

Lung and chest wall mechanics in normal anaesthetized subjects and in patients with COPD at different PEEP levels

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Lung and chest wall mechanics in normal anaesthetized subjects and in patients with COPD at different PEEP levels. G. Musch, G. Foti, M. Cereda, P. Pelosi, D. Poppi, A. Pesenti. ©ERS Journals Ltd 1997.

ABSTRACT: In order to assess the relative contribution of the lung and the chest wall to the derangements of respiratory mechanics in chronic obstructive pulmonary disease (COPD) patients with acute ventilatory failure (AVF), we studied eight COPD patients undergoing controlled mechanical ventilation for AVF and nine normal subjects anaesthetized for surgery as a control group.

With the use of the interrupter technique together with the oesophageal balloon technique we measured: static lung and chest wall elastances ($E_{st,L}$ and $E_{st,w}$, respectively), maximum (RL_{max}), minimum (RL_{min}) and additional (ΔRL) lung resistances, additional chest wall resistance (ΔR_w) and, in the COPD group, total intrinsic positive end-expiratory pressure ($PEEP_{tot}$). Measurements were repeated at 0, 5, 10 and 15 cmH₂O of applied positive end-expiratory pressure (PEEP).

We found that, in the COPD group: 1) both $E_{st,w}$ and ΔR_w were higher than in the normal group; 2) RL_{max} was markedly increased due to an increase of both RL_{min} and ΔRL ; 3) even low levels of PEEP increased $PEEP_{tot}$; 4) PEEP did not reduce elastance or total resistance of either the lung or the chest wall.

We conclude that chest wall mechanics are abnormal in chronic obstructive pulmonary disease patients with acute ventilatory failure undergoing controlled mechanical ventilation and that positive end-expiratory pressure does not seem to be effective in reducing either elastance or resistance of the lung or chest wall.

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The mechanical properties of the total respiratory system in patients with acute exacerbation of chronic obstructive pulmonary disease (COPD) have been extensively investigated, reporting an increase in respiratory resistance as a hallmark [1, 2]. However, few studies evaluated the relative contribution of the lung and the chest wall to total respiratory system mechanics in COPD patients with acute ventilatory failure (AVF). POLESE *et al.* [3] found that, in this condition, the alterations of respiratory mechanics are essentially due to the lung rather than to the chest wall. However, KATZ *et al.* [4] suggested that, at least in some mechanically ventilated patients with acute respiratory failure, chest wall mechanics may be abnormal, and, more recently, an unexpected alteration of chest wall mechanical properties has been reported in patients with adult respiratory distress syndrome [5].

The aim of this study was to further elucidate the alterations of lung and chest wall mechanics during acute exacerbation of COPD requiring mechanical ventilation (MV). We have measured inspiratory resistance and static elastance of the lung and chest wall ($E_{st,L}$ and $E_{st,w}$, respectively) in a selected group of COPD patients with AVF, and compared the results with those obtained in a group of normal anaesthetized subjects. Furthermore, since the use of positive end-expiratory pressure (PEEP) in COPD patients undergoing controlled mechanical ven-

tilation is still controversial [2, 6], we investigated the early effects of acute changes of PEEP upon partitioned respiratory mechanics.

Materials and methods

Study subjects

Two groups of subjects were studied: anaesthetized patients (normal subjects) and COPD patients.

Normal subjects. Nine control subjects (four females, five males) scheduled to undergo elective surgery entered this group. They were nonsmokers and had neither clinical nor radiological evidence of chronic lung disease or chronic heart failure; the mean age was 48 ± 12 yrs, weight 62 ± 7 kg, and height 161 ± 5 cm. Patients received diazepam ($0.14 \text{ mg} \cdot \text{kg}^{-1}$) 30–45 min before the scheduled surgery time, as pre-anaesthetic medication. Anaesthesia was induced with thiopental ($5 \text{ mg} \cdot \text{kg}^{-1}$) and succinylcholine ($1 \text{ mg} \cdot \text{kg}^{-1}$) was given to facilitate orotracheal intubation. Patients were then maintained in air supplemented with oxygen (40% O₂), fentanyl ($2\text{--}3 \text{ } \mu\text{g} \cdot \text{kg}^{-1}$) and droperidol ($0.1 \text{ mg} \cdot \text{kg}^{-1}$) boluses repeated every 30 min, and paralyzed with pancuronium bromide (0.08

mg·kg⁻¹). The patients were transorally intubated with an endotracheal tube (7–8 mm internal diameter (ID)) and ventilated with a Siemens Servo 900 C (Siemens, Elema AB, Berlin, Germany) mechanical ventilator, in volume control mode with constant inspiratory flow (table 1).

