Positive End-expiratory Pressure Influences Echocardiographic Measures of Diastolic Function

A Randomized, Crossover Study in Cardiac Surgery Patients

Peter Juhl-Olsen, M.D.,* Johan Fridolf Hermansen, B.M.Sc.,† Christian Alcaraz Frederiksen, M.D.,* Linda Aagaard Rasmussen, M.H.S.,‡ Carl-Johan Jakobsen, M.D,§ Erik Sloth, Ph.D.||

ABSTRACT

Background: Ultrasonography of the cardiovascular system is pivotal for hemodynamic assessment. Diastolic function is evaluated with a combination of tissue Doppler (e’ and a’) and pulsed Doppler (E and A) measures of transmitral- and mitral valve annuli velocities. However, accurate echocardiographic evaluation in the intensive care unit or perioperative setting is contingent on relative resistance to positive pressure ventilation and changes in preload. This study aimed to evaluate the effects of positive end-expiratory pressure (PEEP) and positioning on echocardiographic measures of diastolic function.

Methods: The study was a prospective, randomized, crossover study. Cardiac surgery patients with ejection fraction greater than 45% and averaged e’ of 9 or more were included. Postoperatively, anesthetized patients were randomized into six combinations of PEEP (0, 6, 12 cm H2O) and positions (horizontal, Trendelenburg). At each combination, e’ (primary endpoint), a’, E, and A were obtained with transthoracic echocardiography along with left ventricular area. Image analysis was performed blinded to the protocol.

Results: Thirty patients completed the study. PEEP decreased lateral e’ from 6.6 ± 3.6 to 5.3 ± 3.0 cm/s (P < 0.001) in the horizontal position and from 7.4 ± 4.2 to 6.5 ± 3.3 cm/s (P < 0.001) in Trendelenburg. Similar results were found for septal e’, a’ bilaterally and transmitral pulsed Doppler measures, and PEEP decreased left ventricular area. E/A, E/e’, and e’/a’ remained unaffected by PEEP and positioning.

Conclusions: When evaluating diastolic function by echocardiography, the levels of PEEP and its effect on ventricular filling pressures in cardiac surgery patients. The presence of positive pressure ventilation should thus be taken into account when evaluating echocardiographic indices of diastolic function.

ULTRASONOGRAPHY is gaining acceptance as a pivotal tool for hemodynamic assessment in intensive care and perioperative settings.¹⁻³ Ultrasonography allows for visualization of obvious pathology and quantification of basic physiological determinants including preload, afterload, contractility, and diastolic function. Diastolic function is a complex reflection of ventricular chamber compliance, active myofilament relaxation, and elastic recoil of potential energy stored in systole.⁴ By current recommendations, echocardiographic assessment of diastolic function incorporates early (E) and atrial (A) transmittal

What We Already Know about This Topic

• Accurate echocardiographic evaluation in the intensive care unit or perioperative setting is contingent on relative resistance to positive pressure ventilation and changes in preload. However, few studies have addressed the effect of positive pressure ventilation on current echocardiographic indices of diastolic function.

• This study aimed to evaluate the effects of positive end-expiratory pressure and positioning on echocardiographic measures of diastolic function in postoperative cardiac surgery patients.

What This Article Tells Us That Is New

• Individual pulsed wave Doppler and tissue Doppler indices of left ventricular diastolic function are subject to change with increasing positive end-expiratory pressure in postoperative cardiac surgery patients. The presence of positive pressure ventilation should thus be taken into account when evaluating echocardiographic indices of diastolic function.
flow velocities as well as the corresponding velocities of the mitral valve annuli (e’ and a’). V

Anesthesia entails positive pressure ventilation and considerable volume shifts occur intra- and postoperatively, especially in major surgery. Therefore, echocardiographic quantification of diastolic function, as an expression of properties intrinsic to the myocardium, needs to be relatively resistant to varying ventilation pressures and preload changes in order to maintain clinical justification. The interactions of positive pressure ventilation with the cardiovascular system are complex and affect both ventricles. Positive pressure ventilation reduces right ventricular preload by impairing venous return. Pulmonary artery resistance is generally increased, but may also decrease if a sufficient amount of collapsed alveoli are recruited and ventilated. These factors determine the influence on left ventricular preload, whereas pressure ventilation lowers left ventricular transmural pressure and, hence, afterload. Overall, mechanical ventilation induces multiple changes in the determinants of ventricular function which may affect diastolic filling velocities and echocardiographic measures.

