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The effects of positive end-expiratory pressure on respiratory system mechanics and hemodynamics in postoperative cardiac surgery patients

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Abstract

We prospectively evaluated the effects of positive end-expiratory pressure (PEEP) on the respiratory mechanical properties and hemodynamics of 10 postoperative adult cardiac patients undergoing mechanical ventilation while still anesthetized and paralyzed. The respiratory mechanics was evaluated by the inflation inspiratory occlusion method and hemodynamics by conventional methods. Each patient was randomized to a different level of PEEP (5, 10 and 15 cmH_2O), while zero end-expiratory pressure (ZEEP) was established as control. PEEP of 15-min duration was applied at 20-min intervals. The frequency dependence of resistance and the viscoelastic properties and elastance of the respiratory system were evaluated together with hemodynamic and respiratory indexes. We observed a significant decrease in total airway resistance (13.12 ± 0.79 $cmH_2O\ l^{-1}\ s^{-1}$ at ZEEP, 11.94 ± 0.55 $cmH_2O\ l^{-1}\ s^{-1}$ ($P<0.0197$) at 5 cmH_2O of PEEP, 11.42 ± 0.71 $cmH_2O\ l^{-1}\ s^{-1}$ ($P<0.0255$) at 10 cmH_2O of PEEP, and 10.32 ± 0.57 $cmH_2O\ l^{-1}\ s^{-1}$ ($P<0.0002$) at 15 cmH_2O of PEEP). The elastance (E_{rs}; cmH_2O/l) was not significantly modified by PEEP from zero (23.49 ± 1.21) to 5 cmH_2O (21.89 ± 0.70). However, a significant decrease ($P<0.0003$) at 10 cmH_2O PEEP (18.86 ± 1.13), as well as ($P<0.0001$) at 15 cmH_2O (18.41 ± 0.82) was observed after PEEP application. Volume dependence of viscoelastic properties showed a slight but not significant tendency to increase with PEEP. The significant decreases in cardiac index ($l\ min^{-1}\ m^{-2}$) due to PEEP increments (3.90 ± 0.22 at ZEEP, 3.43 ± 0.17 ($P<0.0260$) at 5 cmH_2O of PEEP, 3.31 ± 0.22 ($P<0.0260$) at 10 cmH_2O of PEEP, and 3.10 ± 0.22 ($P<0.0113$) at 15 cmH_2O of PEEP) were compensated for by an increase in arterial oxygen content owing to shunt fraction reduction (%) from 22.26 ± 2.28 at ZEEP to 11.66 ± 1.24 at PEEP of 15 cmH_2O ($P<0.0007$). We conclude that increments in PEEP resulted in a reduction of both airway resistance and respiratory elastance. These results could reflect improvement in respiratory mechanics. However, due to possible hemodynamic instability, PEEP should be carefully applied to postoperative cardiac patients.

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- Postoperative cardiac surgery
- PEEP
- Respiratory mechanics
- Hemodynamics

Introduction

Pulmonary dysfunction is a significant cause of postoperative morbidity following open-heart surgery (1,2). The underlying causes seem to be multifactorial, including effects of anesthesia and muscle paralysis, sternotomy, inflammatory reactions due to extracorporeal circulation, increase in extravascular lung water, alveolar collapse and altered chest wall mechanics (3,4). Atelectasis and hypoxemia are the main clinical findings. Atelectasis seems to be caused by reduced lung volume and small airway collapse (5,6). Hypoxemia may reflect increased intrapulmonary shunt due to collapsed lung areas and/or altered ventilation-perfusion ratio (3). To reopen atelectatic lung units and improve arterial oxygenation, different levels of positive end-expiratory pressure (PEEP) have been proposed, most of them based on improvement of the oxygenation index (7,8). To our knowledge, few studies of respiratory mechanical properties are available about postoperative cardiac patients, submitted to PEEP to reopen collapsed lungs (9). Nevertheless, several investigators have shown that PEEP improves arterial oxygenation, although there is controversy regarding the proper level of PEEP to obtain alveolar opening and stabilization, causing minimal hemodynamic instability and barotrauma (10). It is also important to note that postoperative cardiac patients frequently may present severe hypoxemia, due to atelectasis that requires an alveolar recruitment strategy, employing high levels of PEEP. Simple bedside radiography is considered a poor method to detect postoperative atelectasis (6). Therefore, PEEP should be routinely employed in maneuvers for alveolar opening in the presence of hypoxemia. However, even though PEEP is recommended for alveolar reopening, the presence of hemodynamic instability can be further worsened by elevated inspiratory pressures and PEEP. In the present investigation, we studied the effects of different levels of PEEP on respiratory system mechanical properties and oxygenation indexes, as well as its influence on the cardiovascular system in postoperative cardiac surgery patients.

Material and Methods

After approval by the Institutional Ethics Committee, 10 patients (7 males) gave informed written consent to participate in this study. Mean age was 52.3 years (37 to 59) and mean weight 66.7 kg (54 to 87). All patients underwent coronary bypass graft and were studied consecutively during the immediate postoperative period while still under the effects of anesthesia. Surgical procedure and anesthesia were standardized (midazolam, fentanyl and pancuronium bromide), and all patients were submitted to cardiopulmonary bypass with a membrane oxygenator. Inclusion criteria were: previously normal ejection fraction, absence of chronic lung disease, bypass time of 90 to 120 min, satisfactory circulation (absence of vasoactive drugs) and adequate gas exchange parameters upon admission to the intensive care unit.