COPD patients. Eight consecutive patients (three females, five males) admitted to the Intensive Care Unit (ICU) of the University Hospital of Monza, Milan, for acute exacerbation of COPD were studied. The mean age was 61±14 yrs, weight 67±13 kg, height 165±9 cm and duration of intubation at the time of the study 3±3.7 days. The diagnosis of COPD was confirmed by history, physical examination, and chest radiography; pulmonary function tests during a period of clinical stability prior to the study were available in six of the eight patients, their mean±SD forced expiratory volume in one second was 0.68±0.23 L and forced vital capacity 1.34±0.58 L. Chest radiographs taken the day of the study were evaluated by an expert radiologist for the presence of pulmonary infiltrates, pleural effusion and signs of pulmonary oedema. Pulmonary infiltrates were present in four of the eight patients. Unilateral pleural effusions were present in three patients. With reference to a four grade scale (slight, mild, moderate, severe), two were classified as showing slight and one mild pleural effusions. No signs of either interstitial or alveolar pulmonary oedema were detected. In six of the eight patients, in whom a Swan-Ganz catheter had been inserted by the attending physician, pulmonary wedge pressure was 1.5±0.3 kPa (11±2 mmHg) (range 0.9–1.9 kPa (7–14 mmHg)). None of our patients had a history of heart disease; though one was being treated for essential hypertension. Patients were sedated with fentanyl (2–3 µg·kg⁻¹·h⁻¹) and paralyzed with pancuronium bromide boluses (0.06 mg·kg⁻¹). Seven of the eight patients were receiving aminophylline infusion (0.45–0.6 mg·min⁻¹), five methylprednisolone (2 mg·kg⁻¹·day⁻¹ in four doses) and six salbutamol (5–20 µg·min⁻¹) at the time of the study. Seven patients were nasotracheally intubated with a cuffed endotracheal tube (7–8.5 mm) and one had a tracheostomy cannula (9 mm ID). All patients were ventilated with a Siemens Servo 900 C mechanical ventilator, in volume control mode with constant inspiratory flow (table 1).

Baseline ventilatory parameters and gas exchange, before the study, are reported in table 1.

Study design

In both groups, the elastic and flow resistive properties of lung and chest wall were measured at different PEEP levels. Except for changes in applied PEEP the ventilatory parameters, that had been previously set by the attending physician, were kept constant throughout the experiment. PEEP levels of 0, 5, 10 and 15 cmH₂O were applied in random order and maintained for at least 5 min before taking measurements. The entire protocol took 40–50 min in both groups. In all subjects the electrocardiogram, cardiac frequency and arterial oxygen saturation were continuously monitored throughout the study. In the COPD group arterial and central venous pressure were also continuously monitored, whereas in

Table 1. – Baseline ventilatory parameters and arterial blood gases in normal subjects and in patients with chronic obstructive pulmonary disease (COPD)

	Normal	COPD
V _T L	0.59±0.1	0.62±0.1
f _R bpm	13.8±0.4	13.9±2.2
t _I s	1.04±0.05	0.98±0.17
V _I L·s ⁻¹	0.56±0.08	0.65±0.16
PEEP cmH ₂ O	-	4.6±3.9
F _I O ₂	0.4±0.04	0.5±0.1
P _a O ₂ mmHg	171±51	85.3±16.1
P _a CO ₂ mmHg	37.0±2.2	55.2±10.3
pH	7.41±0.04	7.41±0.06

Values are expressed as mean±SD. V_T: tidal volume; f_R: respiratory frequency; bpm: beats per minute; t_I: inspiratory time; V_I: inspiratory flow; PEEP: positive end-expiratory pressure (PEEP set by the attending physician before entry into the study); F_IO₂: inspired oxygen fraction; P_aO₂: arterial oxygen pressure; P_aCO₂: arterial carbon dioxide pressure.

the normal group arterial pressure was measured intermittently and noninvasively. We were able to complete the study protocol in all patients, without significant adverse cardiovascular effects. A physician not involved in the study was always present to provide care for the patients.

The study was approved by the institutional ethics committee and informed consent was obtained from the patients or from their next of kin before entry into the study.

Physiological measurements

Gas flow (V') was measured with a heated pneumotachograph (Fleisch no. 2; Fleisch, Lausanne, Switzerland), placed between the Y-piece of the ventilator and the artificial airway and connected to a Validyne MP 45-1 differential pressure transducer (Validyne Corp., Northridge, CA., USA). The pneumotachograph was calibrated with the experimental gas mixture, and its response was linear over the experimental range of flows. Volume was determined by digital integration of the flow signal.

Airway pressure (P_{aw}) was measured at the proximal end of the endotracheal tube or tracheostomy cannula by means of a polyethylene tubing (2 mm ID, 100 cm long) connected to a Bentley Trantec pressure transducer (Bentley Laboratories, Irvine, CA, USA). Oesophageal pressure (P_{oes}) was measured with a similar transducer connected through a polyethylene catheter (2 mm ID, 100 cm long) to a thin-walled latex oesophageal balloon (Bicore, Irvine, CA, USA), filled with approximately 1 mL of air. The validity of P_{oes} measurements was assessed with the "occlusion test" method [7]. In the normal group after the effect of succinylcholine had ceased, the occlusion test was performed to correctly position the oesophageal balloon and pancuronium bromide was then administered; in the COPD group the occlusion test was performed immediately before paralysis. With this recording system, P_{aw} and P_{oes} measurements were not affected by phase shift or alteration in amplitude up to 20 Hz. Flow and pressure signals were recorded on a four channel pen recorder (Battaglia

Rangoni, Bologna, Italy) and processed *via* an analogue to digital converter (100 Hz sampling rate) by an IBM personal computer (IBM, Armonk, NY, USA) for storage and calculations.

