# Lung and chest wall mechanics in mechanically ventilated COPD patients

C. GUÉRIN, M.-L. COUSSA, N. T. EISSA, C. CORBEIL, M. CHASSÉ, J. BRAIDY, N. MATAR, AND J. MILIC-EMILI

*Respiratory Division, Hôpital Saint-Luc, Université de Montréal, Montreal, Quebec H2X 3J4; and Meakins-Christie Laboratories, McGill University, Montreal, Quebec H2X 2P2, Canada*

GUÉRIN, C., M.-L. COUSSA, N. T. EISSA, C. CORBEIL, M. CHASSÉ, J. BRAIDY, N. MATAR, AND J. MILIC-EMILI. *Lung and chest wall mechanics in mechanically ventilated COPD patients.* J. Appl. Physiol. 74(4): 1570–1580, 1993.—By use of the technique of rapid airway occlusion, the effects of inspiratory flow, volume, and time on lung and chest wall mechanics were investigated in 10 chronic obstructive pulmonary disease (COPD) patients mechanically ventilated for acute respiratory failure. We measured the interrupter resistance (Rint), which in humans reflects airway resistance; the additional resistances due to time constant inequality and viscoelastic pressure dissipations within the lungs (ΔRL) and the chest wall; and the static and dynamic elastances of lung and chest wall. We observed that *1*) static elastances of lung and chest wall in COPD patients were similar to those of normal subjects; *2*) Rint of the lung was markedly increased and flow dependent in COPD patients, whereas Rint of the chest wall was negligible as in normal subjects; and *3*) in COPD patients, ΔRL was markedly increased at all inflation flows and volumes, reflecting increased time constant inequalities within the lungs and/or altered viscoelastic behavior. The results imply increased dynamic work due to Rint and ΔRL and marked time dependency of pulmonary resistance and elastance in COPD patients.

flow resistance; static and dynamic elastances; interrupter resistance; viscoelastic properties; frequency dependence; spring-and-dashpot model of lung and chest wall

CHRONIC OBSTRUCTIVE PULMONARY disease (COPD) is characterized by an increase in airway resistance (Raw) and a loss of lung elastic recoil. As a result, airflow limitation develops, leading to the presence of an intrinsic positive end-expiratory pressure (PEEPi) and dynamic pulmonary hyperinflation (16, 28, 29). Although acute respiratory failure requiring mechanical ventilation is a frequent event in COPD patients, there are relatively few reports dealing with the mechanical properties of the respiratory system in this situation. Using the technique of rapid airway occlusion during constant-flow ($\dot{V}$) inflation, Bernasconi et al. (7) and Broseghini et al. (9) measured *1*) the total resistance of the respiratory system (Rrs); *2*) the interrupter resistance of the respiratory system (Rint,rs), which in humans reflects Raw (11, 17); and *3*) the difference between Rrs and Rint,rs, namely, the additional resistance (ΔRrs), which reflects dynamic pressure dissipations due to viscoelastic properties of the thoracic tissues and/or time constant inequality within the lungs (2, 11, 26). These measurements, which were carried out at a single baseline inflation $\dot{V}$ and volume ($\Delta V$), showed that Raw, ΔRrs, and Rrs were markedly increased in COPD patients with acute respiratory failure. Tantucci et al. (32) extended these observations by determining the V and $\Delta V$ dependence of Rrs in mechanically ventilated COPD patients. However, they did not partition between lung and chest wall mechanics. In the present study on mechanically ventilated COPD patients, we used the rapid airway occlusion method combined with measurement of esophageal pressure to assess the effects of inflation $\dot{V}$, $\Delta V$, and time on the mechanical properties of the lungs and chest wall.