Respiratory mechanical data

The patients were anesthetized and paralyzed and initially ventilated with a constant flow ventilator (Bear 5, Bear Medical Systems, Riverside, CA, USA) using an FIO_2 of 0.6, tidal volume (V_t) of 8 to 10 ml/kg, inspiratory square-wave flow of 1 l/s and respiratory frequency of 10 cycles/min. The end inflation occlusion method was used to measure the resistive and elastic properties of the respiratory system (11). Respiratory elastance (E_{rs}) was computed by dividing $P_{el,rs}$ by the tidal volume (12). Care was taken to avoid leaks in the system. Airflow (V) changes in lung volume (V_l) and tracheal pressure (P_{tr}) were obtained directly from the ventilator and stored on an IBM personal

computer (IBM PC, IBM Computers, São Paulo, SP, Brazil) through a 12-bit analog to digital converter (DT 2801^{A}, Data Transition, Marlboro, MA, USA) at a sampling frequency of 200 Hz (13). V_t was obtained by digital integration of the flow signal. The accuracy of the flow signal provided was tested by comparing different volume values from the ventilator (electronically integrated flow signal) with volumes simultaneously measured with a dry spirometer within the V_t range. The transducer that provided P_{tr} was tested by applying 5-s PEEP plateaux (5, 10, 15 and 20 cmH_2O) during the ventilation of a rubber balloon. The values observed on the electronic display were compared with those measured with a calibrated pressure transducer (270, Hewlett-Packard, Waltham, MA, USA). The flow resistive properties of the equipment (endotracheal tube plus connectors) were experimentally calculated (14) and subtracted from the obtained resistance. A power function fitting this relationship was determined and used to calculate the resistive pressures dissipated along the equipment at any given flow during the tests (13). The equipment resistance was subtracted whenever necessary, so that the results reported here represent intrinsic resistance values. Expiratory flow became nil before the end of expiration and the onset of inspiratory flow was synchronous with the beginning of the positive pressure, showing that auto-PEEP was not present in any patient.

The end inflation occlusion method consists of inflating the relaxed respiratory system with a constant square wave flow provided by a ventilator, followed by a rapid airway occlusion at end inspiration, which is maintained until a plateau in tracheal pressure is achieved. In the present study, a rapid airway occlusion was performed during a constant inspiratory flow and was held for 2s of inspiratory pause. Initially, there is a fast drop in tracheal pressure (ΔP_1) from the peak airway pressure (P_0 or P_{trmax}) to a deflection in the pressure curve (P_1), followed by a slower decay (ΔP_2) until an apparent plateau is reached, which represents respiratory system static elastic recoil pressure (P_2 or $P_{el,rs}$) (Figure 1). ΔP_1 corresponds to the pressure loss across the airways, with some contribution of rapid resistive components of the chest wall, where ΔP_2 represents pressure dissipation due to lung and chest wall viscoelastic properties. ($\Delta P_1 + \Delta P_2$) divided by the previous inspiratory flow gives the total resistance of the respiratory system (R_{rsmax}). ΔP_1 divided by the preceding flow gives minimal value of resistance (R_{init}), which is due mainly to airway resistive properties. ΔP_2 divided by the inspiratory flow immediately preceding airway occlusion indicates tissue initial resistance (R_{diff}) or (ΔP_2). Bates et al. (11) propose two values for respiratory system resistance: one that would be obtained in the absence of unequal time constants within the system and that is not affected by stress relaxation, corresponding to R_{init} (ΔP_1); the other reflects the mechanical unevenness within the system and stress relaxation R_{diff} (ΔP_2). The overall R_{rsmax} corresponds to addition of R_{diff} and R_{init} (15). To avoid auto-PEEP each maneuver was performed at the bedside by allowing a complete expiration to zero end-expiratory pressure (ZEEP) at each step of increasing PEEP, and observing the straight part of the P-V curve.

Hemodynamic data acquisition

Mean arterial pressure (MAP, mmHg), mean pulmonary artery pressure (MPAP, mmHg), pulmonary capillary wedge pressure (PCWP, mmHg) and right atrial pressure (RAP, mmHg) were measured. Cardiac output (CO, l/min) was measured in triplicate and each reported value was the mean of the three successive measurements (Model 9520, American Edwards Laboratories, Santa Ana, CA, USA). Immediately after CO was measured, arterial and mixed venous blood samples were collected and arterial and

venous saturation (SaO_2, SvO_2) was measured with a Radiometer OSM 3 hemoxymeter and partial oxygen pressures (PaO_2, PvO_2; mmHg) were measured using standard electrodes (Radiometer, Copenhagen, Denmark). Cardiac index (CI, l min^{-1} m^{-2}), systemic and pulmonary vascular resistance (SVR, PVR, dyne s^{-1} cm^{-5}), right ventricular stroke work index (RVSWI, g m^{-1} m^{-2}), left ventricular stroke work index (LVSWI, g m^{-1} m^{-2}), intrapulmonary shunt (Qs/Qt), alveolar arterial oxygen gradient ($G(A\text{-}a)O_2$), oxygen transport (DO_2, ml min^{-1} m^{-2}), oxygen consumption (VO_2, ml min^{-1} m^{-2}), and oxygen extraction rate (O_2 ER, %) were calculated using standard formulas.