Few studies have addressed the effect of positive pressure ventilation on current echocardiographic indices of diastolic function. A previous study, in healthy volunteers, showed that both E and e’ decrease with successively higher inspiratory pressures, and that this effect varies with preload status. However, postoperative cardiac surgery patients are characterized by hemodynamic instability, myocardial stunning, and pulmonary atelectasis. It is under these conditions that diastolic evaluation is often warranted and therefore requires clinical validation.

Thus, the primary aim of this study was to evaluate the influence of increasing positive end-expiratory pressure (PEEP) on established echocardiographic measures of diastolic function in postoperative cardiac surgery patients. The secondary aim was to elucidate whether such an effect could be altered or eliminated with increasing preload. We hypothesized that e’, a’, E, and A were dependent on PEEP levels in the horizontal position, but not so with increased preload in the Trendelenburg position.

**Materials and Methods**

The study was approved by the Central Denmark Region Committees on Biomedical Research Ethics, Viborg, Denmark. Participation was conditional upon written, informed consent.

**Study Design**

This single-site study was a prospective, randomized, cross-over study conducted at Aarhus University Hospital, Denmark, in the period July 2012 through October 2012. Patients aged more than 18 yr, undergoing elective cardiac surgery, including routine transthoracic echocardiography, were eligible for inclusion. Patients were recruited the day before surgery by a dedicated study nurse. Inclusion criteria were sinus rhythm and a preoperative averaged early (e’) velocity of the mitral valve annuli of 9 or less measured with transthoracic echocardiography. Exclusion criteria were mitral valve surgery and ejection fraction of less than 45%. Predefined drop-out criteria were postoperative hemodynamic instability, the need for ventricular pacing, or left ventricular failure necessitating the use of inotropes after surgery. Atrial pacing, vasoconstriction with norepinephrine in the presence of ejection fraction greater than 45% and vasodilation with nitroprusside sodium were allowed.

**Study Protocol**

In order to facilitate postoperative hemodynamic stabilization, the study protocol started 90–120 min after surgery when the patients were still anesthetized and coupled to a ventilator (Evita Infinity V500; Dräger, Lübeck, Germany). Infusion rates of vasoactive drugs were kept steady, and volume infusion was restricted to less than 100 ml/h throughout the protocol. Each patient was randomized in a 1:6 ratio into two positions (horizontal and Trendelenburg position) and three levels of PEEP (0, 6, 12 cm H2O). Hence, patients underwent a total of six random combinations of positioning and PEEP. Single-block randomization was performed before study initiation using a publically available website. On enrollment, patients were consecutively allocated a study number corresponding exactly to the number of enrolled patients at the time. Each study number thus had a predefined randomization order. During the study, the randomization plan was administered by the study nurse.

At each combination of positioning and PEEP, measurements started when invasive pressures had stabilized and after a period of at least 60 s. Any carry-over effect from the previous positioning and PEEP setting was neutralized by positioning the patient horizontally at the PEEP level attained before protocol commencement in between each combination. The Trendelenburg position was a tilt of either 13 degrees or 9 degrees (according to the maximal capacity of the individual patient bed).

**Outcomes**

The primary endpoint was the effect of increasing PEEP on e’ in the horizontal position. Secondary endpoints were the effect of increasing PEEP on e’ in the Trendelenburg position, the effects of positioning on e’, and interaction between PEEP and positioning. In addition, secondary endpoints included a’, E, A, E deceleration time, E/e’, E/A, e’/a’, left ventricular area, and how these measures were affected by both PEEP and positioning.

