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Airway Occlusion Pressure to Titrate Positive End-expiratory Pressure in Patients with Dynamic Hyperinflation

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Background: **Although the use of external positive end-expiratory pressure (PEEP) is recommended for patients with intrinsic PEEP, no simple method exists for bedside titration. We hypothesized that the occlusion pressure, measured from airway pressure during the phase of ventilator triggering ($P_{0.1t}$), could help to indicate the effects of PEEP on the work of breathing (WOB).**

Methods: **Twenty patients under assisted ventilation with chronic obstructive pulmonary disease were studied with 0, 5, and 10 cm H_2O of PEEP while ventilated with a fixed level of pressure support.**

Results: **PEEP 5 significantly reduced intrinsic PEEP (mean ± SD, 5.2 ± 2.4 cm H_2O at PEEP 0 to 3.6 ± 1.9 at PEEP 5; $P < 0.001$), WOB per min (12.6 ± 6.7 J/min to 9.1 ± 5.9 J/min; $P = 0.003$), WOB per liter (1.2 ± 0.4 J/l to 0.8 ± 0.4 J/l; $P < 0.001$), pressure time product of the diaphragm (216 ± 86 cm $H_2O \cdot s^{-1} \cdot min^{-1}$ to 155 ± 179 cm $H_2O \cdot s^{-1} \cdot min^{-1}$; $P = 0.001$) and $P_{0.1t}$ (3.3 ± 1.5 cm H_2O to 2.3 ± 1.4 cm H_2O; $P = 0.002$). At PEEP 10, no further significant reduction in muscle effort nor in $P_{0.1t}$ (2.5 ± 2.1 cm H_2O) occurred, and transpulmonary pressure indicated an increase in end-expiratory lung volume. Significant correlations were found between WOB per min and $P_{0.1t}$ at the three levels of PEEP ($P < 0.001$), and between the changes in $P_{0.1t}$ *versus* the changes in WOB per min ($P < 0.005$), indicating that $P_{0.1t}$ and WOB changed in the same direction. A decrease in P0.1 with PEEP indicated a decrease in intrinsic PEEP with a specificity of 71% and a sensitivity of 88% and a decrease in WOB with a specificity of 86% and a sensitivity of 91%.**

Conclusion: **These results show that $P_{0.1t}$ may help to assess the effects of PEEP in patients with intrinsic PEEP. (Key words: Chronic obstructive lung disease; intrinsic PEEP; mechanical ventilation; work of breathing.)**

PATIENTS with acute exacerbation of chronic obstructive pulmonary disease (COPD) who require intubation and mechanical ventilation frequently exhibit dynamic hyperinflation responsible for an auto or intrinsic positive end-expiratory pressure (PEEPi).[1,2] The presence of PEEPi implies that alveolar pressure at end expiration is higher than airway opening pressure. This phenomenon may occur because the expiratory time is too short to allow complete lung emptying in the case of abnormalities in lung compliance and lung and airway resistances (including those of the endotracheal tube and the expiratory circuit of the ventilator) and in the presence of a high minute ventilation. More importantly, expiratory dynamic flow limitation is a frequent cause of air trapping and dynamic hyperinflation with PEEPi.

The presence of dynamic hyperinflation with PEEPi has several clinical implications. It increases the work of spontaneous breathing, can flatten the diaphragm and alter its performance, and can cause hemodynamic disturbances.[1–5] It has been shown that the addition of external PEEP in patients with PEEPi and flow limitation

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Table 1. Characteristics of the Patients

Patient	Age (yr)	Sex	Cause of Decompensation	Duration of Ventilation (days)	Outcome	PEEPi (cm H_2O)
1	70	M	Pneumonia	9	S	9.3
2	72	M	Bronchial infection	7	S	4.4
3	43	F	Thoracic surgery	20	S	3.6
4	62	M	Bronchial infection	2	S	3.6
5	36	F	Pneumonia	6	S	3.1
6	72	F	Bronchospasm	5	S	4.3
7	67	M	Bronchial infection	6	D	1.1
8	63	M	Bronchial infection	3	S	8.2
9	66	F	Sepsis	9	S	6.5
10	40	M	Pneumonia	5	S	3.1
11	74	M	Pneumonia	10	S	11.4
12	68	M	Septic shock	10	D	5.4
13	58	M	Acute renal failure	16	S	4.5
14	70	M	Bronchospasm	8	S	6.4
15	79	F	Pneumonia	7	S	5.4
16	66	M	Bronchial infection	7	S	6.3
17	74	F	Aortic valve replacement	121	S	4.7
18	72	F	Peritonitis	43	S	4.1
19	82	F	Peritonitis	12	D	3.8
20	78	F	Peritonitis	20	S	4.4

PEEPi = dynamic intrinsic positive end-expiratory pressure, measured at zero end-expiratory pressure; S = survived; D = died.

frequently decreases the inspiratory effort done to initiate an assisted breath.[2] This effect is highly variable from one patient to another, however.[2] Moreover, the addition of external PEEP can also increase the degree of pulmonary hyperinflation.[6-8] Accordingly, a method to titrate external PEEP is desirable to allow an optimal setting of mechanical ventilation in patients with dynamic hyperinflation.