The pressure-flow relationship of the artificial airway was determined *in vitro* with the same gas mixture used during the *in vivo* experiments. These relationships were then used to estimate the resistive pressure drop across the endotracheal tube or tracheostomy cannula for any given flow during tests. This method has been extensively described and validated by BEHRAKIS *et al.* [8]. Subjects were connected to the ventilator by standard adult low-compliance tubing (2 cm ID, 110 cm long) and the humidifier was removed during the experiments in order to reduce the effects of resistance and compliance of the system upon physiological measurements.

Respiratory mechanics were measured using the end-inspiratory occlusion (EIO) technique during constant flow inflation [9] and the end-expiratory occlusion (EEO) method [10]. The oesophageal balloon technique allowed partitioning of total respiratory system mechanics into their lung and chest wall components [3, 11].

As shown in figure 1, the EIO was followed by an immediate drop in P_{aw} from a maximum value ($P_{aw,max}$) to a lower, zero flow, value ($P_{aw,1}$), and then by a slow decay to a plateau ($P_{aw,2}$); on the P_{oes} tracing, only a maximum ($P_{oes,max}$) and a plateau ($P_{oes,2}$) value were clearly identified and no rapid decrease was evident following airway occlusion (*i.e.* $P_{oes,1}$ could not be identified) in line with what has already been reported by

other authors [5, 11, 12]. $P_{aw,max}$ was corrected for the resistive pressure drop due to the artificial airway, as described above, and the corrected value was used for all calculations involving $P_{aw,max}$. $P_{aw,1}$ was measured by back extrapolation of a computer fitted curve to the time corresponding to $P_{aw,max}$. Measurements of $P_{aw,2}$ and $P_{oes,2}$ were taken 4 s after the onset of the EIO. We were thus able to compute:

$$\begin{aligned} \text{minimum lung resistance } (R_{L,min}) &= (P_{aw,max} - P_{aw,1}) / V' \\ \text{additional lung resistance } (\Delta RL) &= ((P_{aw,1} - P_{oes,max}) - \\ &\quad (P_{aw,2} - P_{oes,2})) / V' \\ \text{maximum lung resistance } (R_{L,max}) &= ((P_{aw,max} - P_{oes,max}) - \\ &\quad (P_{aw,2} - P_{oes,2})) / V' = R_{L,min} + \Delta RL \end{aligned}$$

where V' is the gas flow immediately preceding the EIO.

Values of $R_{L,min}$ were corrected for the closing time of the Servo 900C ventilator valve as previously described [13]. Since no $P_{oes,1}$ value could be clearly identified in either normal or COPD subjects, it follows that we were not able to detect any appreciable purely ohmic chest wall resistance. This implies that:

$$\text{chest wall resistance } R_{w,max} = \Delta R_w = (P_{oes,max} - P_{oes,2}) / V'$$

According to the analysis by BATES *et al.* [9], R_{min} represents airway resistance and is, therefore, also referred to as "ohmic" resistance, whereas additional resistance, denoted as ΔR , should reflect viscoelastic phenomena (*i.e.* stress relaxation) of thoracic tissues and/or gas redistribution due to time constant inequalities (*i.e.* pendel-luft) among alveolar units.