**Data Acquisition and Analyses**

As a routine part of the anesthetic procedure, all patients had a radial artery catheter and a pulmonary artery catheter (744 HF75; Edwards Lifesciences, Irvine, CA) inserted for measurements of mean systemic arterial pressure (MAP), mean pulmonary artery pressure, central venous pressure, heart rate, and mixed venous saturation (SvO2). Pressure transducers were fixed to the patients’ chests for correct measurements at different positions. A multiplane transthoracic
Probe (6T; GE Healthcare, Horten, Norway) was placed for intraoperative cardiac monitoring. Standard anesthesia consisted of propofol, sufentanyl, and rocuronium, and postoperative sedation was facilitated with propofol alone.

The study echocardiography was performed by the same physician. All echocardiographic endpoints were obtained with a Vivid E9 echocardiography system (GE Healthcare) from the mid-esophageal four-chamber view, precluding random variation from changing image planes. Grey-scale four-chamber cine loops were obtained and pulsed wave Doppler was used to obtain transmitral E and A along with E deceleration time (Fig. 1A). c’ and a’ were quantified with a combination of tissue and pulsed wave Doppler (Fig. 1B). The automatic respiratory tracing function was active allowing for off-line identification of respiratory phases.

Commercially available software (Echopac; GE Healthcare) was used for subsequent image analyses. Values were averaged from triplicates and measured during the apnea period between expiratory and inspiratory phases. c’ and a’ were averaged from septal- and lateral mitral valve annuli. The composite ratios, E/A, E/c’, and E/a’, of which E/A represents a conventional approach to diastolic evaluation, whereas E/e’ and E/a’, are established as sensitive markers of diastolic function and correlate well with left atrial pressure, were calculated. As tissue Doppler values from the septal mitral valve annulus often do not align well with the Doppler beam during transesophageal echocardiography, thereby introducing considerable random variation, E/e’ and E/a’ were calculated from both lateral tissue Doppler values alone as well as averaged from both mitral valve annuli. End-diastolic areas of the left ventricle were traced from four-chamber views and the relative area change calculated. A single observer who was blinded to positioning and PEEP levels assessed all echocardiograms for sufficient image quality and performed image analysis. All measurements were repeated by a similarly blinded second observer.

**Statistical Analyses**

The sample size was based on between-group analysis and derived from Juhl-Olsen et al. showing a decrease in e’ from 19.5 to 17.1 cm/s (high PEEP to no PEEP in the horizontal position) and SDs of 3.0 and 3.3, respectively, in healthy participants. Given a power of 90% and an α of 0.05, 20 patients were necessary. As patients in the current study had stunned myocardiums, a more blunted response was expected and it was decided to include 30 patients.

A two-way (2 × 3) ANOVA for repeated measurements incorporating variance analysis of two positions, three PEEP levels, and patient id was used for overall analysis. This analysis yields the effects of both position and PEEP as well as the probability of interaction between position and PEEP. A one-way ANOVA for repeated measurements was used for the analysis of PEEP in individual positions. The effect of positioning at individual PEEP levels was estimated with a two-tailed Student t test for paired samples. For ANOVAs, P value less than 0.05 was considered significant due to the inherent correction for number of repetitions. In case of statistically significant interaction between PEEP and positioning (e.g., significant effect of PEEP in the horizontal position, but not in Trendelenburg), significance level was corrected in accordance with the Bonferroni principle at individual PEEP levels (3) and positions (2).

Interobserver variation was calculated as the average difference in values divided by the averaged values, expressed as a percentage and presented in accordance with the Bland and Altman approach for repeated measurements with limits of agreement.

All analyses were performed with STATA (StataCorp LP, College Station, TX). Results are given as mean ± SD (CI).