Study design

After admission to the ICU, the patients had their volemic status adjusted, maintaining an end point of PCWP of 6 mmHg and RAP of 4 mmHg throughout the study. During data acquisition the patients were randomized and remained anesthetized and paralyzed. Additional doses of fentanyl, midazolam and pancuronium bromide were given whenever necessary. Respiratory mechanics and hemodynamics were measured after 15 min of application of three different PEEP levels: 5, 10 and 15 cmH_2O including ZEEP. A pause of 20 min was allowed between each PEEP application period, when the ventilatory parameters returned to initial values. In order to avoid interference during the measurement period, neither end expiratory nor sustained inflation was used during or between measurement periods. In each set of measurements, including ZEEP, 7 to 10 breath cycles were pooled and averaged to provide one data point. In order to remove time from the end of surgery as an influencing variable, the sequence of PEEP level application was randomized.

Statistical method

Data were analyzed statistically by analysis of variance (ANOVA) for repeated measures followed by the Tukey test to determine the differences between the established study points within groups, and by the Student *t*-test to determine differences between groups. The level of significance was set at $P<0.05$.

Results

All patients had an uncomplicated clinical course and were discharged from the ICU within 48 h after admission. No patient required re-operation for bleeding or for any other cause. The results are shown in Tables 1 to 4.

Respiratory mechanical data

Along with PEEP application we can observe a progressive decrease of respiratory elastance (Table 1). The elastance (cmH_2O/l) was not significantly modified by PEEP from zero (23.49 ± 1.21) to 5 cmH_2O (21.89 ± 0.70). However, a significant decrease ($P<0.0003$) at 10 cmH_2O PEEP (18.86 ± 1.13), as well as ($P<0.0001$) at 15 cmH_2O (18.41 ± 0.82) was observed after PEEP application.

A progressive reduction of the total resistance of respiratory system along with PEEP increment was observed. Values of R_{rsmax} decreased significantly from 13.12 ± 0.79

Table 1 - Respiratory mechanical data.

E_{rs}, Respiratory system elastance (cmH_2O/l); R_{rsmax}, respiratory system resistance (cmH_2O l^{-1} s^{-1}); ΔP_1, airway resistance (cmH_2O l^{-1} s^{-1}); ΔP_2, viscoelastic resistance (cmH_2O l^{-1} s^{-1}); ZEEP, zero end-expiratory pressure (0 cmH_2O); PEEP, positive end-expiratory pressure (5, 10 and 15 cmH_2O). E_{rs}: *P<0.05 compared to 5 cm H_2O PEEP and ZEEP. R_{rsmax} and ΔP_1: *P<0.05 compared to their respective ZEEP (ANOVA).

	ZEEP	PEEP		
	0	5	10	15
E_{rs}	23.49 ± 1.21	21.89 ± 0.70	18.86 ± 1.13*	18.41 ± 0.82*
R_{rsmax}	13.12 ± 0.79	11.94 ± 0.55*	11.42 ± 0.71*	10.32 ± 0.57*
ΔP_1	11.60 ± 0.75	10.85 ± 0.58*	10.43 ± 0.66*	9.42 ± 0.57*
ΔP_2	3.76 ± 0.49	3.96 ± 0.55	4.41 ± 0.66	4.51 ± 0.63

($cmH_2O\ l^{-1}\ s^{-1}$) at ZEEP to 11.94 ± 0.55 ($P<0.0197$) at 5 cmH_2O, 11.42 ± 0.71 ($P<0.0255$) at 10 cmH_2O and 10.32 ± 0.57 ($P<0.0002$) at 15 cmH_2O of PEEP. The same phenomenon was observed in airway resistance. ΔP_1 represents the fast decay phase of airway pressure after inspiratory airway occlusion and is represented by the interval between P_0 and P_1 (Figure 1). The ΔP_1 values decreased significantly from 11.60 ± 0.75 (cmH_2O) without any PEEP to 10.85 ± 0.58 ($P<0.0242$) at 5 cmH_2O of PEEP, 10.43 ± 0.66 ($P<0.0491$) at 10 cmH_2O of PEEP, and 9.42 ± 0.57 ($P<0.0003$) at PEEP of 15 cmH_2O (Figure 2).

ΔP_2 represents the slow decay phase of airway pressure after inspiratory airway occlusion and is represented by the interval between P_1 and P_2 (Figure 1). ΔP_2 (cmH_2O) did not change significantly with PEEP. A slight increase of this parameter was observed from 3.76 ± 0.49 (ZEEP) to 3.96 ± 0.55 (5 cmH_2O of PEEP), 4.41 ± 0.66 (10 cmH_2O of PEEP), and 4.51 ± 0.63 (15 cmH_2O of PEEP) ($P<0.4869$). The variation of total resistance and its subcomponents data along with PEEP are represented in the Figure 2.