## METHODS

Ten COPD patients (7 men) in acute respiratory failure requiring orotracheal intubation and mechanical ventilation for exacerbation of their disease, due to infection of the upper respiratory tract, were investigated in a semirecumbent position. Their anthropometric characteristics are given in Table 1. The mean duration of mechanical ventilation before the investigation was 4.4 ± 1.4 (SE) days. The diagnosis of COPD was made according to clinical history, chest X rays, and pulmonary function tests. The mean values of forced expiratory volume in 1 s, forced vital capacity, and the ratio of forced expiratory volume in 1 s to forced vital capacity before admission to the intensive care unit were 1.04 ± 0.30 liters (47 ± 11% of predicted), 2.37 ± 0.47 liters (71 ± 12% of predicted), and 0.50 ± 0.03, respectively. The predicted values were those of Morris et al. (22). The investigation was approved by the Institutional Ethics Committee, and informed consent was obtained from each patient or next of kin.

The patients were intubated (cuffed-endotracheal tube of 8 or 8.5 mm ID and 27 cm length; Sheridan, New York, NY) and mechanically ventilated (900C servo ventilator, Siemens-Elema). During the study, all patients were sedated with fentanyl (2–3 μg/kg) and paralyzed with pancuronium bromide (0.1–0.2 mg/kg). The baseline ventilatory settings, which were kept constant throughout the experiment, are listed in Table 1. The respiratory frequency was 12.5 ± 0.6 breaths/min, and the inspiratory-to-total cycle duration ratio (TI/TT) was 0.19 ± 0.01. All measurements were done with zero applied end-expiratory pressure. Flow was measured with a

TABLE 1. *Anthropometric characteristics and baseline ventilatory settings of 10 COPD patients*

| | Age, yr | Height, cm | Weight, kg | $FI_{O_2}$ | ΔV, liter | $\dot{V}$, l/s | TI, s | TT, s |
|---|---|---|---|---|---|---|---|---|
| Mean ± SE | 73±2.8 | 164±3.4 | 61±4.4 | 0.41±0.03 | 0.73±0.02 | 0.80±0.03 | 0.92±0.01 | 4.90±0.24 |

COPD, chronic obstructive pulmonary disease; $FI_{O_2}$, fraction of inspired oxygen; ΔV, tidal volume; $\dot{V}$, inspiratory flow; TI, inspiratory time; TT, total duration of respiratory cycle.

heated pneumotachograph (no. 2, Fleisch, Lausanne, Switzerland) inserted between the endotracheal tube and the Y-piece of the ventilator. The pressure drop across the two ports of the pneumotachograph was measured with a differential solid-state pressure transducer (163PC01D36 ±12.7 $cmH_2O$, Micro switch, Freeport, IL). The response of the pneumotachograph was linear over the experimental range of $\dot{V}$. ΔV was obtained by numerical integration of the $\dot{V}$ signal (model 8815A; Hewlett-Packard, Andover, MA). Pressure at the airway opening (Pao) was measured proximal to the endotracheal tube with a solid-state pressure transducer (143PC03D ±176 $cmH_2O$, Micro switch). Tracheal pressure (Ptr) was measured with a polyethylene catheter (1.5 mm ID) with multiple side holes and an occluded end hole, placed 2–3 cm past the carinal end of the endotracheal tube, and connected to a solid-state pressure transducer (143PC03D ±176 $cmH_2O$, Micro switch). Esophageal pressure (Pes) was measured with a thin-walled latex balloon (10 cm long, 3 cm in circumference) sealed over one end of a polyethylene catheter (2 mm ID, 120 cm long), inflated with 0.6–1.0 ml of air, and connected to a solid-state pressure transducer (143PC03D ±176 $cmH_2O$, Micro switch). The validity of Pes was assessed with the occlusion test immediately before the paralysis (5). With the system used to measure Pao, Ptr, and Pes, there was no appreciable shift or alteration in amplitude ≤20 Hz. The equipment dead space (not including the endotracheal tube) was 150 ml. All variables were recorded on an eight-channel pen recorder (7718A; Hewlett-Packard, Cupertino, CA) at a paper speed of 10 mm/s and on an IBM-compatible personal computer by a 12-bit analog-to-digital board at a sample frequency of 200 Hz for subsequent data analysis. In this analysis ΔV was obtained by digital integration of the $\dot{V}$ signal. Special care was taken to avoid gas leaks in the equipment and around the tracheal cuff. To reduce the effects of the compliance of the system connecting the subjects to the ventilator on the mechanics measurements (12), a single length of standard low-compliance adult tubing was used (2 cm ID, 60 cm long) and the humidifier was omitted from the inspiratory line. The compliance of the system connecting the subjects to the ventilator was 0.4 ml/$cmH_2O$.

