the usefulness of a corrected filling pressure in evaluating left ventricular preload. However, a change in left ventricular compliance$^{6,18,19}$ would be directly relevant, and might, under some circumstances, prevent complete correction of intracavitary filling pressures. The extent to which PEEP alters left ventricular compliance, the responsible mechanisms, and whether changes in compliance depend on the intravascular volume present when PEEP is applied have not been clearly established. However, it is tempting to speculate that correction for changes in right-sided intracardiac pressures might compensate partially for any decrease in compliance mediated through changes in right ventricular volume and septal configuration.

In summary, we found that intracavitary left ventricular filling pressures measured in the presence of PEEP and corrected by subtracting the effects of PEEP on right-sided intracardiac pressures have approximately the same relationship to ventricular performance as intracavitary pressures measured under baseline conditions. It seems reasonable to suggest, therefore, that pressures corrected in this manner can be interpreted in accordance with the same guidelines$^{1,2}$ applied to pressures measured in the presence of atmospheric airway pressure. This potentially represents an attractive alternative to esophageal manometry (which is the only practical method of estimating changes in intrathoracic pressure in most clinical settings). Right-sided intracardiac pressures can be measured easily, while esophageal recordings require additional instrumentation and may not accurately reflect changes in pressure around the left ventricle in the presence of PEEP.$^{21}$ In practice, our proposal could be implemented with standard, double-lumen catheters for measuring pulmonary arterial wedge and central venous pressures. It would be necessary to ensure that the tip of the catheter was positioned in a dependent portion of the lung to avoid potential discrepancies between wedge and left atrial pressures in the presence of PEEP.$^{22,23}$ Wedge pressures could then be corrected by simply subtracting the difference between central venous pressures recorded with and without positive airway pressure at any given level of filling. Although the appropriate correction factor would need to be determined whenever airway pressure or ventricular filling conditions were altered significantly, we believe that careful application of these techniques would strengthen the relationship between wedge pressures and ventricular performance in this setting.

However, it is important to recognize the limitations of the present study. Our conclusions are based on a comparison of pressure-flow relationships derived under steady-state conditions with and without 15 cm of water of PEEP in dogs. We purposefully suspended respiration for several seconds at end-expiration to allow a relatively pure comparison of pressures and flows in the presence and absence of positive airway pressure. We have not yet validated this method of correction at other levels of PEEP, during cyclic positive pressure ventilation (with or without PEEP) over the range of ventilatory patterns that might be encountered clinically, or in human subjects. Furthermore, the similarity between the effects of PEEP on intrapericardial and right-sided intracardiac pressures is largely a chance occurrence, and depends on the combined effects of several factors that could vary independently in the clinical setting. It remains to be determined whether the method of correction proposed in this study is equally valid in the presence of diseases that alter either right ventricular compliance or the effects of PEEP on intrathoracic pressure and pulmonary vascular resistance.

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References
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