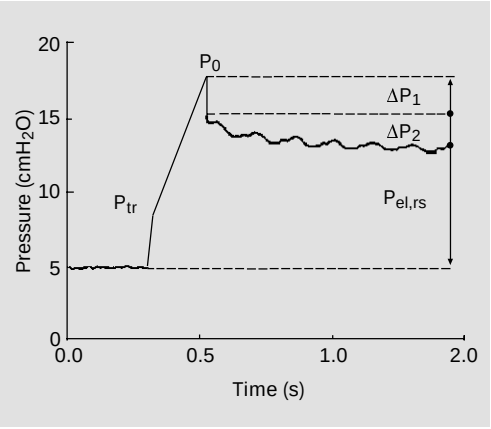

Figure 1 - Flow and pressure curves used for the evaluation of respiratory mechanical properties by the end inspiratory occlusion method. P_{tr}: Tracheal pressure; P_0 or P_{trmax}: peak airway pressure; P_2 or $P_{el,rs}$: static elastic recoil pressure; R_{init} (ΔP_1): minimal value of resistance; R_{diff} (ΔP_2): mechanical unevenness within the system and stress relaxation; R_{rsmax}: total respiratory system resistance, corresponding to the sum of R_{diff} and R_{init}.

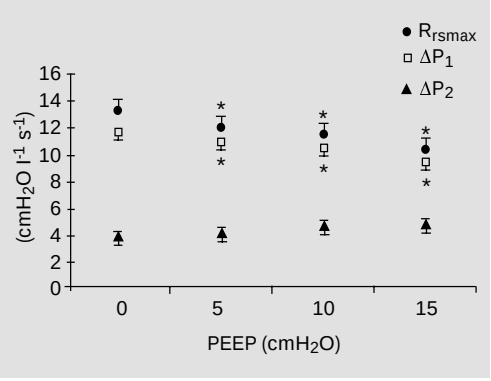

Figure 2 - Total resistance (R_{rsmax}) variance and subcomponents (ΔP_1 and ΔP_2). Airway resistance-dependent pressure gradient (ΔP_1) shows a significant and progressive fall along with positive end-expiratory pressure (PEEP) application from baseline to 5 ($P<0.0242$), 10 ($P<0.0491$) and 15 ($P<0.0003$) cmH_2O. The viscoelastic resistance-dependent pressure gradient (ΔP_2) presents a nonsignificant tendency to increase with PEEP increase (ANOVA).

Table 2 - Hemodynamic data.

CI, Cardiac index ($l\ min^{-1}\ m^{-2}$); MAP, mean pulmonary artery pressure; PCWP, mean pulmonary capillary wedge pressure (mmHg); RAP, right atrium pressure (mmHg); MAP, mean arterial pressure (mmHg); LVSWI, left ventricular stroke work index ($g\ m^{-1}\ m^{-2}$); RVSWI, right ventricular stroke work index ($g\ m^{-1}\ m^{-2}$); PVR, pulmonary vascular resistance ($dyne\ s^{-1}\ cm^{-5}$); SVR, systemic vascular resistance ($dyne\ s^{-1}\ cm^{-5}$); ZEEP, zero end-expiratory pressure (0 cmH_2O); PEEP, positive end-expiratory pressure (5, 10 and 15 cmH_2O). *$P<0.05$ compared to respective ZEEP (ANOVA).

	ZEEP	PEEP		
	0	5	10	15
CI	3.90 ± 0.22	3.43 ± 0.17*	3.31 ± 0.22*	3.10 ± 0.22*
MPAP	14.30 ± 1.09	14.40 ± 1.00	17.30 ± 1.07*	19.10 ± 1.04*
PCWP	8.90 ± 1.21	8.30 ± 0.80	10.30 ± 0.64	11.80 ± 0.79*
RAP	6.30 ± 0.94	5.80 ± 0.78	7.20 ± 0.84	9.10 ± 1.10*
MAP	86.20 ± 4.01	87.80 ± 2.99	86.50 ± 3.22	88.00 ± 3.87
LVSWI	41.90 ± 3.65	38.96 ± 3.59	36.93 ± 3.29	33.92 ± 3.54
RVSWI	4.31 ± 0.49	3.80 ± 0.44	4.66 ± 0.34	4.43 ± 0.55
PVR	61.80 ± 6.02	78.90 ± 6.94*	98.40 ± 13.81*	109.30 ± 11.34*
SVR	983.30 ± 100.60	1070.50 ± 83.48*	1022.69 ± 135.56*	1169.50 ± 81.40*