**Fig. 1.** Examples of pulsed wave Doppler tracking of diastolic transmitral blood flow (A) and tissue Doppler analysis of the medial mitral valve annulus velocities (B). Simultaneous electrocardiogram and automated respiratory tracing facilitated precise identification of cardiac and respiratory phases. A = peak atrial diastolic transmitral flow; a’ = peak atrial diastolic velocity of the mitral valve annulus; E = peak early diastolic transmitral flow; e’ = peak early diastolic velocity of the mitral annulus; FPS = frames per second.
PERIOPERATIVE MEDICINE

Results

Thirty-six patients were included in the study. Six patients dropped out due to: hemodynamic instability (1), ventricular pacing (1), withdrawal of patient consent (1), atrial fibrillation (1), inability to insert a transesophageal echocardiography probe (1), and logistical reasons (1), leaving 30 for analysis. No patient suffered adverse events during the study protocol. Patient demographics and echocardiographic characteristics are displayed in table 1. Twenty-four patients were tilted 13 degrees for Trendelenburg position and six patients tilted 9 degrees as determined by the beds’ capacities.

Effects of PEEP

An increase in PEEP from 0 to 12 cm H₂O reduced lateral e’ significantly from 6.6 ± 3.6 cm/s (CI, 5.1–8) to 5.3 ± 3.0 cm/s (CI, 4.2–6.4) in the horizontal position and from 7.2 ± 4.2 cm/s (CI, 5.7–8.8) to 6.5 ± 3.4 cm/s (CI, 5.2–7.8) in the Trendelenburg position. As for septal e’, the corresponding values were 5.4 ± 1.8 cm/s (CI, 4.7–6.1) to 4.8 ± 1.5 cm/s (CI, 4.2–5.4) (horizontal) and 5.6 ± 1.7 cm/s (CI, 4.9–6.2) to 5.0 ± 1.6 cm/s (CI, 4.2–5.7) (Trendelenburg); a’ was affected similarly (fig. 2, A and B for details).

E decreased with higher PEEP from 76.1 ± 22.0 cm/s (CI, 67.2–84.6) (0 cm H₂O) to 65.7 ± 23.2 cm/s (CI, 56.8–74.5) (12 cm H₂O) in the horizontal position with a concomitant increase in E deceleration time from 208.5 ± 36.0 ms (CI, 190.0–227.1) to 227.5 ± 50.4 ms (CI, 199.0–256.0). Parallel results were found in the Trendelenburg position (fig. 2, C and D).

The composite values, E/A, E/e’ average, E/e’ lateral, e’/a’ average, and e’/a’ lateral remained unaffected by PEEP (fig. 2, D, E, and F).

Mean pulmonary artery pressure and central venous pressure increased with PEEP in conjunction with a decrease in SvO₂ and heart rate (P ≤ 0.005). Increasing PEEP caused a decrease in MAP in the horizontal position, but MAP did not change with higher PEEP in the Trendelenburg position (table 2).

Left ventricular area diminished with PEEP from 24.7 ± 5.4 cm² (CI, 22.2–27.2) (PEEP = 0 cm H₂O) to 22.6 ± 4.7 cm² (CI, 20.4–24.7) (PEEP = 12 cm H₂O) in the horizontal position. The corresponding values in the Trendelenburg position were 26.1 ± 5.2 cm² (CI, 23.8–28.5) and 25.2 ± 5.6 cm² (CI, 22.6–27.7; fig. 3).

Effects of Positioning

Positioning of patients in Trendelenburg increased lateral e’ by 0.7–1.2 cm/s according to PEEP level. The effect on septal e’ was statistically significant as well, but less pronounced (fig. 2A). Similar findings were found for a’.

The Trendelenburg position consistently increased E and A at all PEEP levels, whereas E deceleration time was reduced by 25–30 ms (fig. 2, C and D).