Theoretically, titration of external PEEP should be based on repeated measurements of PEEPi. This is scarcely done in the clinical setting, however, for several reasons. Bedside measurement of dynamic PEEPi in spontaneously breathing patients may, at best, require estimation of the pleural pressure by means of esophageal balloon catheter and estimation of abdominal pressure to take into account the effect of abdominal muscle contraction during expiration.[9-11] The simple occlusion method is subject to false estimates of PEEPi because of expiratory muscle activity,[11] a frequent finding in patients with COPD. Consequently, the adjustment of external PEEP in spontaneously breathing patients is frequently based on poorly reliable subjective criteria or arbitrary values.

Because changes in PEEPi should primarily modify the work of breathing (WOB)[12] and the central respiratory drive,[2,13] we hypothesized that the measurement of the airway occlusion pressure (P0.1) could be a simple and noninvasive way to titrate the amount of external PEEP in patients in whom PEEPi with dynamic hyperinflation is suspected. We expected to see a similar direction of changes between the two indexes, WOB and P0.1, and we also wanted to observe the correlation between WOB and P0.1.

Materials and Methods

Patients

We studied 20 consecutive patients with COPD who needed intubation and mechanical ventilation for any reason. The patients were recruited among two multidisciplinary intensive care units (Créteil and Barcelona). Diagnosis of COPD was based on clinical history, chest radiograph, arterial blood gases, and clinical examination on admission. Only a few patients had pulmonary function tests before admission, and it was not possible to give a precise assessment of respiratory function for all patients. Clinical characteristics of the patients are shown in table 1. All patients gave their informed consent to participate in the study, and the protocol was approved by the Henri Mondor Ethics Committee (Comité Consultatif de Protection des Personnes dans la Recherche Biomédicale).

Protocol

Patients were studied during the weaning phase of mechanical ventilation while breathing in the pressure support mode. All patients were orotracheally intubated and were ventilated with an Evita 2 (Dräger, Lübeck, Germany) or a Servo 900C (Siemens, Solna, Sweden) ventilator. The trigger was adjusted at its most sensitive level. The level of pressure support was adjusted by the attending physician to keep each patient's respiratory frequency equal to or less than 30 breaths/min and ranged from 10 to 25 cm H_2O (mean, 16 ± 5 cm H_2O). This level was kept unchanged during the study period.

For the purpose of the study, patients were randomly ventilated with three different levels of external PEEP: 0, 5, and 10 cm H_2O. After 15–30 min of changing the external PEEP, measurements and calculations were performed as explained in the following section.

Measurements

Flow at the airway opening was measured with a heated Fleish #2 pneumotachograph (Metabo, Epalinges, Switzerland) placed between the endotracheal tube and the Y-piece of the ventilator, connected to a differential pressure transducer (Validyne MP 45, ±2.25 cm H_2O, Northridge, CA) and calibrated with a 1-l syringe containing room air.

Airway pressure (P_{aw}) was measured between the endotracheal tube and the pneumotachograph by means of a lateral pressure port connected to a differential pressure transducer (Validyne MP 45, ±225 cm H_2O). Esophageal (P_{es}) and gastric pressures (P_{ga}) were measured by means of latex balloons attached to a double-lumen polyethylene catheter (Marquat, Boissy-St. Léger, France). The catheter–balloon system was introduced through the nostril, and each catheter was connected to a differential pressure transducer (Validyne MP 45, ±80 cm H_2O). After insertion, the esophageal and gastric balloons were filled with 0.5 and 1 ml of air, respectively. The correct position of the esophageal balloon was assessed by means of an occlusion test.[14] We checked the effects of swallowing, which induces a sharp increase in P_{es} without changes in the P_{ga} tracing, and also looked at the latter while gently pushing on the belly.[15]

Calculations

The analog signals of airflow, P_{aw}, P_{es}, and P_{ga}, were digitized at a sampling rate of 128 Hz using a 12-bit analog-to-digital board (DT 2901, Data Translation, Marlboro, MA) and stored in a microcomputer for subsequent calculations. Data acquisition was performed during a 60–90 s period 15–30 min after changing the external PEEP. Volume was obtained by numerical integration of flow signal. From the flow signal, respiratory rate (f), minute ventilation (V_E), inspiratory-to-total cycle duration (T_i/T_{tot}) and V_T-T_i were calculated. Transdiaphragmatic pressure (P_{di}) was obtained by electronic subtraction of P_{es} from P_{ga}.