Hemodynamic data

As demonstrated below, the augmentation of intra-thoracic pressure caused by PEEP application determined a depression of the cardiac function expressed by a decrease of cardiac output and derived indexes (Table 2). The elevation of atrial filling pressures as pulmonary arterial pressure also represents the effects of intra-thoracic distending pressure. Cardiac index (1 min^{-1} m^{-2}) showed a significant and progressive decrease from 3.90 ± 0.22 at ZEEP to 3.43 ± 0.17 (P<0.0260) at 5 cmH_2O of PEEP, 3.31 ± 0.22 (P<0.0260) at 10 cmH_2O of PEEP, and 3.10 ± 0.22 (P<0.0113) at 15 cmH_2O of PEEP. Mean pulmonary artery pressure (mmHg) remained unchanged from ZEEP (14.3 ± 1.09) to 5 cmH_2O of PEEP (14.4 ± 1.00; P<0.8760). However, at PEEP of 10 cmH_2O and at PEEP of 15 cmH_2O (17.3 ± 1.07, P<0.0048 and 19.1 ± 1.04, P<0.0005, respectively) it increased significantly. There was no significant change in PCWP when comparing values at ZEEP (8.9 ± 1.21) and at PEEP of 5 cmH_2O (8.3 ± 0.80; P<0.4151) and 10 cmH_2O (10.3 ± 0.64; P<0.4707). However, a significant variation occurred at 15 cmH_2O of PEEP (11.8 ± 0.79; P<0.0326). The right atrium pressure did not change at ZEEP (6.3 ± 0.94), and 5 and 10 cmH_2O of PEEP (5.8 ± 0.78, P<0.5366 and 7.2 ± 0.84, P<0.2091, respectively). On the other hand, at 15 cmH_2O of PEEP, it showed a significant elevation (9.1 ± 1.10; P<0.0056). No significant changes in mean arterial pressure

Table 3 - Respiratory data.

PaO_2, Arterial oxygen tension (mmHg); $PaCO_2$, arterial carbon dioxide tension (mmHg); Qs/Qt, intrapulmonary shunt (%); $G(A\text{-}a)O_2$, alveolar arterial gradient of oxygen (mmHg); ZEEP, zero end-expiratory pressure (0 cmH_2O); PEEP, positive end-expiratory pressure (5, 10 and 15 cmH_2O). *P<0.05 compared to respective ZEEP (ANOVA).

	ZEEP	PEEP		
	0	5	10	15
PaO_2	261.90 ± 22.98	282.00 ± 26.28	333.60 ± 24.47*	369.05 ± 18.91*
$PaCO_2$	31.60 ± 1.15	28.76 ± 1.18	27.90 ± 1.32	28.50 ± 1.55
Qs/Qt	22.26 ± 2.28	19.64 ± 2.06	15.71 ± 1.40*	11.66 ± 1.24*
$G(A\text{-}a)O_2$	125.50 ± 12.59	103.80 ± 10.12	52.80 ± 14.07*	16.33 ± 6.28*

Table 4 - Peripheral oxygenation indexes.

CaO_2, Arterial oxygen content (ml/dl); DO_2, oxygen delivery (ml min^{-1} m^{-2}); VO_2, oxygen consumption (ml min^{-1} m^{-2}); O_2ER, oxygen extraction rate (%); SvO_2, mixed venous saturation (%); ZEEP, zero end-expiratory pressure (0 cmH_2O); PEEP, positive end-expiratory pressure (5, 10 and 15 cmH_2O). *P<0.05 compared to respective ZEEP (ANOVA).

	ZEEP	PEEP		
	0	5	10	15
CaO_2	15.89 ± 0.80	15.96 ± 0.77	16.17 ± 0.76*	16.38 ± 0.76*
DO_2	481.29 ± 40.11	435.74 ± 35.13	423.02 ± 36.83	432.16 ± 38.63
VO_2	121.93 ± 11.94	125.42 ± 14.53	124.97 ± 11.24	138.24 ± 15.21
O_2ER	0.26 ± 0.02	0.29 ± 0.02	0.30 ± 0.02	0.33 ± 0.029
SvO_2	76.99 ± 2.19	74.04 ± 2.47	73.71 ± 3.04	71.82 ± 3.04

were observed when compared to basal values (86.2 ± 4.01 at ZEEP, 87.8 ± 2.99 at 5 cmH_2O of PEEP, 86.5 ± 3.22 at 10 cmH_2O of PEEP and 88 ± 3.87 at 15 cmH_2O of PEEP (P<0.3104)). When compared with baseline LVSWI (41.9 ± 3.65 at ZEEP), it decreased to 38.96 ± 3.59 at 5 cmH_2O, 36.93 ± 3.29 at 10 cmH_2O and 33.92 ± 3.54 at 15 cmH_2O (P<0.4680). On the other hand, when compared with baseline parameters (4.31 ± 0.49), RVSWI showed a nonsignificant variation (P<0.1073) obtained at the PEEP levels of 5 cmH_2O (3.8 ± 0.44), 10 cmH_2O (4.66 ± 0.34), and 15 cmH_2O (4.43 ± 0.55). When compared with basal values (61.8 ± 6.02), PVR presented a significant increase with PEEP levels of 5 cmH_2O (78.9 ± 6.94; P<0.0141), 10 cmH_2O (98.4 ± 13.81; P<0.0083), and 15 cmH_2O (109.3 ± 11.34; P<0.0011). Finally, a variation in SVR was observed when basal values (943.3 ± 100.60) were compared to PEEP levels of 5 cmH_2O (1070.5 ± 83.48; P<0.0047), 10 cmH_2O (1022.69 ± 135.56; P<0.0472), and 15 cmH_2O (1169.5 ± 81.40; P<0.0186).