Table 1. Patient Demographics and Preoperative Echocardiographic Characteristics

<table>
<thead>
<tr>
<th>Surgery Type</th>
<th>AS (n = 17)</th>
<th>CABG (n = 6)</th>
<th>AS + CABG (n = 3)</th>
<th>OPCAB (n = 4)</th>
<th>All Together (n = 30)</th>
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</thead>
<tbody>
<tr>
<td>Male</td>
<td>12 (70.6%)</td>
<td>4 (66.7%)</td>
<td>3 (100%)</td>
<td>1 (25.0%)</td>
<td>20 (66.7%)</td>
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<tr>
<td>Age (years)</td>
<td>70.3 ± 10.8</td>
<td>65.6 ± 6.2</td>
<td>76.7 ± 15.8</td>
<td>69.9 ± 7.7</td>
<td>69.9 ± 10.1</td>
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<tr>
<td>Body mass index (kg/m²)</td>
<td>26.8 ± 2.7</td>
<td>28.2 ± 4.5</td>
<td>30.0 ± 2.8</td>
<td>30.7 ± 2.9</td>
<td>27.9 ± 4.3</td>
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<tr>
<td>Transthoracic echocardiography</td>
<td></td>
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<tr>
<td>Left ventricular mass index (g/m²)</td>
<td>128.7 ± 32.4</td>
<td>116.6 ± 32.3</td>
<td>140.5 ± 13.5</td>
<td>92.2 ± 24.4</td>
<td>123 ± 32</td>
</tr>
<tr>
<td>Ejection fraction (%)</td>
<td>63.8 ± 9.0</td>
<td>64.2 ± 4.7</td>
<td>57.7 ± 6.4</td>
<td>68.5 ± 2.4</td>
<td>63.9 ± 7.7</td>
</tr>
<tr>
<td>E (cm/s)</td>
<td>82.1 ± 22.4</td>
<td>66.0 ± 20.0</td>
<td>86.3 ± 24.3</td>
<td>87.8 ± 32.2</td>
<td>80.1 ± 23.4</td>
</tr>
<tr>
<td>E/A</td>
<td>0.93 ± 0.33</td>
<td>0.79 ± 0.21</td>
<td>11.8 ± 0.37</td>
<td>0.87 ± 0.24</td>
<td>0.91 ± 0.30</td>
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<tr>
<td>E deceleration time (ms)</td>
<td>217.7 ± 70.0</td>
<td>224.8 ± 28.6</td>
<td>160.7 ± 26.0</td>
<td>233.3 ± 34.3</td>
<td>215 ± 56</td>
</tr>
<tr>
<td>e’ average (cm/s)</td>
<td>7.5 (3.5–9)</td>
<td>9 (5–9)</td>
<td>6.5 (4–9)</td>
<td>8 (6.5–9)</td>
<td>7.75 (3.5–9)</td>
</tr>
<tr>
<td>E/e’ average</td>
<td>11.4 (6–32.6)</td>
<td>9.0 (5.7–10.2)</td>
<td>14 (5.7–27)</td>
<td>11.3 (6.3–16.5)</td>
<td>11.0 (5.7–32.6)</td>
</tr>
<tr>
<td>e’/a’ average</td>
<td>0.67 (0.30–1.2)</td>
<td>0.75 (0.45–0.95)</td>
<td>1.05 (0.87–1.33)</td>
<td>0.67 (0.55–0.82)</td>
<td>0.68 (0.52–1.33)</td>
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<tr>
<td>Aortic valve gradient (mmHg)</td>
<td>72.0 ± 27.5</td>
<td>—</td>
<td>70.3 ± 24.5</td>
<td>—</td>
<td>71.8 ± 25.5</td>
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<tr>
<td>Tapse (mm)</td>
<td>23.5 ± 4.1</td>
<td>21.0 ± 2.4</td>
<td>26.7 ± 1.5</td>
<td>24.0 ± 4.2</td>
<td>23.5 ± 3.8</td>
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</tbody>
</table>

Demographics of the 30 patients included in the study as well as their echocardiographic characteristics on the day before surgery. Data are presented as mean ± SD or median (range) according to distribution profile.

A = peak atrial diastolic transmitral flow; a’ average = averaged atrial peak diastolic velocity of the septal and lateral mitral valve annuli; AS = aortic valve stenosis; CABG = coronary artery bypass graft; E = peak early diastolic transmitral flow; e’ average = averaged early peak diastolic velocity of the septal and lateral mitral valve annuli; OPCAB = off-pump coronary artery; Tapse = tricuspid annular plane systolic excursion.