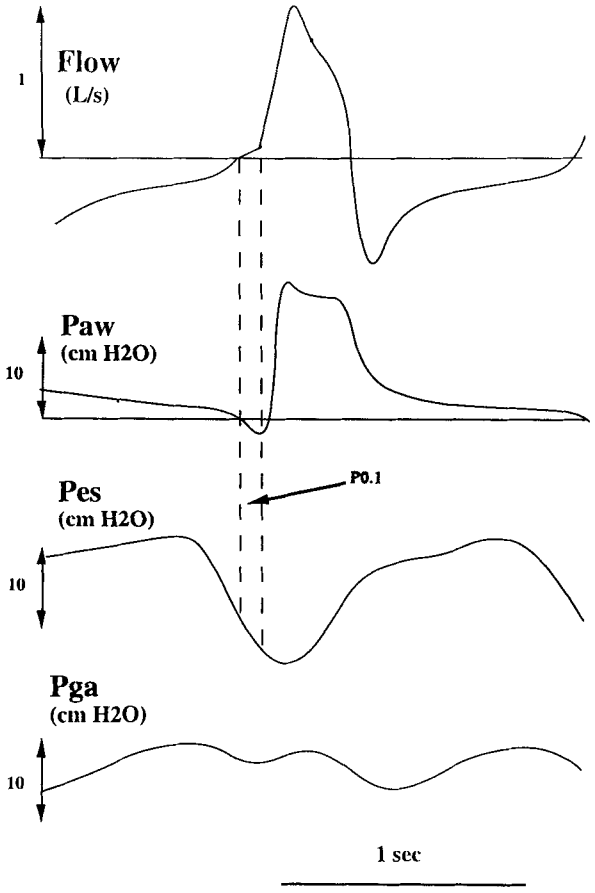

Fig. 1. Recordings of flow and airway, esophageal, and gastric pressures (P_{aw}, P_{es}, and P_{ga}) around the triggering phase during pressure support ventilation. Although the inspiratory effort has started before the breath, as indicated by the P_{es} decay with a slight concomitant decay in P_{ga}, the occluded triggering phase allows estimation of airway occlusion pressure (P0.1) during this phase.

Airway Occlusion Pressure. Airway occlusion pressure, or the pressure generated at the airway opening in the first 100 ms of an occluded inspiration (P0.1), was estimated from the P_{aw} tracing during the effort to trigger the ventilator ($P_{0.1t}$). Figure 1 illustrates the triggering phase and shows the concomitant respiratory signals. The problems encountered with the measurement

of P0.1 during ventilator triggering are twofold. First, the occlusion time is frequently shorter than 100 ms. For this reason, we measured the drop in pressure over 50 ms and extrapolated its value to 100 ms. Assuming that the period of complete occlusion corresponded to the steepest slope, we measured it over several windows of 50 ms and looked for the steepest slope among these values. Second, the time at which this "P0.1" is measured may be late relative to the beginning of the inspiratory effort in patients with dynamic hyperinflation. This problem is intrinsic to the method of measuring P0.1, but measuring P0.1 during this period is still a reliable indicator of the beginning of the effort.[16] $P_{0.1t}$ was calculated as follows: (1) the minimal value of P_{aw} during the triggering of the breath was detected, corresponding to the last point of zero flow before it becomes inspiratory; (2) 10 consecutive regression lines (P_{aw} over time) were calculated in windows of 50 ms in backward direction, and a total time of near 120 ms was evaluated (the last point corresponding to the minimal P_{aw} and the first point corresponding to the P_{aw} value 120 ms before); (3) the regression line with the steepest negative slope was chosen to calculate the $P_{0.1t}$; and (4) $P_{0.1t}$ was extrapolated over 100 ms from this slope. The values reported here are the average of all $P_{0.1t}$ obtained in a 60–90 s period of acquisition, with a variable number of respiratory cycles depending on the respiratory rate.

Inspiratory Work of Breathing and Pressure Time Product. The inspiratory WOB per breath was computed from the surface included between the inspiratory tidal volume–esophageal pressure loop and the relaxation curve of the chest wall, as previously described.[17–19] We used the Campbell diagram and measurements of P_{es} and P_{ga} to estimate the "true" PEEPi, as explained in the next section. Static elastic recoil pressure of the chest wall was assumed to be linear in the tidal volume range and was calculated according to its predicted value for normal subjects.[19] Measurement of the actual characteristics of the chest wall would have been preferable, but this often necessitates sedating the patient. However, even large errors in chest wall mechanics have relatively minor influence on the work performed by the patients in the range of effort evaluated here, and this does not invalidate the comparisons between different ventilatory settings. The Campbell diagram was drawn by passing this line through the end-expiratory static elastic recoil pressure of the chest wall, which is similar to the P_{es} at the beginning of inspiratory flow if the relaxation volume of the respiratory system has been reached. This is different, however, if PEEPi and dynamic hyperinflation are present, as explained in the next section. Figure 2 shows the schema of the Campbell diagram and explains its computation. The use of P_{es} (referenced to atmosphere) allows calculation of the patient's work under any form of mechanical ventilation. Indeed, if P_{es} recording follows the relaxation characteristics of the chest wall, this indicates that no active work is performed by the respiratory muscles, whatever the magnitude of the ventilator's work performed on the lungs. Every time the curve drops below this relaxation curve (or to the left of the curve on the diagram), this indicates that some active effort has been performed (*e.g.*, to trigger the ventilator). This computes the active part performed by the respiratory muscles.