Respiratory data

As can be seen in Table 3, the increase of PEEP improved oxygenation, without any interference with carbon oxide excretion. Compared to the baseline parameters (261.9 ± 22.98) there was a nonsignificant change in PaO_2 at PEEP of 5 cmH_2O (282 ± 26.28; P<0.4696), whereas a significant increase was observed at PEEP of 10 cmH_2O (333.6 ± 24.47; P<0.0011) and 15 cmH_2O (399.05 ± 18.91; P<0.0001). $PaCO_2$ did not vary significantly from basal value (31.6 ± 1.15) (P<0.1293) with PEEP of 5 cmH_2O (28.76 ± 1.18), 10 cmH_2O (27.9 ± 1.32) and 15 cmH_2O (28.5 ± 1.55).

Intrapulmonary shunt and alveolar arterial gradient of oxygen represent indexes of oxygenation. The decreasing of both means improvement of gas exchange in the lungs. $G(A\text{-}a)O_2$ decreased significantly from basal values of 125.50 ± 12.59 to 103.80 ± 10.12 at 5 cmH_2O of PEEP. There were additional and significant decreases in the levels measured at PEEP of 10 cmH_2O (52.80 ± 14.07; P<0.0023) and 15 cmH_2O (16.33 ± 6.28; P<0.0001). There was a decrease in Qs/Qt from control (22.26 ± 2.28), which was nonsignificant at 5 cmH_2O of PEEP (19.64 ± 2.06; P<0.2829), but strongly significant at 10 cmH_2O of PEEP (15.41 ± 1.40; P<0.0064) and 15 cmH_2O of PEEP (11.66 ± 1.24; P<0.0007).

Peripheral oxygenation indexes

In comparison with basal values of arterial oxygen content (CaO_2 = 15.89 ± 0.80 ml/dl), there was no significant change at PEEP levels of 5 cmH_2O (15.96 ± 0.776; P<0.4468), but a significant change occurred at PEEP of 10 cmH_2O (16.17 ± 0.763; P<0.0016) and 15 cmH_2O (16.38 ± 0.76; P<0.0001) (Table 4). There was no significant variation in DO_2 ($ml\,min^{-1}\,m^{-2}$) (P<0.097) at PEEP of 5 cmH_2O (435.74 ± 35.13), 10 cmH_2O (423.02 ± 36.83) and 15 cmH_2O (432.16 ± 38.63), compared to basal parameters (481.29 ± 40.11). The basal value of oxygen consumption ($ml\,min^{-1}\,m^{-2}$) was 121.93 ± 11.94, 125.42 ± 14.53 at PEEP of 5 cmH_2O, 124.97 ± 11.24 at 10 cmH_2O, and 138.24 ± 15.21 at 15 cmH_2O. Oxygen consumption did not vary significantly (P<0.0790). Compared to baseline parameters (0.26 ± 0.020), a slight but not significant increase in O_2 ER (%) (P<0.379) was observed at PEEP of 5 (0.29 ± 0.024), 10 (0.30 ± 0.21) and 15 cmH_2O (0.33 ± 0.029). Compared to baseline parameters (76.99 ± 2.19), no significant difference in SvO_2 (%) (P<0.2475) was observed at PEEP levels of 5 (74.04 ± 2.47), 10 (73.71 ± 2.39) or 15 cmH_2O (71.82 ± 3.04).

Discussion

The usefulness of PEEP throughout the respiratory cycle for the correction of hy-

poxemia caused by acute respiratory failure has been clinically demonstrated since 1967 (16). Since then, several studies have been performed in order to establish the ideal PEEP that could restore the oxygenation with minimal impairment of oxygen delivery (4,5,17). In order to minimize pulmonary and circulatory negative influences, many authors recommend adjusting PEEP values according to respiratory mechanical properties (3,18,19).

Recently, several methods have been proposed to assess respiratory mechanical properties in artificially ventilated patients (18,20). Respiratory compliance or elastance and airway resistance can be readily calculated using the flow and pressure transducers incorporated into modern mechanical ventilators, if the raw signals can be connected to an external recording device (21). Among these, the constant flow inflation method has been employed by many authors (12,13,22,23). This technique was developed by Bates et al. (11), who reexamined an early analysis by Rattenborg and Holaday (24) of the behavior of the multicompartmental model of the respiratory system. Utilizing the end inflation occlusion method it is possible to measure the elasticity, resistance and its subcomponents of respiratory system.

In the present study a significant change was observed in pulmonary elastance or compliance at PEEP levels of 10 and 15 cmH_2O. The decrease in respiratory elastance with PEEP can be explained by a supplementary alveolar recruitment. Normal airway resistance is of the order of 2.5 $cmH_2O\ l^{-1}\ s^{-1}$ and significant increases have been described in patients with chronic air flow limitation (26.4 $cmH_2O\ l^{-1}\ s^{-1}$) (21). The increase in airway resistance observed after cardiac surgery may reflect airway wall edema, presence of fluid or secretions within the airway lumen as well as losses of functional lung volume.