Anesthesiology 2013; 119:1078-86 1081  Juhl-Olsen et al.
None of the composite ratios, E/A, E/e’ average, E/e’ lateral, e’/a’ average, and e’/a’ lateral, reached statistical significance as positions changed (fig. 2, D, E, and F).

MAP, mean pulmonary artery pressure, central venous pressure, and SvO2 all increased with Trendelenburg position \((P < 0.001; \text{table 2})\). Heart rate was independent of position \((P = 0.646)\).

Left ventricular area was significantly larger in the Trendelenburg position (fig. 3).

**Interaction between PEEP and Positioning**

Variance analyses did not show any statistically significant interaction between PEEP and positioning for any echocardiographic parameter \((P > 0.161)\). Therefore, the effects of PEEP were not significantly affected by positioning. This was also the result for all invasive measurements \((P > 0.102)\), except for MAP as described previously \((P < 0.001)\).

The time consumption for completing the protocol was 25.8 ± 4.8 min (CI, 23.9–27.8). The difference between

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**Fig. 2.** The effects of positioning (horizontal and Trendelenburg) and positive end-expiratory pressure (PEEP) on echocardiographic indices of diastolic function including tissue Doppler peak early (e’) and atrial (a’) diastolic velocities of the mitral valve annuli (A and B), pulsed Doppler peak early (E) and atrial (A) diastolic transmitral flow (C) and E deceleration time (D). In addition, the effects of positioning and PEEP on the composite ratios E/A, E/e’, and e’/a’ are shown (D–F). ANOVA, \(P_{\text{PEEP}} = P\) values of PEEP; ANOVA; Average = averaged from the septal and lateral mitral valve annuli; \(P_{\text{positioning}} = P\) values of positioning.
PEEP settings and PEEP actually measured by the ventilator was $-0.23 \pm 0.70$ (CI, $-0.34$ to $-0.12$) cm H$_2$O.

After off-line evaluation of echocardiographic image quality, 92.5% of theoretically available data were included in the analyses. Mean interobserver variation was $-2.2\%$ (95% limits of agreement: $-18.4$ to $13.9\%$) for pulsed wave Doppler velocities, $2.9\%$ (95% limits of agreement: $-17.6$ to $23.3\%$) for tissue Doppler measurements, and $-4.3\%$ (95% limits of agreement: $-23.1$ to $14.4\%$) for ventricular area tracings.

**Discussion**

This study unequivocally showed that individual pulsed wave Doppler and tissue Doppler indices of left ventricular diastolic function are subject to change with increasing PEEP in postoperative cardiac surgery patients. In addition, a clear effect of positioning was seen on all parameters. In the overall ANOVA analysis, the effects of PEEP were independent of positioning and therefore seen in both the horizontal and Trendelenburg positions. The composite values E/A, e'/a', and E/e' remained unaffected throughout the study.

The potential influence of mechanical ventilation on diastolic filling velocities is complex because positive pressure ventilation affects the cardiovascular system in numerous ways. First, the transmission of higher intrathoracic pressure to the right side cavities impairs systemic venous return. The drop in preload will, a few beats later, reach the left ventricle effectively lowering the diastolic atrial-to-ventricular pressure gradient; this decreases both E and e'.

Second, the hyperinflation of lung volume mediated by positive pressure ventilation influences pulmonary resistance and, hence, right ventricular cardiac output and left ventricular filling. Increasing lung volume up to functional residual capacity decreases pulmonary resistance, whereas inflation beyond this volume has the opposite effect. In addition, opening of pulmonary vasoconstriction and augments pulmonary flow. This is highly relevant in cardiac surgery as lungs are deflated during intraoperative cardiopulmonary bypass.