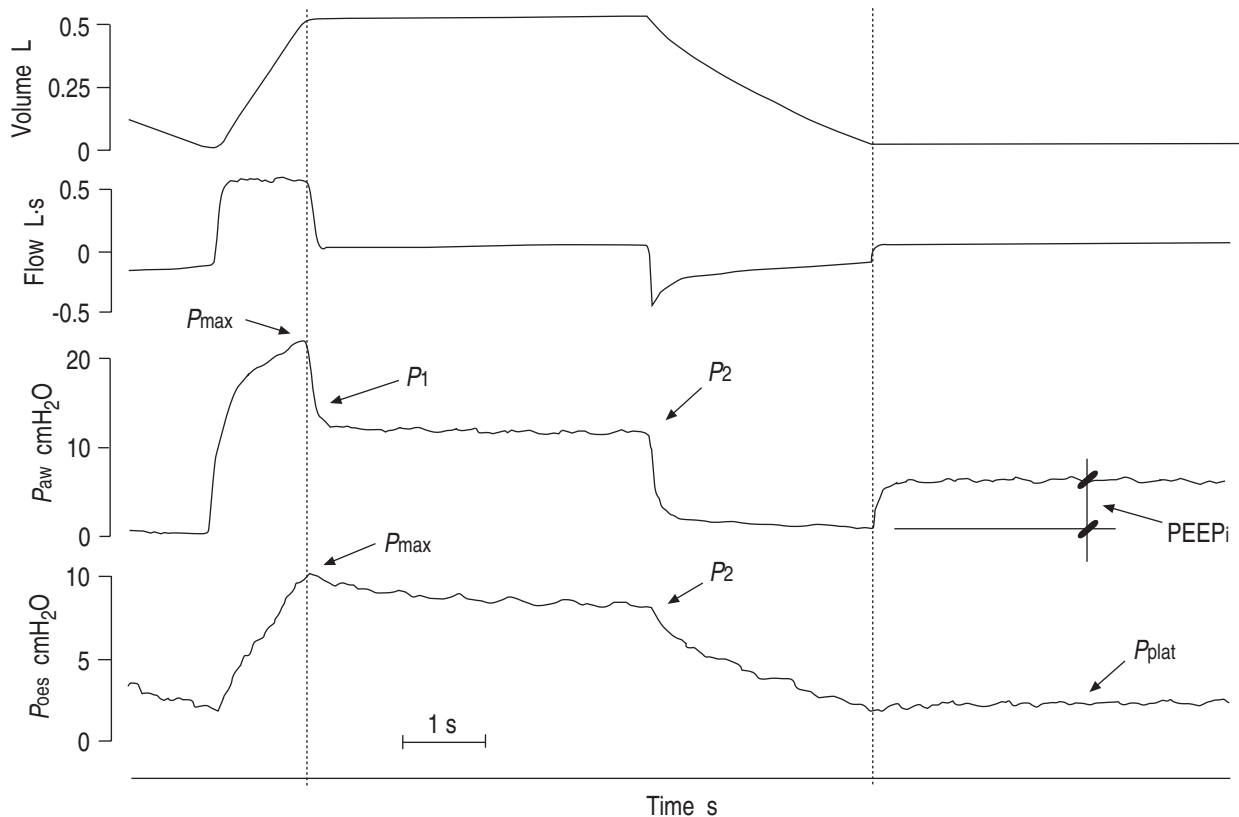


Fig. 1. — Tracings of volume (obtained by integration of the flow signal), flow, airway pressure (P_{aw}) and oesophageal pressure (P_{oes}) in a representative patient with chronic obstructive pulmonary disease (COPD) during an end inspiratory occlusion followed by an end expiratory occlusion. : indicate timing of occlusions. P_{max} : maximum value; P_1 : zero flow value; P_2 : plateau value; PEEP_i: intrinsic positive end-expiratory pressure is the static end-expiratory recoil pressure of the respiratory system; P_{plat} : plateau value of P_{oes} after end-expiratory occlusion. Values of $P_{aw,max}$, used for calculations were corrected for the resistive pressure drop due to the artificial airway. See text for further explanations.

An EEO from a COPD patient is shown in figure 1. Whereas in the normal subjects P_{aw} did not appreciably change after the occlusion, in the COPD patients there was a rise in P_{aw} following the occlusion towards a plateau value, which represents the static end-expiratory recoil pressure of the respiratory system, and that has been referred to as intrinsic PEEP (PEEP_i) [1], auto-PEEP [2] or occult PEEP [10]. All of our COPD patients exhibited a PEEP_i. We will henceforth denote the absolute postocclusion plateau P_{aw} value as PEEP_{tot} and the difference between PEEP_{tot} and the preocclusion end-expiratory P_{aw} value as PEEP_i. On the P_{oes} tracing, the postocclusion plateau P_{oes} pressure ($P_{oes,plat}$) was used to compute elastances.

$E_{st,L}$ and $E_{st,w}$ were calculated as follows:

$$E_{st,L} = ((P_{aw,2} - P_{oes,2}) - (PEEP_{tot} - P_{oes,plat})) / V_{T,I}$$

$$E_{st,w} = (P_{oes,2} - P_{oes,plat}) / V_{T,I}$$

where $V_{T,I}$ is inspiratory tidal volume.

Statistical analysis

Values are expressed as mean \pm SEM unless otherwise specified. The study was planned according to a split-plot experimental design in which each patient represented a randomized block and analysis of variance (ANOVA) allowed evaluation of the global effect of disease, of the effect of PEEP and of the eventual interaction between groups and PEEP [14]. Only when ANOVA revealed significant overall differences between the two groups, were further comparisons between selected means from the two groups performed by Student's t-test for unpaired data. Zero end-expiratory pressure (ZEEP) was arbitrarily chosen for these comparisons, and differences at higher PEEP levels were tested only when differences at ZEEP were not statistically significant, despite significant overall differences between the two groups as revealed by ANOVA. When a significant interaction between groups and PEEP was detected, the effect of PEEP was assessed separately in the COPD and normal groups by two-way ANOVA [14]. Student's t-test for paired data was used for within group comparisons between different levels of PEEP. A p-value of less than 0.05 was considered significant.

Results

Elastances of the lung and chest wall are shown in table 2. At ZEEP, $E_{st,w}$ was significantly higher in patients with COPD than in the normal subjects ($p < 0.01$). Furthermore, PEEP decreased $E_{st,w}$ in the normal group ($p < 0.05$), whereas it did not significantly affect $E_{st,w}$ in the COPD group. $E_{st,L}$ did not differ between the two groups and it increased with PEEP in both COPD and normal subjects ($p < 0.05$) with no significant interaction between groups and PEEP.