Arterial blood gases were measured with a blood gas analyzer (ABL 330; Radiometer, Copenhagen, Denmark). During the experiment, arterial $P_{O_2}$ averaged 110 ± 3 Torr, arterial $P_{CO_2}$ averaged 43 ± 1.2 Torr, and pH was 7.45 ± 0.005. The electrocardiogram, heart rate, systemic arterial blood pressure, and arterial $O_2$ saturation (model 11A, Biox, Mississauga, Ontario, Canada) were continuously monitored. During the study a physician not involved in the experiment was always present to provide for patient care.

*Procedure and Data Analysis*

Respiratory mechanics were assessed by the constant-$\dot{V}$ rapid airway occlusion method previously described in detail (10, 11). Two sets of experiments were done in each subject. *1)* Iso-ΔV experiment: while baseline ΔV was kept constant, $\dot{V}$ was varied randomly from 0.2 to 1.2 l/s for single test breaths by regulating TI with the appropriate knob of the ventilator. *2)* Iso-$\dot{V}$ experiment: while baseline $\dot{V}$ was kept constant, ΔV was changed randomly from 0.2 to 0.7 liter for single test breaths by changing the frequency of the ventilator. The end-inspiratory occlusion, obtained by pressing the end-inspiratory hold knob on the ventilator, lasted 5–6 s. Before each test breath an end-expiratory occlusion was performed by pressing the end-expiratory hold knob on the ventilator. This allowed us to quantify PEEPi and to start the test breath from a fixed static elastic equilibrium condition. Because PEEPi implies dynamic pulmonary hyperinflation [i.e., that the end-expiratory lung volume during mechanical ventilation exceeds the relaxation volume of the respiratory system (Vr)], we also measured the difference between end-expiratory lung volume and Vr (here termed the change in functional residual capacity) by reducing the ventilator frequency to its lowest value during baseline expiration, thus prolonging expiratory duration to allow the patient to exhale to Vr (12). Vr was achieved when expiratory flow became nil and end-expiratory occlusion resulted in no change in airway pressure (i.e., no PEEPi). After each test breath, the baseline ventilation was resumed until ΔV, $\dot{V}$, and pressures returned to their baseline values (usually in a few breaths). Each measurement was done twice.

After end-inspiratory airway occlusions, Ptr and Pao, but not Pes except in one patient (*patient 3*), exhibited an initial rapid drop [maximum pressure (Pmax) − pressure after first drop ($P_1$)] followed by a slow decay to an apparent plateau pressure ($P_2$) (Fig. 1). During this period, the contribution of reduction in pressure due to volume loss by continuing gas exchange should be negligible. Ptr, Pes, and transpulmonary pressures (PL) measured at 5 s were taken as the static end-inspiratory elastic recoil pressures of the respiratory system (Pst,rs), chest wall (Pst,w), and lung (Pst,L), respectively. By dividing tracheal values $Pmax,tr - P_2,tr$ and $Pmax,tr - P_1,tr$ by the $\dot{V}$ immediately preceding the occlusion, Rrs and Rint,rs were obtained. ΔRrs was calculated as the difference between Rrs and Rint,rs. By dividing the esophageal value $Pmax,es - P_2,es$ by the $\dot{V}$ preceding the occlusion, the total resistance of the chest wall (Rw) was obtained. Because Pes did not exhibit any immediate drop after end-inspiratory occlusion, except for *patient 3*, Rw represents the additional resistance of the chest wall (ΔRw). In *patient 3*, the interrupter resistance of the