Third, a lowering of the transmural pressure gradients decreases afterload of left side chambers. The resulting increase in left atrial contractility augments ventricular filling with a theoretical increase in A and a'. Furthermore, enhanced left ventricular contractility secondary to reduced afterload may accumulate more elastic energy for release as elastic recoil during the subsequent diastole affecting E and e' in a similar way.

Thus, positive pressure ventilation acts on left ventricular diastolic filling in many, often, opposing ways, and the net effect is difficult to predict.

The current study showed a decrease in e', E, and E deceleration time with higher PEEP, and these changes were associated with lower end-diastolic left ventricular areas (fig. 3). When patients were placed in the Trendelenburg position, greater left ventricular areas were seen, and e' and E increased. The consistent association between area and indices of diastolic function suggests that PEEP influences e' and E by its effect on left ventricular volume rather than a direct effect on myofilament relaxation. For example, in the horizontal position with PEEP = 0 cm H$_2$O, left ventricular area was $24.7 \pm 5.4$ cm$^2$. This area was identical in the Trendelenburg position with PEEP = 12 cm H$_2$O ($25.2 \pm 5.6$ cm$^2$; $P = 0.105$). Under these different physiological conditions, but with similar left ventricular areas, e', a', E, and A were also similar (fig. 2, D–F).

The volumetric relationship is consistent with a previous publication stating that E increases and E deceleration time decreases with a greater left atrial-to-ventricular pressure gradient. By definition, this gradient is determined by the early diastolic pressures of the left atrium and the left ventricle. If left ventricular external pressure is kept constant (with unchanged PEEP), we can conclude that the effects of the Trendelenburg position on E and E deceleration time are mediated by increasing early diastolic left atrial pressure resulting in a larger end-diastolic volume. The increase in volume may itself by increasing the force diastolic elastic recoil contribute further to both pulsed wave and tissue Doppler velocities.

With regard to PEEP, the physiology is more complex. The effects of PEEP on early pulsed wave and tissue Doppler indices may have been mediated by both lower atrial pressure and increased left ventricular external pressure by direct pleural compression. Both result in lower ventricular area. The transmission of alveolar pressure to the heart is directly correlated with lung compliance. Patients after cardiopulmonary bypass have reduced lung compliance. This suggests that reduced left atrial filling pressure likely contributes more than external pleural compression by PEEP to reduce left ventricular areas seen with higher PEEP.

The effects of positioning on pulsed wave and tissue Doppler indices are in parallel with previous studies. Although results on e' have been conflicting, the prevailing picture is that e' is preload dependent, but to a lesser degree than E. This is part of the physiological rationale underlying the linear relationship between E/e' and left atrial pressure demonstrated previously.

In this study, left ventricular area increased in the Trendelenburg position at constant PEEP. As mentioned, a constant PEEP implies unchanged external pressure to heart, and the area change must have been facilitated by a higher left atrial pressure. Despite this, E/e' remained unaffected in the Trendelenburg position (fig. 2E) and therefore did not track the intraindividual change in atrial pressure. E/e' was unchanged, as e' and E showed identical relative changes with shifting position. Therefore, in serial measurements of the same individual, the linear relationship between E/e' and left atrial pressure could not be confirmed in this study.

When PEEP increased, the left ventricular area decreased implying a lower transmural pressure or lower filling pressure secondary to reduced venous return. E/e' did not show a statistically significant change with PEEP and actually displayed a trend toward higher values with increasing PEEP. An
Table 2. Effects of PEEP and Positioning on Invasive Measurements

<table>
<thead>
<tr>
<th></th>
<th>MAP (mmHg)</th>
<th>mPAP (mmHg)*</th>
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<tbody>
<tr>
<td></td>
<td>Horizontal</td>
<td>Trendelenburg</td>
</tr>
<tr>
<td>PEEP 0 (cm H₂O)</td>
<td>83.4 ± 11.2</td>
<td>87.6 ± 9.5</td>
</tr>
<tr>
<td>PEEP 6 (cm H₂O)</td>
<td>81.8 ± 12.4</td>
<td>89.9 ± 9.5</td>
</tr>
<tr>
<td>PEEP 12 (cm H₂O)</td>
<td>75.9 ± 12.1</td>
<td>86.3 ± 10.4</td>
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P_{Positioning} <0.002†
P_{PEEP} <0.001 0.123 <0.001

The effects of increasing PEEP and varying positioning on invasive hemodynamic parameters in postoperative cardiac surgery patients. Data are presented as mean ± SD.