Resistances of the lung and chest wall are shown in table 3. At ZEEP, RL_{max} was markedly elevated in patients with COPD compared to the normal subjects ($p < 0.01$). This increase in RL_{max} was due mainly to higher RL_{min} ($p < 0.01$) but also to an increased ΔRL

Table 2. – Static lung and chest wall elastance ($E_{st,L}$ and $E_{st,w}$, respectively) in normal subjects and in patients with chronic obstructive pulmonary disease (COPD)

	PEEP cmH ₂ O			
	0	5	10	15
$E_{st,L}$ cmH ₂ O·L ⁻¹				
Normal*	8.7 \pm 0.5	9.5 \pm 0.5	9.6 \pm 0.5	9.7 \pm 0.6
COPD*	9.2 \pm 2.0	9.7 \pm 2.0	10.3 \pm 2.6	12.6 \pm 2.9
$E_{st,w}$ cmH ₂ O·L ⁻¹ †‡				
Normal*	6.2 \pm 0.3	4.5 \pm 0.5	4.2 \pm 0.4	3.9 \pm 0.5
COPD	8.9 \pm 0.9§	8.7 \pm 0.8	8.6 \pm 0.6	9.4 \pm 1.2

Values are expressed as mean \pm SEM. PEEP: positive end-expiratory pressure. *: Significantly different between PEEP 0, 5, 10 and 15 cmH₂O ($p < 0.05$); †: significant interaction between groups and PEEP ($p < 0.05$); ‡: significantly different between COPD and Normal ($p < 0.01$); §: significantly different from the corresponding value of the normal group ($p < 0.01$).

Table 3. – Lung and chest wall resistances in normal subjects and in patients with COPD

	PEEP cmH ₂ O			
	0	5	10	15
RL_{max} cmH ₂ O·L ⁻¹ ·s ⁺				
Normal	3.2 \pm 0.4	2.7 \pm 0.3	2.5 \pm 0.2	2.3 \pm 0.3
COPD	17.6 \pm 2.9**	18.1 \pm 3.2	17.8 \pm 3.0	17.2 \pm 2.9
RL_{min} cmH ₂ O·L ⁻¹ ·s ^{††}				
Normal§	2.1 \pm 0.4	1.8 \pm 0.3	1.6 \pm 0.2	1.0 \pm 0.2
COPD§	11.5 \pm 1.8**	11.1 \pm 1.8	9.6 \pm 1.8	7.8 \pm 1.3
ΔRL cmH ₂ O·L ⁻¹ ·s ^{††}				
Normal	1.1 \pm 0.2	0.9 \pm 0.2	0.9 \pm 0.2	1.2 \pm 0.4
COPD§	6.1 \pm 2.0*	7.0 \pm 2.1	8.2 \pm 2.0	9.4 \pm 2.2
ΔR_w cmH ₂ O·L ⁻¹ ·s ^{††}				
Normal	0.9 \pm 0.2	0.7 \pm 0.1	0.8 \pm 0.1	0.7 \pm 0.1
COPD§	1.4 \pm 0.2	1.6 \pm 0.3**	2.3 \pm 0.4**	3.0 \pm 0.6**

Values are expressed as mean \pm SEM. RL_{max} : maximum lung resistance; RL_{min} : minimum lung resistance; ΔRL : additional lung resistance; ΔR_w : additional chest wall resistance; †: significantly different between COPD and Normal ($p < 0.01$); ††: significantly different from the corresponding value of the normal group ($p < 0.01$); ‡: significant interaction between groups and PEEP ($p < 0.01$); §: significantly different between PEEP 0, 5, 10 and 15 cm H₂O ($p < 0.01$); *: significantly different from the corresponding value of the normal group ($p < 0.05$). For further definitions refer to table 1.

($p < 0.05$) compared with the normal group. PEEP did not affect RL_{max} in the COPD subjects, although it did cause a substantial redistribution between its components by increasing ΔRL ($p < 0.01$) and decreasing RL_{min} ($p < 0.01$). At ZEEP, ΔR_w was higher in the COPD than in the normal group, although it did not reach statistical significance ($p < 0.1$); split-plot analysis, however, revealed a significant interaction between groups and PEEP ($p < 0.01$), due to the fact that ΔR_w increased with PEEP in the COPD patients ($p < 0.01$), whereas it did not in the normal subjects. At PEEP 5 cmH₂O and higher, ΔR_w was significantly higher in the COPD than in the normal group ($p < 0.01$).