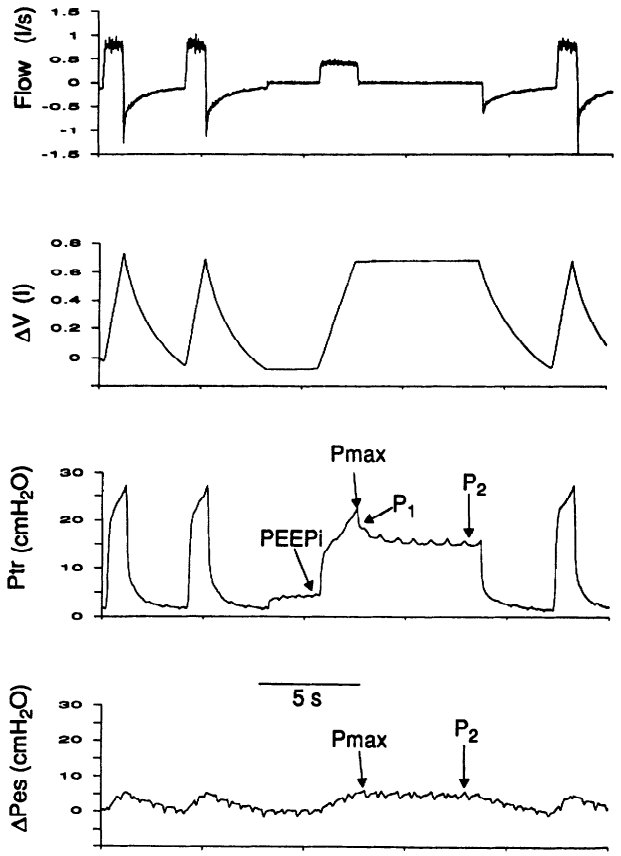


FIG. 1. Records of flow, volume ($\Delta V$), tracheal pressure (Ptr), and esophageal pressure ($\Delta Pes$) vs. time in chronic obstructive pulmonary disease (COPD) *patient 9*. Tracings show 2 baseline breaths followed by test breath comprising end-expiratory occlusion followed by end-inspiratory occlusion. In this test breath, inflation flow was decreased while inflation volume was kept at its baseline value (iso-$\Delta V$ experiment). PEEPi, intrinsic PEEP; Pmax, maximal pressures during lung inflation; $P_1$, immediate drop in tracheal pressure after airway occlusion; $P_2$, static end-inspiratory pressures. Note absence of immediate drop in $\Delta Pes$ after end-inspiratory occlusion.

chest wall (Rint,W) was obtained by dividing Pmax,es − $P_1$,es by the $\dot{V}$ preceding the end-inspiratory occlusion and $\Delta R_W$ was obtained by subtracting Rint,W from $R_W$. Total ($R_L$), interrupter (Rint,L), and additional ($\Delta R_L$) resistances of the lung were obtained by subtracting the corresponding values of the chest wall from those pertaining to the total respiratory system. In computation of Rint, the errors caused by the closing time of the ventilator valve were corrected as previously described (10). The static elastances of the lung (Est,L) and chest wall (Est,W) were computed by dividing the corresponding values of $P_2$ − PEEPi by $\Delta V$. Our values of PEEPi include a slightly positive end-expiratory pressure, ranging from 0.2 to 1.25 $cmH_2O$, due to the ventilator (29). The dynamic elastance of the lung (Edyn,L) was obtained by dividing the difference between the lung value $P_1$,L and the static end-expiratory $P_L$ by $\Delta V$ (29). The dynamic elastance of the chest wall (Edyn,W) was determined by dividing the difference between Pmax,es and the static end-expiratory Pes by $\Delta V$ in the nine patients whose Pes did not exhibit any immediate drop after end-inspiratory airway occlusion and by dividing $P_1$,es − static end-expiratory Pes by $\Delta V$ in *patient 3*, who exhibited an immediate drop in Pes after end-inspiratory airway occlusion.