† No significant interaction between positioning and PEEP.

CVP = central venous pressure; HR = heart rate; MAP = mean systemic arterial pressure; mPAP = mean pulmonary arterial pressure; PEEP = positive end-expiratory pressure; P_{PEEP} = P values of PEEP; ANOVA, P_{Positioning} = P values of positioning. ANOVA; SvO₂ = mixed venous saturation.

unchanged or slightly greater filling pressure, as suggested by the trend in E/e’, may be compatible with a lower transmural pressure when PEEP increased from 0 to 12 cm H₂O.

This study found no interaction between the effects of PEEP and positioning for all echocardiographic parameters of diastolic function. It has been demonstrated previously in healthy volunteers that the effects of PEEP and pressure support can be cancelled out in 30 degrees Trendelenburg with a concomitant fluid bolus. In the current study, preload augmentation was limited to the tilting capacity of patient beds. This may have been insufficient to reach the flat part of the Frank–Starling curve where pressure changes do not facilitate volume changes. Thus, a greater tilt may have revealed a statistically significant interaction between PEEP and positioning. However, we still believe that the beds’ Trendelenburg capacities are representative of a clinically relevant preload increase as demonstrated quantitatively by the increase in left ventricular volume.

Clinical Implications

This study shows that the presence of positive pressure ventilation should be taken into account when evaluating diastolic function. Initial diastolic assessment is often a question of the presence or absence of diastolic dysfunction. The starting point for this is, by current recommendations, E’. Values less than 8 (E’ septal) and less than 10 (E’ lateral) suggest the presence of diastolic dysfunction which can be further divided into subcategories. As especially lateral E’ decreased with PEEP in our study, the use of these specific cutoff values should be used with caution during mechanical ventilation. Although fluctuations were less prominent for septal E’, alignment of the Doppler beam with the septal mitral valve annulus is often difficult with transesophageal echocardiography and necessitates measurements at a high angle. This increases random variation and minimizes the practical use of septal E’ diastolic motion to individuals with adequate alignment (<20 degrees).

Despite these limitations, we recommend that both septal and lateral E’ are measured routinely in cardiac surgery patients showing hemodynamic compromise and, acknowledging the nonperfect predictive values of all echocardiographic indices, be related to the clinical context.

This study does not discredit the use of E’ for following the diastolic relaxation of individual patients over time. As PEEP levels influence E’, we recommend that measurements are to be performed at the same PEEP if possible. In addition, one should be aware of the influence of other sources of preload variation on tissue Doppler parameters.

The current study underscores previous concerns that E/e’ lacks sensitivity for tracking changes in left atrial pressure. Therefore, the use of E/e’ for this purpose is dissuaded during mechanical ventilation. This also applies to c’/a’.

Limitations

Ethical concerns precluded direct measurements of intracavitary left ventricular and pericardial pressures. Likewise, the trending capability of continuous cardiac output readings with pulmonary artery catheters is insufficient to pick up the...
### Table 2. (Continued)

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<thead>
<tr>
<th></th>
<th>CVP (mmHg)*</th>
<th>Svo₂ (%)*</th>
<th>HR (min⁻¹)*</th>
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<td>Trendelenburg</td>
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<td>10.3 ± 3.2</td>
<td>14.4 ± 4.0</td>
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<td>69.3 ± 5.8</td>
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<tr>
<td>10.9 ± 3.2</td>
<td>15.1 ± 3.6</td>
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<td>68.6 ± 5.6</td>
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<tr>
<td>12.1 ± 3.0</td>
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<td>66.8 ± 7.4</td>
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<td>&lt;0.001</td>
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**References**