Values of PEEP_i and PEEP_{tot} in the COPD group are shown in figure 2. As applied PEEP was raised from 0 to 15 cm H₂O, PEEP_i significantly decreased ($p < 0.01$) and PEEP_{tot} increased ($p < 0.01$). PEEP_{tot} was significantly higher at 5 cmH₂O than at ZEEP (9.3 \pm 1.0 versus 7.5 \pm 1.2 cmH₂O, $p < 0.01$) the values at 10 and 15 cmH₂O

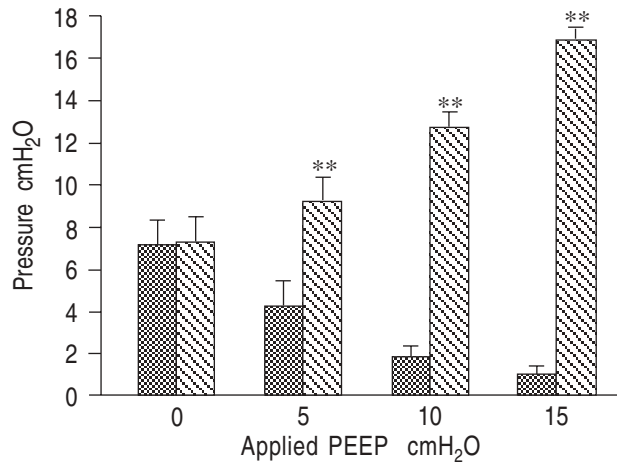


Fig. 2. — Intrinsic positive end-expiratory pressure (PEEP_i; ■) and postocclusion plateau airway pressure (PEEP_{tot}; ▨) in patients with chronic obstructive pulmonary disease at five levels of applied positive end-expiratory pressure (PEEP). Values are presented as mean ± SEM. **: p < 0.01 versus 0 cmH₂O applied PEEP.

were also significantly higher than ZEEP (p < 0.01). In two COPD patients, PEEP_i at ZEEP was lower than 5 cmH₂O. We then repeated the above analysis of PEEP_{tot} in only the six patients who had a PEEP_i at ZEEP greater than 5 cmH₂O, and found that PEEP_{tot} still increased significantly with PEEP, even at PEEP 5 cmH₂O (in these six patients PEEP_{tot} was 8.7 ± 1.1 cmH₂O at ZEEP versus 10.4 ± 1.0 cmH₂O at PEEP 5 cmH₂O, p < 0.01).

Discussion

The main results of this study are that: 1) the chest wall showed altered mechanical properties in our mechanically ventilated COPD patients, since both $E_{st,w}$ and ΔR_w were increased when compared with the normal subjects; 2) the lung showed higher total resistance in the COPD group due to an increase of both $R_{L,min}$ and ΔR_L ; 3) even low levels of PEEP increased PEEP_{tot} in the COPD group; 4) PEEP decreased $E_{st,w}$ in the normal subjects but not in the COPD patients and increased ΔR_w in the COPD but not in the normal group. Unexpectedly, PEEP did not decrease $R_{L,max}$ in the COPD group.

Comparison of COPD versus normal groups

Chest wall and lung elastance. $E_{st,w}$ was significantly higher in our COPD than in our normal subjects: this result was unexpected on the basis of previous experimental and clinical work that failed to show an increase in $E_{st,w}$ in either emphysematous animals [15] or subjects [12, 16, 17]. RANIERI *et al.* [18] reported even higher values of $E_{st,w}$ in COPD patients with AVF undergoing MV (10.7 ± 1.4 cmH₂O · L⁻¹). Therefore, it seems that an increased $E_{st,w}$ often adds to the derangements of respiratory mechanics that characterize exacerbated COPD. We may hypothesize that several factors contributed to our finding. Altered intestinal, especially colonic motility, eventually leading to colonic pseudo-obstruction, has been shown to occur with an unexpectedly high frequency in mechanically ventilated COPD patients with

AVF [19]; narcotic sedation, which is frequently used in the ICU, may further aggravate this condition [20]. The resulting abdominal distension might increase $E_{st,w}$ [21]. In four of our eight patients the attending physician reported intestinal hypomotility and abdominal distension as a relevant clinical problem. Narcotics, especially fentanyl, may also cause chest wall rigidity through a central effect [22]. It is unlikely, though, that this effect contributed to the observed abnormal $E_{st,w}$, since our patients were receiving neuromuscular blocking agents at the time of the study. In patients with AVF undergoing MV, the chest wall static mechanical properties might be also altered by tissue oedema [4]. Furthermore, a recent experimental study has demonstrated that volume infusion induces chest wall stiffening [23]; although extrapolation of these experimental data to the clinical setting must be taken with caution, it might be that fluid loading, which is frequent in ICU patients undergoing MV, contributed to chest wall stiffening. Finally, the presence of pleural effusions might have contributed to increased $E_{st,w}$ in three of our COPD patients. All these factors are peculiar to exacerbations of COPD so severe as to require MV, and this might explain the discrepancy between our results and those of previous investigators who did not observe an increase in $E_{st,w}$ in stable COPD subjects who volunteered to undergo anaesthesia paralysis for the purpose of the study [16, 17]. Although the effect of age cannot be completely discarded, we think that the relatively small difference in age between COPD and control groups did not substantially affect our results.