*Model and Curve-Fitting*

Our data were analyzed in terms of the model of the respiratory system proposed by D'Angelo et al. (11) for humans. This model comprises three compartments in parallel (Fig. 2). The first is a dashpot representing Rint,L, which explains the initial fast pressure drop observed in $P_L$ immediately after the end-inspiratory occlusion. Using the alveolar capsule technique, Bates et al. (2) found that in dogs Rint,L reflected Raw, indicating that the pulmonary tissues did not exhibit any appreciable Newtonian resistance. According to Liistro et al. (17) this is also probably true in humans. Contrary to dogs (31) and cats (30), in normal anesthetized paralyzed humans there is no appreciable immediate drop in Pes after end-inspiratory occlusion, indicating an absence of Rint,W (11). With one exception (*patient 3*), this was also the case in the COPD patients of the present study. The second and third compartments of the model in Fig. 2 are Kelvin bodies, corresponding to the lung and chest wall. Each consists of a standard static elastance (Est) in parallel with a Maxwell body, i.e., a spring ($E_2$) and a dashpot ($R_2$) arranged serially. In normal anesthetized paralyzed subjects, $E_2$ and $R_2$ probably virtually entirely reflect the viscoelastic properties of the tissues of the lungs and chest wall (11).

During constant-$\dot{V}$ inflation, the model in Fig. 2 predicts that $\Delta R$ should increase with TI according to the following function (11)

$$\Delta R = R_2(1 - e^{-TI/\tau_2}) \quad (1)$$

where the viscoelastic time constant ($\tau_2$) = $R_2/E_2$.

Because during constant-$\dot{V}$ inflation TI = $\Delta V/\dot{V}$, *Eq. 1* can be rewritten (11)

$$\Delta R = R_2(1 - e^{-\Delta V/\dot{V}\tau_2}) \quad (2)$$

The model also predicts that during constant-$\dot{V}$ inflation the tension in the spring $E_2$ will increase the effective stiffness (elastance) of the system. The additional elastance ($\Delta E$) imposed by $E_2$ varies as a function of TI and inflation $\dot{V}$, according to the following functions (21)

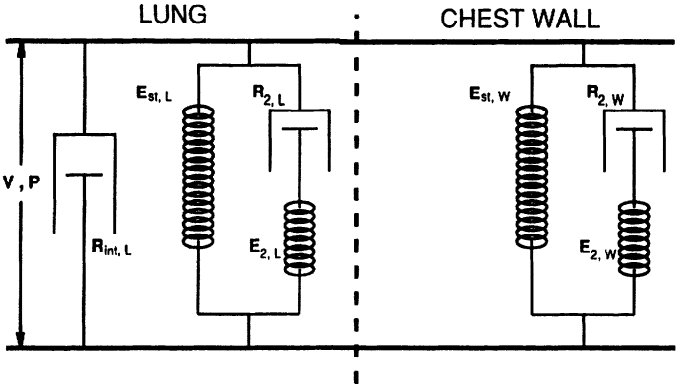


FIG. 2. Scheme of spring-and-dashpot model for interpretation of lung (L) and chest wall (W) mechanics during inflation flow interruption. Respiratory system consists of airway resistance (Rint,L) in parallel with 2 Kelvin bodies, corresponding to lung and chest wall. Each consists of standard static elastance (Est) in parallel with a Maxwell body, i.e., spring $E_2$ and dashpot $R_2$ arranged serially. $E_2$ and $R_2$ represent viscoelastic (stress adaptation) units. Distance between 2 horizontal bars is analogue of $\Delta V$, and tension between these bars is analogue of pressure at airway opening (P). [Modified from D'Angelo et al. (11).]

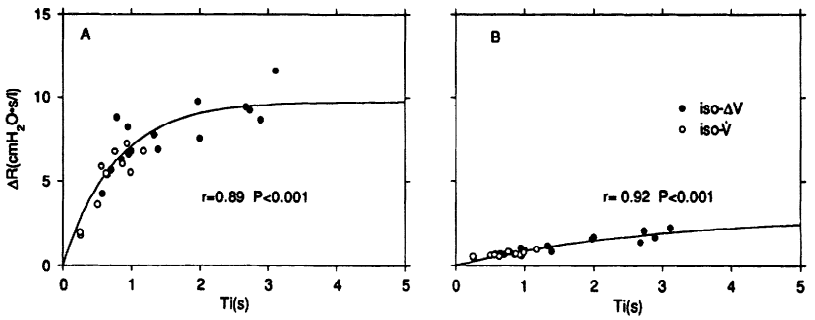


FIG. 3. Relationships of additional resistance (ΔR) to inspiratory time (TI) for lung (*A*) and chest wall (*B*) in COPD *patient 4*. Results were obtained in both iso-ΔV and iso-flow (V̇) experiments. Curves were computed according to *Eq. 1*.

$$\Delta E = R_2(1 - e^{-TI/\tau_2})/TI \quad (3)$$

$$\Delta E = R_2\dot{V}(1 - e^{-\Delta V/\dot{V}\tau_2})/\Delta V \quad (4)$$

*Equations 1* and *3* indicate that ΔR and ΔE are TI dependent.