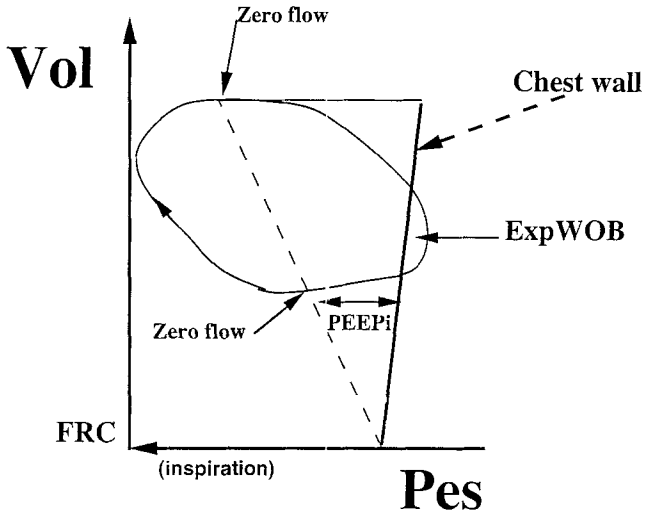

Fig. 2. Schematic representation of the Campbell diagram, used to calculate the work of breathing (WOB). For one entire breath, the esophageal pressure change is plotted against tidal volume to generate a loop. The relaxation line of the chest wall is traced for the corresponding tidal volume. The negative lung static pressure volume curve passes through the zero flow points. The increase in lung volume relative to functional residual capacity (FRC) due to dynamic hyperinflation indicates that the beginning of the inspiratory effort is shifted to the right of the zero flow point (or to the right of the beginning of inspiratory flow) by an amount equal to the intrinsic positive end-expiratory pressure (PEEPi). This value is further corrected for expiratory muscle activity (not shown). The inspiratory WOB is the area enclosed between the chest wall relaxation line and the inspiratory pressure volume loop. The area right of the chest wall relaxation line during expiration represents active expiratory work (ExpWOB).

The inspiratory WOB per breath, expressed in Joules, was multiplied by the respiratory rate to obtain the power of breathing (J/min), and the power was divided by V_E to obtain the work per liter of ventilation (J/l).

The esophageal pressure time product (PTP_{es}) was cal-

culated as the surface enclosed within the P_{es} and the relaxation line of the chest wall over inspiratory time.[20] Another index of each patient's muscle effort, the PTP for the diaphragm (PTP_{di}) was computed as the surface under P_{di} swings *versus* time, as described elsewhere.[21,22] The PTP_{es} and PTP_{di} are expressed in cm $H_2O \cdot s^{-1} \cdot min^{-1}$.

Correction of the Inspiratory Work of Breathing and Esophageal Pressure Time Product for the Presence of Intrinsic Positive End-expiratory Pressure. In nonparalyzed mechanically ventilated patients, dynamic PEEPi is classically referred to as the sudden decay of P_{es} that occurs before flow reaches the zero value; there is then an additional decay in P_{es} before inspiration due to the demand valve triggering. This value of dynamic PEEPi measured on the P_{es} tracing was corrected for expiratory muscle activity, as explained here. Expiratory muscle activity frequently occurs in COPD patients, thus increasing end-expiratory alveolar pressure independently of dynamic hyperinflation. The pressure changes resulting from the activation of expiratory abdominal muscles (*i.e.*, the positive expiratory swing measured during expiration on the P_{ga} tracings) was subtracted from the total dynamic PEEPi, because the initial decay in P_{es} is not entirely due to contraction of inspiratory muscles but is also caused by relaxation of the expiratory muscles.[9-11] Although this method has limitations,[23] it was recently validated against electromyographic measurements.[24] The value of dynamic PEEPi obtained after the above-mentioned correction was used in all the calculations.

Estimation of the Active Expiratory Work of Breathing. The presence of active expiration implies that some amount of additional work is performed by expiratory muscles. This additional work was evaluated as follows[25]: the pressure developed by the expiratory muscles is represented by the departure of P_{es} to the right of the relaxation pressure-volume curve of the chest wall and is integrated over the volume change during such active expiration (fig. 2). Because the expiratory work may be small, this calculation is dependent on the accuracy of the slope of the static elastic recoil pressure-volume relation of the chest wall. Because we used the theoretical value for this curve, this method primarily allows us to assess the changes in expiratory effort from one situation to another, whereas the absolute value may be debatable.

Estimation of the Changes in Lung Volume. Because external PEEP may increase lung volume, we calculated end-expiratory transpulmonary pressure as an estimate of end-expiratory lung volume, calculated as P_{aw} minus P_{es}.

Statistical Analysis

All data are expressed as mean ± SD. Statistical analysis was performed by means of an analysis of variance for repeated measures. When the F value showed a significant difference ($P < 0.05$ was considered as significant), we carried out a Tukey test to detect differences among groups (PEEP 0, PEEP 5, and PEEP 10). Additionally, we performed correlation analysis to assess the relation between continuous variables. Spearman ρ correlations were performed independently for each level of PEEP so that, for each correlation, one patient was represented by one set of measurements. We also looked at correlations between the individual changes in $P_{0.1t}$ and the individual changes in WOB or in PTP to see whether the variations in $P_{0.1t}$ could reliably indicate the direction of the changes in patient's effort. Finally, we looked at the predictive value of the changes in P0.1 using the classical formula for sensitivity and specificity.

Results

Tracings of P_{aw}, airflow, P_{es} and P_{ga} at PEEP 0 and PEEP 10, obtained in a representative patient, are shown in figure 3.

Breathing Pattern Parameters

Results concerning breathing pattern and PEEPi at the different levels of external PEEP are shown in table 2. Respiratory rate did not significantly change among the different levels of PEEP, and a slight but significant increase in V_T was observed with PEEP 10 as a result of an increase in T_i-T_{tot}, whereas V_E did not change. External PEEP (both 5 and 10 cm H_2O) decreased the magnitude of PEEPi by 31% between PEEP 0 and PEEP 5, by 24% between PEEP 5 and 10, and by 47% between PEEP 0 and PEEP 10.