Previously we described variations of the overall R_{rsmax} and its airway (ΔP_1) and viscoelastic (ΔP_2) components in patients immediately before and after cardiac surgery (13). There are few studies comparing R_{rsmax}, ΔP_1 and ΔP_2 at different PEEP levels during the postoperative period after cardiac surgery. The significance of R_{init} ((P_{trmax} - P_1)/ flow) or (ΔP_1) has only recently been clarified in human beings, as essentially representing airway resistance (24). As described above, the difference between P_1 and P_2 (i.e., ΔP_2) represents the slow postocclusion decay in tracheal pressure and may reflect stress relaxation due to the viscoelastic properties of the respiratory system and possibly the "Pendelluft" phenomenon that represents distribution of air among the different lung regions (11,25-27). In normal subjects, "Pendelluft" probably has a relatively small role, however, this phenomenon may be more evident if there were an increase in time constant inhomogeneities of alveolar inflation and deflation within the lung. It is important to emphasize that R_{rsmax} corresponds to the effective resistance at zero respiratory frequency, while ΔP_1 reflects the resistance at high frequency (11). Therefore, ΔP_2, that reflects tissue viscance, is a measure of the frequency dependence of resistance, a considerably important clinical parameter (28). It is important to emphasize that R_{rsmax} is always greater than R_{init} (ΔP_1). In chronic or acute lung diseases this difference tends to be higher owing to R_{diff} (ΔP_2) elevation (20). In the present study we observed a significant decrease in R_{rsmax} due to a significant decrease in ΔP_1, with increasing levels of PEEP. This effect can be explained by a probable increase in airway radius due to radial forces applied by the alveolar parenchyma on the airway wall. These data confirm a basic principle of respiratory mechanics, i.e., that flow resistance decreases with increasing lung volume, as determined by changes in ΔP_1 (29,30). The decrease in ΔP_1 and the nonsignificant effect of PEEP on ΔP_2 lead to a decrease in R_{rsmax}. These findings in

humans are in contrast with those observed in cats, since it was demonstrated in this species that R_{rsmax} increases with lung volume (30) because of the increase in parenchyma viscoelastic losses. On the other hand, at fixed tidal volume, R_{rsmax} could decrease with increased flow as demonstrated in adult respiratory distress syndrome patients (23).

Although ΔP_2 increased with increasing PEEP, this variation was not considered to be statistically significant. As previously mentioned, ΔP_2 reflects "Pendelluft" phenomena and stress relaxation; however, it is difficult to say which of the two was more prominent in the present study. The term stress relaxation used in this text refers to the phenomena of lung accommodation to positive intra-alveolar pressure, probably caused by the interstitial lung fibrillar matrix realignment and/or by a decrease of the forces generated by superficial tension. A stress relaxation increase is normally related to tissue edema and/or collapsed alveoli, a common situation after cardiac surgery, which is resolved by the alveolar recruitment effect of PEEP. On the other hand, ΔP_2 may increase with PEEP, thus reflecting the volume dependency of stress relaxation. The elevation of tissue viscance observed in our study was not significant, but further studies are necessary to better characterize the effects of PEEP on lung viscance. The current methods frequently employed in ICU to evaluate mechanical properties in artificially ventilated patients (i.e., dynamic and static compliance as well as total airway resistance) are probably not enough to detect changes in tissue viscance. Whether the observed PEEP-associated tendency to tissue viscance elevation in this study represents a mechanical adverse effect that speaks against the use of PEEP is a point that needs more study. Probably the use of other approaches, such as increasing inspiratory flow, may cancel the small increase in tissue viscance observed in the present data (27).

Qs/Qt and $G(A\text{-}a)O_2$ decreased concurrently with the changes in respiratory elastance. It is important to point out that PEEP values above 10 cmH_2O are not commonly recommended after cardiac surgery due to a possible decrease in cardiac output. Although the cardiac index fell from 3.31 to 3.10 l min^{-1} m^{-2}, when we changed the PEEP level from 10 to 15 cmH_2O the oxygenation improvement caused by the decrease in Qs/Qt maintained DO_2 at adequate levels. Therefore, considering a Qs/Qt reduction from 19.64 ± 2.06% at PEEP of 5 cmH_2O to 15.71 ± 1.40% and 11.66 ± 1.24% at PEEP of 10 and 15 cmH_2O, respectively, values from 10 to 15 cmH_2O may be necessary to reduce the shunt fraction after cardiac surgery.

In this study there was a significant increase in atrial filling pressure as well as in pulmonary vascular resistance, an effect which is probably related to increased intrathoracic and pleural pressure observed with increasing PEEP. As demonstrated by other studies at 10 cmH_2O or higher, PCWP overestimates left ventricular filling pressure, even if the occluded catheter tip is positioned in the inferior regions of the lung (31,32). One of the critiques of our study is the lack of any correction for increased pleural pressure during PEEP application and making hemodynamic measurements with the patient connected to the ventilator. As expected, we observed a significant variation in right and left pressures mainly at 15 cmH_2O of PEEP. On the right side of the heart, this fact is probably caused by an obstruction-like effect in venous return (31) on the left; the PCWP elevation is probably due to an artifact transmitted during lung distention which is more evident with increasing PEEP (33). Lozman et al. (34) observed a good correlation between PCWP and left atrium pressure at low levels of PEEP after cardiac surgery; however, at 10 and 15 cmH_2O of PEEP, a discrepancy was observed between PCWP and left atrium