$E_{st,L}$ did not differ between our COPD and normal subjects and $E_{st,L}$ in our COPD group was only slightly higher than that reported by other authors in similar patients [3, 12], but much higher than that reported for stable COPD subjects (3.8 cmH₂O · L⁻¹) [17]. Several hypotheses may account for this result. Firstly, it is possible that the patients of VAN LITH *et al.* [17] had a greater degree of pulmonary emphysema. Secondly, this result may be attributed to the acute inflammatory lung process responsible for the exacerbation of COPD. Pulmonary infiltrates and pleural effusions, which were present in some of our patients were likely implicated in this increase of $E_{st,L}$ as compared to stable COPD. A recent experimental study has demonstrated that effusate loading of the pleural space may in fact result in increased lung elastance [24].

Lung and chest wall resistance. $R_{L,min}$, which represents airway resistance [9, 11] was significantly higher in COPD compared to normal subjects as expected.

The increase of $R_{L,max}$ in the COPD group, though, was due not only to a higher $R_{L,min}$ but also to a significantly higher ΔR_L . Since inspiratory time was quite similar in our two groups, this finding might reflect increased stress relaxation of lung tissues but also substantial time constant inhomogeneities among different alveolar units which are likely to exist in COPD patients [2, 25].

Similarly to other authors [5, 11, 12], we did not measure an appreciable ohmic (interrupter) resistance of the chest wall, as we did not identify $P_{oes,1}$. A different technical approach, such as the use of a more rapid airway shutter valve [26], may allow the recognition of $P_{oes,1}$.

However, the interrupter resistance of the chest wall that can be thus measured is rather small ($0.4 \text{ cmH}_2\text{O}\cdot\text{L}\cdot\text{s}$ [26]) and is, probably, not a significant portion of the high RL_{\min} observed in our COPD patients.

Chest wall resistance was higher in our COPD than in our normal group. GUERIN *et al.* [12] measured ΔR_w at different inspiratory flows and inflation volumes in 10 COPD patients and found consistently higher values than for the 18 normal subjects studied by D'ANGELO *et al.* [11], at the same age and volume. They suggested that the older age of the COPD subjects might partially explain the difference in ΔR_w . However, in our study there was only a relatively minor difference in age between COPD and control group and, in any case, the age gap between the two groups was much narrower than in the study of GUERIN *et al.* [12]. SHARP *et al.* [27] found an increased stress relaxation of the chest wall in patients with ankylosing spondylitis, suggesting that rheological properties of chest wall tissues may be abnormal in restrictive disease of the thorax. Our data seem to suggest that rheology of chest wall tissues is also altered in exacerbated obstructive pulmonary disease.

Effects of PEEP

PEEP_i in the COPD group. The presence of flow limitation during passive exhalation and of heterogeneous lung emptying was suggested, in our patients, by expiratory flow-volume curves that showed an upward concavity due to the presence of a flow spike at the beginning of exhalation followed by lower expiratory flows [28, 29]. A flow-volume curve, obtained during passive exhalation at ZEEP in one of our patients, is shown in figure 3. The interaction between PEEP_i and externally applied PEEP, and hence the effects that PEEP might exert upon respiratory mechanics in COPD, depend upon the underlying mechanism generating PEEP_i [2, 6]. If flow limitation is prevalent and homogeneous among different alveolar units, then PEEP values lower than airway pressure at the "choke point" (P_{crit}) should not

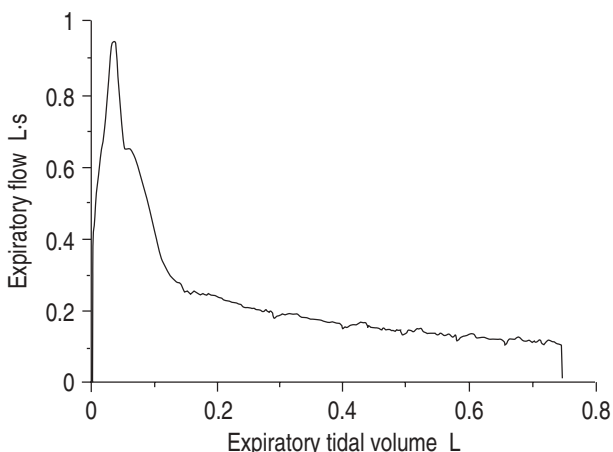


Fig. 3. — Expiratory flow volume curve during passive exhalation at zero end-expiratory pressure in a patient with chronic obstructive pulmonary disease. Notice the bowing towards the volume axis (*i.e.* upward concavity) especially during the first part of exhalation, which suggests the presence of flow limitation [26, 27].