Work of Breathing, Respiratory Muscle Effort, and Airway Pressure during the Phase of Ventilator Triggering

We observed a significant decrease in the values of WOB, PTP_{es}, PTP_{di}, and $P_{0.1t}$ when external PEEP was added. As shown in table 3, WOB, expressed either as power or as per liter of ventilation, was significantly lower during PEEP 5 and PEEP 10 in comparison with PEEP 0 (both $P < 0.005$). Both PTP_{es} and PTP_{di} signifi-

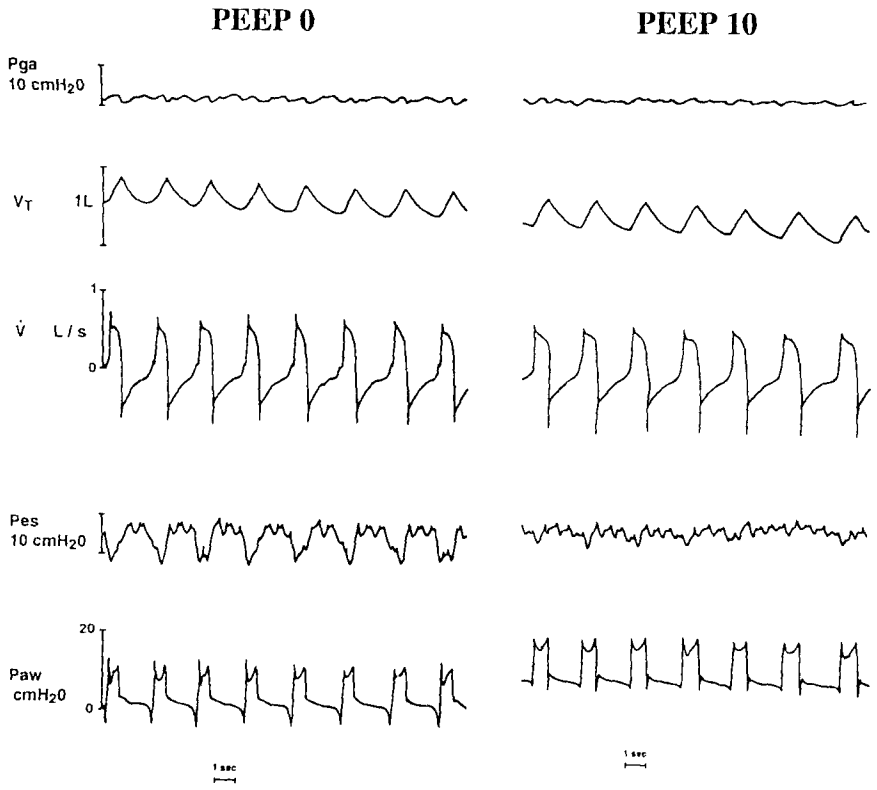

Fig. 3. From *top* to *bottom*, tracings of gastric pressure (P_{ga}), tidal volume (V_T), airflow (V), esophageal pressure (P_{es}) and airway pressure (P_{aw}) obtained in a representative patient during ventilation at positive end-expiratory pressure (PEEP) 0 and PEEP 10. Intrinsic PEEP (PEEPi), airway pressure during the phase of ventilator triggering ($P_{0.1t}$), and work of breathing (WOB) were maximal at PEEP 0. Note the marked inspiratory P_{es} swings and the presence of abdominal muscle recruitment during expiration at PEEP 0.

cantly decreased during PEEP 5 and PEEP 10. $P_{0.1t}$ also significantly decreased, by 29% between PEEP 0 and PEEP 5 and by 22% between PEEP 0 and PEEP 10. There was no difference in any of these parameters between PEEP 5 and 10. Finally, the expiratory WOB was significantly higher at PEEP 0 than at PEEP 5 and 10.

Correlations between External Positive End-expiratory Pressure and Changes in Patients' Effort and Drive

Most of the correlation coefficients (ρ) between WOB (expressed as power) and respiratory rate or V_T were low or not significant (NS): 0.30 (P = NS) and 0.72 (P = 0.002) at PEEP 0, 0.24 (P = NS) and 0.47 (P = 0.04) at PEEP 5, and 0.57 (P = 0.02) and 0.27 (P = NS) at PEEP 10. In contrast, $P_{0.1t}$ correlated strongly ($P < 0.005$) with the power of breathing, as shown in figures 4, 5, and 6. Correlations between $P_{0.1t}$ and PTP_{es} were also significant: ρ = 0.64 (P = 0.005) at PEEP 0, 0.62 (P = 0.007) at PEEP 5, and 0.83 ($P < 0.001$) at PEEP 10. $P_{0.1t}$ also correlated with PEEPi; ρ = 0.48 (P = 0.04) at PEEP 0 (fig. 7), 0.65 (P = 0.002) at PEEP 5, and 0.84 at PEEP 10 ($P <$ 0.001).

The directional changes in $P_{0.1t}$ followed the individual

Table 2. Breathing Pattern Components and Intrinsic Positive End-expiratory Pressure (PEEP)

	PEEP 0	PEEP 5	PEEP 10	*P* Value
f (per min)	26.9 ± 7.1	25.5 ± 6.7	25.1 ± 8.3	0.18
V_T (ml)	399 ± 118*	432 ± 136	459 ± 137	0.003
V_E (l/min)	10.7 ± 4.3	10.8 ± 4.1	11.1 ± 4.4	0.27
Ti/Tt (%)	32 ± 6*	33 ± 5	34 ± 5	0.025
V_T/Ti (ml/s)	561 ± 170	551 ± 160	556 ± 180	0.74
PEEPi (cm H_2O)	5.2 ± 2.4†	3.6 ± 1.9	2.7 ± 1.9	<0.001

* Significantly different from PEEP 10 cm H_2O.