pressure and no statistical correlation was found between these values. In their study, Pinsky et al. (31) found that in postoperative patients PCWP does not reflect or change with PEEP. However, PCWP reflects transmural pressure (left pressure) only during low levels of PEEP (<5 cmH_2O) whereas nadir PEEP obtained by abrupt airway disconnection accurately reflects transmural pressure to at least 15 cmH_2O. To minimize a possible interference with respiratory mechanical data acquisition, we did not disconnect our patients from the ventilator to obtain atrial filling pressures. In contrast, Van den Berg et al. (35) employed sustained inspiratory hold maneuver (24 s) in postoperative coronary bypass surgery patients to determine the dynamic changes in right and left ventricular output and found that sustained inspiratory pressure induces proportionally similar decreases in both right and left ventricle output. They concluded that the hemodynamic effects of positive inspiratory pressure ventilation will depend on the degree of lung inflation, on the inspiratory time, and on the time when measurements are made within the ventilatory cycle. In normal volunteers, Huemer et al. (36) employed Doppler hemodynamic indices to show that the fall in cardiac output during PEEP is caused by a reduction in ventricular filling due to decreased venous return. Our data, despite the fall in cardiac index, showed that DO_2 and VO_2 were preserved; in addition, CaO_2 increments due to the PEEP-related increase in oxygen saturation were also able to partially compensate for the hemodynamic impairment. According to our results, although PEEP therapy above 10 cmH_2O substantially increases oxygenation, it should be cautiously applied, especially in patients with marginal cardiac function due to contractility disturbances or hypovolemia. The positive results from PEEP higher than 10 cmH_2O related to reduction in airway resistance and compliance restoration due to alveolar recruitment should be carefully weighed against undesirable hemodynamic effects.

Validity and limitations of measurements of respiratory mechanics in patients

Among the several techniques available to study respiratory mechanics during mechanical ventilation, the single breath method (SBM) (37), the end-inflation occlusion method (EIOM) (11), and the interrupter technique (IT) (38) have been successfully applied to normal humans or patients with acute respiratory failure (1,21-23,39). SBM allows a detailed account of respiratory system resistive properties throughout relaxed expiration. At a particular constant inspiratory flow, EIOM analyzes the frequency-dependent behavior of respiratory system resistance (giving the infinite frequency and zero frequency resistances) and splits it into its homogeneous and uneven components, i.e., that corresponding to the combined summation of series/parallel elements, and that resulting from time constant inequalities within the system and/or stress relaxation, respectively. IT allows the study of volume and flow dependence of the resistive and elastic mechanical properties of the respiratory system by means of brief airway occlusions during relaxed expiration. In the present study, we utilized the EIOM because we are more confident in this procedure. Some conditions may modify the values obtained by EIOM. First, the magnitude of ΔP_2 can be influenced by the compliance and the resistance of the equipment. Unless equilibration of airway and alveolar pressure is complete, airway open pressure does not reflect the elastic recoil pressure of the respiratory system. An overestimation of ΔP_2 because of insufficient expiratory pause results in underestimation of resistive pressure and overestimation elastance. The ideal application of EIOM requires an instantaneous occlusion of the open airway pressure, which is possible to achieve since the occlusion valve

of the ventilator has a latency in occlusion time. There could be an underestimation of the resistive pressures used to compute R_{rsmax} and ΔP_1 because during the closure of the system some flow is still present and will cause an increase in lung volume and consequently in elastic recoil pressure and ΔP_1.

At a constant flow R_{rsmax} increases with lung volume, reflecting the volume dependence of stress relaxation. At a constant inflation volume R_{rsmax} decreases with increasing flow, exhibiting a minimum value at a flow rate substantially higher than the eupneic flow range. In order to interpret measurements of respiratory system mechanics correctly, the investigator must be aware of the underlying assumptions and the clinical conditions under which they are violated (39). Throughout this study, we assumed that volume, pressure and flow data are derived from appropriately calibrated instruments and that inspired gas has been delivered at a constant flow (square wave flow on the ventilator), situations that, if unrecognized, will lead to erroneous results. Particular emphasis is placed on the need for absence of spontaneous respiratory activity, errors due to time-constant inequalities within the lung, the recognition of dynamic hyperinflation, and errors in determining volumes, flows and pressures due to leaks, gas compression, tubing compliance, ventilator malfunction and intrinsic resistance of tracheal tube and inspiratory circuit. The increased values of airway resistance and elastance in our patients obtained at ZEEP conditions suggest that some degree of injury is caused in the lung during the surgical procedure (40).

In conclusion, even though most of the investigations involving PEEP therapy have been carried out on patients with acute respiratory failure, data on its effects on respiratory mechanics in postoperative cardiac patients without respiratory failure are scarce (41). Along with the increase in PEEP we observed a significant decrease in total and airway resistance and in elastance. The dependence of volume on viscoelastic properties showed a slight but not significant tendency to increase with reduction in airway resistance.

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