affect expiratory flow and hence neither upstream alveolar pressure nor lung volume. This implies that PEEP_i is expected to decrease by an amount equal to applied PEEP, with the consequence that PEEP_{tot} should not change until applied PEEP equals P_{crit} . Data reported by RANIERI *et al.* [18] are consistent with the above reasoning and indicate 85% of PEEP_i on ZEEP as the PEEP threshold that does not affect PEEP_{tot} (P_{crit}). Our results are not as clear-cut as theirs, since even our low PEEP level of $5 \text{ cmH}_2\text{O}$, which represented only 70% of average PEEP_i on ZEEP ($7.1 \pm 1.2 \text{ cmH}_2\text{O}$), was associated with an increase in PEEP_{tot} from 7.5 ± 1.2 to $9.3 \pm 1.0 \text{ cmH}_2\text{O}$ (fig. 2). When data only from the patients with PEEP_i on ZEEP greater than $5 \text{ cmH}_2\text{O}$ were compared, PEEP_{tot} was still found to increase significantly from 8.7 ± 1.1 to $10.4 \pm 1.0 \text{ cmH}_2\text{O}$ with $5 \text{ cmH}_2\text{O}$ of applied PEEP. This implies that even low PEEP, below 85% of PEEP_i on ZEEP, induced further, although presumably small, hyperinflation in our patients. At present there is theoretical, experimental and clinical evidence to suggest that lung mechanics in obstructive disease is highly heterogeneous [2, 29]: open non-flow-limited alveolar units are likely to coexist with flow-limited and functionally closed ones. In such a nonhomogeneous lung model, even low levels of applied PEEP would cause further hyperinflation by increasing upstream alveolar pressure in both non-flow-limited units and in flow-limited units with the lowest P_{crit} once PEEP reverses dynamic airway collapse.

Although we wished to investigate the effects of PEEP on respiratory mechanics, we can speculate that PEEP might have affected gas exchange. Moderate levels of PEEP can lead to improvements in gas exchange and decreases in the ventilation-perfusion mismatch, in COPD patients [30].

Chest wall and lung elastance. The progressive decrease in $E_{\text{st},w}$ with PEEP in our normal individuals could have been anticipated on the basis of the chest wall V-P curve which shows a progressively increasing slope over the whole vital capacity range [31]. In contrast, PEEP did not significantly modify $E_{\text{st},w}$ in our COPD patients, although average $E_{\text{st},w}$ increased slightly at high PEEP. Information on the chest wall V-P curve in COPD patients is still sparse. SHARP *et al.* [16] found that, in emphysema, V-P curves of the thorax remained linear up to volumes higher than predicted total lung capacity. Their chest wall mechanics data, however, were obtained from stable COPD patients. Since we did not measure end-expiratory lung volume, we were not able to draw V-P curves in our patients. However, this was done in a very recent study by RANIERI *et al.* [32] in which the authors found that COPD patients undergoing MV for AVF showed a downward concave chest wall V-P curve, in marked contrast to what happens in normal subjects [31]. The discrepancy in the behaviour of $E_{\text{st},w}$ with PEEP between normal and COPD subjects, found in the present study, is consistent with their findings.

$E_{\text{st},L}$ increased with PEEP in both groups as expected from the shape of the lung V-P curve [31, 33]. In our COPD group the largest increase of $E_{\text{st},L}$ was observed when PEEP was raised from 10 to $15 \text{ cmH}_2\text{O}$; that was presumably the pressure range in which relevant lung overdistension occurred.

Lung and chest wall resistances. A decrease of RL_{\min} with PEEP, observed in both our groups, was expected from the relationship between lung volume and airway resistance [34].

PELOSI *et al.* [5] and D'ANGELO *et al.* [35] reported no change in either ΔRL or ΔR_w when moderate PEEP levels (10 and 7.8 cmH₂O, respectively) were applied to normal anaesthetized paralyzed subjects, in line with the results of the present study. In contrast, both ΔRL and ΔR_w increased with PEEP in our COPD subjects. It may be hypothesized that, in the mechanically heterogeneous COPD lung, PEEP enhances time constant inequalities among different alveolar units by dilating open, non-flow-limited alveolar pathways on one hand, while, on the other hand, recruiting previously flow-limited or functionally closed ones, which were virtually excluded from ventilation, to participate more actively in inspiratory VT distribution. In this respect it should be noted that PEEP might actually result in a more even distribution of ventilation in COPD patients [2, 36], and that the increased additional resistance at higher PEEP levels might be due to the fact that a larger number of alveolar units with different time constants participate in ventilation. The increase of additional resistance with PEEP might also be due, at least in part, to enhanced stress relaxation. SHARP *et al.* [27] have shown that pressure losses due to stress relaxation increase considerably only when significant pulmonary hyperinflation occurs: this might have been the case in our COPD patients as suggested by the increase of $E_{st,L}$ at high PEEP. Unfortunately, the interrupter technique does not allow differentiation between pendelluft and stress relaxation [9]. Independent of the underlying mechanism, the increase of ARL with PEEP offset the concomitant decrease of RL_{\min} , with the consequence that PEEP did not prove effective in reducing total inspiratory lung resistance.

In conclusion, we have shown that, in patients with chronic obstructive pulmonary disease undergoing controlled mechanical ventilation for acute ventilatory failure, the chest wall may show markedly altered mechanical properties that add to the widely reported increase of lung resistance. Furthermore, positive end-expiratory pressure does not seem to acutely reduce total resistance or elastance of either the chest wall or the lung in these patients, at least during controlled mechanical ventilation.

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