† Significantly different from PEEP 5 and PEEP 10 cm H_2O.

Table 3. Work of Breathing (WOB), Pressure Time Product (PTP), and $P_{0.1t}$

	PEEP 0	PEEP 5	PEEP 10	*P* Value
WOB (J/min)	12.6 ± 6.7*	9.1 ± 5.9	8.8 ± 8.6	0.003
WOB (J/l)	1.17 ± 0.44*	0.82 ± 0.43	0.69 ± 0.43	<0.001
WOB_{ex} (J/min)	1.44 ± 1.3*	0.84 ± 0.6	0.68 ± 0.6	0.006
WOB_{ex} (J/l)	0.14 ± 0.12*	0.08 ± 0.05	0.06 ± 0.04	0.002
PTPes (cm $H_2O \cdot s^{-1} \cdot min^{-1}$)	213 ± 89*	158 ± 88	137 ± 94	<0.001
PTPdi (cm $H_2O \cdot s^{-1} \cdot min^{-1}$)	216 ± 86*	155 ± 79	143 ± 108	0.001
$P_{0.1t}$ (cm H_2O)	3.3 ± 1.5*	2.3 ± 1.4	2.5 ± 2.1	0.002

* Significantly different from PEEP 5 and PEEP 10 cm H_2O.

PTPdi = pressure time product for the diaphragm; PTPes = pressure time product for the esophagus; WOBex = active expiratory work of breathing.

changes in power of breathing, both from PEEP 0 to 5 and from PEEP 5 to 10 ($P < 0.005$), as shown in figure 8. A correlation was also found with the changes in PTP_{es} ($P < 0.05$). Correlation coefficients between $P_{0.1t}$ and respiratory rate or V_T were much poorer: respectively, 0.43 and 0.37 at PEEP 0, 0.39 and 0.34 at PEEP 5, and 0.54 ($P = 0.01$) and 0.26 at PEEP 10.

Reasoning that P0.1 may be useful for the clinician to detect whether a change in external PEEP has decreased PEEPi or WOB, we used this classification to calculate the predictive value of a change in $P_{0.1t}$. We found that a decrease in $P_{0.1t}$ in response to PEEP indicated a decrease in PEEPi with a specificity of 71% and a sensitivity of 88%, and indicated a decrease in WOB with a specificity of 86% and a sensitivity of 91%.

Transpulmonary Pressure and Lung Volume

From 0 to 5 cm H_2O of PEEP, no significant change in end-expiratory transpulmonary pressure was observed, whereas it was significantly raised by PEEP 10 (1.6 ± 6.4 cm H_2O at PEEP 0, 2.1 ± 5.4 cm H_2O at PEEP 5, and 5.2 ± 7.2 cm H_2O at PEEP 10; $P < 0.05$).

Discussion

The results of this study suggest that the measurement of $P_{0.1t}$ during the assisted breaths of mechanical ventilation can help to estimate the effects of external PEEP to reduce the inspiratory WOB.

The main interest of adding external PEEP in mechanically ventilated COPD patients with dynamic hyperinflation is to decrease the elastic workload that inspiratory muscles must overcome before triggering the ventilator. In part because of the frequent activity of the expiratory muscles,[8,9,11] optimal measurements of PEEPi in patients under assisted modes of mechanical ventilation may require the insertion of esophageal and gastric catheters, which is not applicable in routine practice. Moreover, the response to external PEEP in these pa-

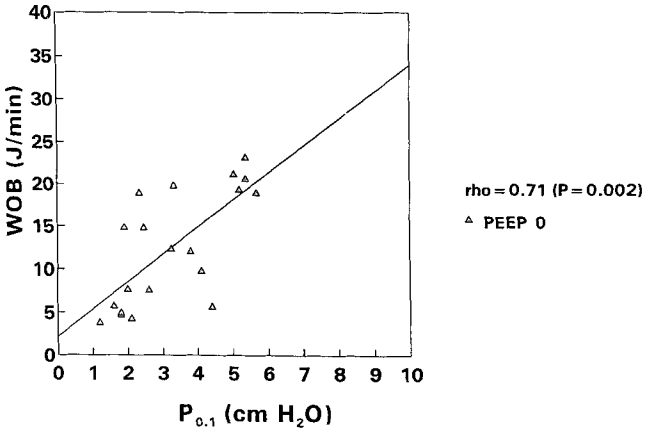

Fig. 4. Correlation between power of breathing (WOB in J/min) and airway occlusion pressure ($P_{0.1t}$) at positive end-expiratory pressure (PEEP) 0. Each triangle represents an individual patient. Correlation was highly significant (r = 0.71; $P = 0.002$).

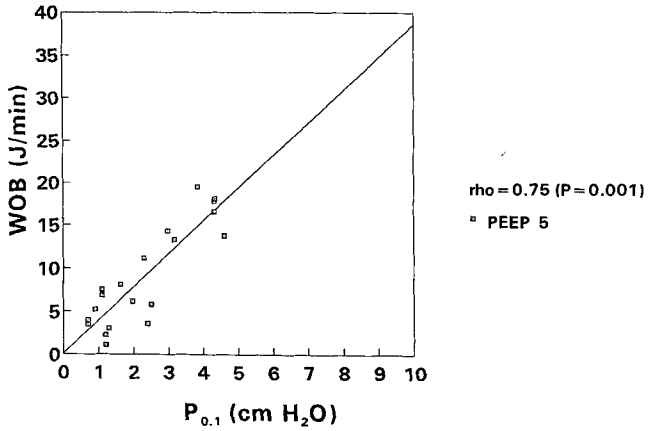

Fig. 5. Correlation between power of breathing (WOB in J/min) and airway occlusion pressure ($P_{0.1t}$) at positive end-expiratory pressure (PEEP) 5. Each square represents an individual patient. Correlation was highly significant (r = 0.75; $P = 0.001$).

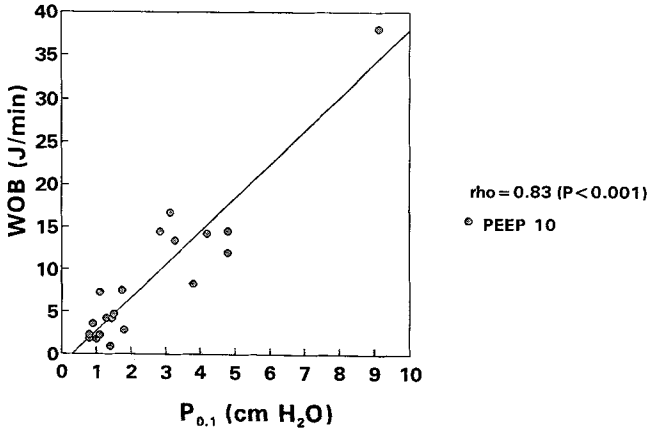

Fig. 6. Correlation between power of breathing (WOB in J/min) and airway occlusion pressure ($P_{0.1t}$) at positive end-expiratory pressure (PEEP) 10. Each dot represents an individual patient. Correlation was highly significant (r = 0.83; *P* < 0.001).

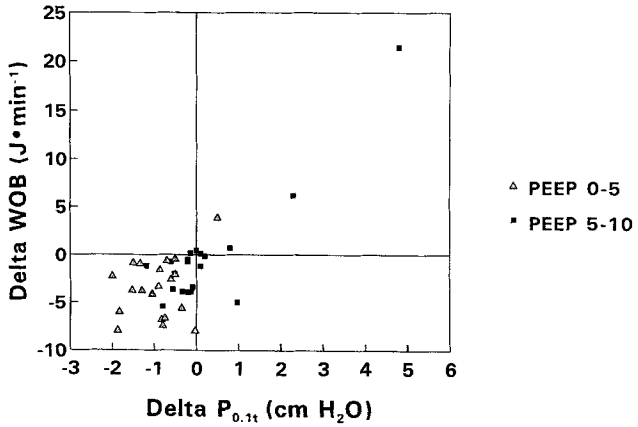

Fig. 8. Individual changes in work of breathing (ΔWOB in J/min) and in airway occlusion pressure ($\Delta P_{0.1t}$) observed during changes in external positive end-expiratory pressure (PEEP) from 0 to 5 cm H_2O (triangles) and from 5 to 10 cm H_2O (squares). Only 1 of 20 patients exhibited a clear increase in $P_{0.1t}$ (+ 1 cm H_2O), whereas WOB decreased (−5 J/min; ρ = 0.47; *P* = 0.003). In every case in which the addition of PEEP increased the WOB, $P_{0.1t}$ also increased.

tients can be hard to predict in terms of reduction in WOB and further hyperinflation,[6,26] thus warranting a clinically rigorous approach to safely adjust external PEEP. Until now, a clinically simple, noninvasive, and reliable method helpful to titrate external PEEP in patients with dynamic hyperinflation under assisted ventilation has not been described.

Because of the time lag between the onset of inspiratory effort on the Peso tracing and the depression observed on the P_{aw} tracing ($P_{0.1t}$), $P_{0.1t}$ could theoretically poorly reflect the real occlusion pressure (supposed to parallel the inspiratory drive) in case of PEEPi.[27] In intubated patients with COPD exhibiting different levels of PEEPi, however, Conti *et al.*[16] have shown that the airway occlusion pressure and the $P_{0.1t}$ closely reflect the occluded P_{es}. In addition, several patients exhibited abdominal muscle contraction, as reflected by expiratory WOB and expiratory positive swings in gastric pressure. This implies that the initial decay in the P_{es} tracing before inspiration begins is not only due to inspiratory muscle contraction but also to the relaxation of expiratory muscles.[11,28] This finding could potentially affect the interpretation of occlusion pressures, both as an index of respiratory drive and as a surrogate for WOB. The correlation between $P_{0.1t}$ and WOB remained acceptable even with the highest levels of expiratory WOB (at PEEP 0).

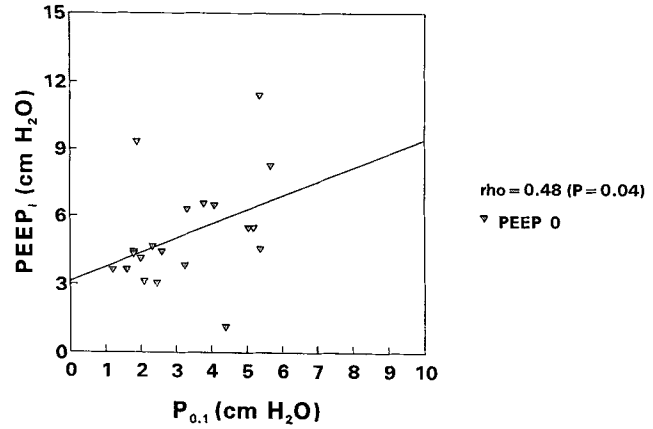

Fig. 7. Plot of individual values of intrinsic positive end-expiratory pressure (PEEPi) and airway occlusion pressure ($P_{0.1t}$) measured at PEEP 0 (ρ = 0.48; *P* = 0.04).

Another factor that can influence the measurement of both WOB and $P_{0.1t}$ is lung volume.[29] Absolute lung volume was indirectly assessed through transpulmonary pressure measured at end expiration and indicated that no change in lung volume seemed to occur with PEEP 5, making the measurement of WOB and $P_{0.1t}$ reliable in this setting. The values of WOB at PEEP 10 could be influenced by an altered diaphragmatic geometry leading to a decreased muscle effectiveness. Measurement of $P_{0.1t}$ can not be used to indicate changes in lung volume. Interestingly, however, there was no drop and even a slight increase in $P_{0.1t}$ between PEEP 5 and 10, whereas lung volume increased.

Changes in arterial blood gases and thus in chemoreceptor sensitivity could modify the $P_{0.1t}$ measurements at the different levels of external PEEP. This is unlikely, however, because the addition of external PEEP in this

setting has repeatedly been shown to have no significant influence on arterial blood gases.[1,7,26] Moreover, in COPD patients, a high neural drive indicate a high mechanical load rather than a high chemical drive.[30,31]

There was a weak but significant correlation between individual changes in $P_{0.1t}$ and in WOB when external PEEP was increased (fig. 8). No patient exhibited a decrease in $P_{0.1t}$ and a simultaneous increase in WOB, and only one patient showed an increase in $P_{0.1t}$ and a decrease in WOB. This study did not investigate whether P0.1 might be an indicator of the best PEEP on PEEPi during pressure support, but the fact that $P_{0.1t}$ parallels the changes in WOB make this parameter helpful in individually titrating the level of external PEEP in terms of respiratory muscle unloading. There was no change in WOB or $P_{0.1t}$ when external PEEP was increased from 5 to 10 cm H_2O. Three patients exhibited increases in both WOB and $P_{0.1t}$, thus suggesting an inadequate titration of external PEEP. For the purpose of this study, arbitrary levels of PEEP were used in these patients. On an individual basis, one can imagine this could be tailored differently.

We used a specific algorithm to measure $P_{0.1t}$.[32] The way $P_{0.1t}$ was measured had probably no influence on the results, because we checked that the results obtained in intubated patients were very similar to hand calculations on paper tracings. The method was robust and could be easily incorporated in a microprocessor-driven ventilator for monitoring purposes or for providing information to a knowledge-based system.[33] One limit, however, is that in the case of flow triggering, this calculation of P0.1 can not be used.

The correlation between WOB and respiratory rate, a parameter used to adjust pressure support ventilation level at the bedside,[17,20] was weaker than the correlation between WOB and $P_{0.1t}$. Berger *et al.*[34] found a good correlation between P0.1 and WOB in patients recovering from acute respiratory failure; whereas respiratory rate continued to decrease at levels of support higher than those providing a near complete unloading, P0.1 remained almost constant at these levels of support, suggesting that P0.1 may be more useful than respiratory rate in indicating the effects of pressure support on WOB. Alberti *et al.*[35] showed in mechanically ventilated patients without PEEPi that P0.1, estimated from the deflection on the Peso, was better correlated with inspiratory WOB than tidal volume or respiratory frequency over different levels of pressure support.

Although changes in breathing pattern are commonly observed when levels of pressure support ventilation are modified[17] and are thus clinically useful to titrate pressure support ventilation,[20] the current investigation indicates that this is not the case when the level of PSV is held constant and the only modification is the external PEEP. MacIntyre *et al.*[36] also observed that in COPD patients under PSV, the respiratory rate was unchanged when external PEEP was increased in a stepwise fashion to the values of PEEPi.

The decrease in $P_{0.1t}$ observed in our study was concomitant with the decrease in patient's inspiratory WOB. Partitioning of the transpulmonary (not esophageal) WOB into its three components (elastic work due to PEEPi, elastic work not due to PEEPi, and resistive work) showed that only the work related to PEEPi[28] was significantly decreased (data not shown).

There was a possibility that the work had been shifted from inspiratory to expiratory muscles. We used two different indexes to evaluate expiratory muscle activity. The active expiratory work, assessed using the Campbell diagram, was certainly a gross approximation,[23] because the position of the chest wall is crucial with regards to the small magnitude of the expiratory work. This calculation helped, however, to give an estimate of the direction of the change. Indeed, because it decreased when external PEEP was increased, it is very likely that the "true" expiratory work did decrease. The other index was the expiratory rise in P_{ga} (data not shown), which also decreased with PEEP. The decrease in inspiratory work was not accompanied by an increase in expiratory WOB. Expiratory muscle recruitment is a nonspecific response that mainly happens when a greater than resting stimulation occurs.

This study describes the use of $P_{0.1t}$ as a possible useful adjunct to adjust external PEEP in COPD patients with dynamic hyperinflation who are under assisted mechanical ventilation. The airway occlusion pressure measured during the effort done to trigger the mechanical breaths followed the direction of the changes in the external WOB dissipated by the respiratory muscles at different external PEEP levels, thus providing a simple and noninvasive tool of assessing the effect of external PEEP in patients with dynamic hyperinflation.

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