In the present study, we could also fit *Eq. 1* to our experimental data of ΔRL and ΔRW as shown in Fig. 3 for a representative patient. In all patients, the relationships of both ΔRL and ΔRW with TI closely fit *Eq. 1* ($P < 0.001$). In line with previous results with normal subjects (11), there were no apparent differences between the individual iso-V̇ and iso-ΔV relationships for both ΔRL and ΔRW with TI. Accordingly, a single curve was fitted to the combined experimental points, and the parameters $R_2$ and $\tau_2$ of the lung and chest wall were thus determined. $E_2$ values of the lung and chest wall were computed as respective ratios $R_2/\tau_2$. As in normal subjects, ΔRW in our COPD patients is probably due virtually entirely to viscoelastic behavior of chest wall tissues. In contrast to normal subjects, however, ΔRL in COPD patients is likely to reflect to a major extent time constant inequalities within the lungs (pendelluft) (11). It should be noted that *Eqs. 1–4* apply not only to the viscoelastic model in Fig. 2 but also to a two-compartment model of the lung with unequal time constants (4).

### *Statistical Analysis*

Regression analysis was made using the least-squares method. The results of the 10 COPD patients and of 18 normal anesthetized paralyzed humans of D'Angelo et al. (11) were compared with use of Student's unpaired *t* test and two-way analysis of variance. $P < 0.05$ was accepted as statistically significant. Values are means ± SE.

## RESULTS

### *Rint*

As in the normal subjects, in the COPD patients Rint,L increased linearly with increasing V̇ according to

$$Rint,L = K_1 + K_2\dot{V} \quad (5)$$

where $K_1$ and $K_2$ are Rohrer's constants (Fig. 4*A*). The values of $K_1$ and $K_2$ were significantly higher in COPD patients (Table 2).

As shown in Fig. 4*B*, during constant-V̇ inflation there was a linear relationship between interrupter pulmonary conductance (Gint,L, the reciprocal of Rint,L) and ΔV

$$Gint,L = a' + b'\Delta V \quad (6)$$

where $a'$ and $b'$ are constants (11). The average values of $a'$ and $b'$ of the 10 COPD patients are given in Table 2 together with the corresponding values for normal subjects. The values of $a'$ and $b'$ were significantly lower in the COPD patients.

Except for *patient 3*, Pes did not exhibit any appreciable immediate drop after end-inspiratory occlusion (Fig. 1). In *patient 3*, Rint,W amounted to 2.84 $cmH_2O \cdot l^{-1} \cdot s$ at his baseline ventilatory settings (Table 1) and did not change significantly with either V̇ or ΔV. Thus, in most COPD patients, Rint,W appears to be negligible as in normal individuals (11).

### *ΔR*

Table 3 provides the average values of the "viscoelastic" constants for both lung and chest wall of 10 COPD patients and 18 normal subjects (11). $R_2$,L, $E_2$,L, $R_2$,W, and $\tau_2$,W were significantly higher in the COPD patients. In the COPD patients, the values of $R_2$ and $E_2$ were significantly higher for the lung than the chest wall ($P < 0.001$), whereas the opposite was true for $\tau_2$ ($P < 0.001$).

Figure 5 illustrates the average relationships of RL with V̇ (*A*) and ΔV (*B*) in 10 COPD patients and 18 normal subjects (11). In both conditions, the values of RL were significantly higher in the COPD patients. In both groups at constant ΔV, RL decreased progressively with increasing V̇, whereas at constant V̇, RL increased progressively with increasing ΔV.

Both under iso-ΔV and iso-V̇ conditions, the values of ΔRL were significantly higher in the COPD patients than

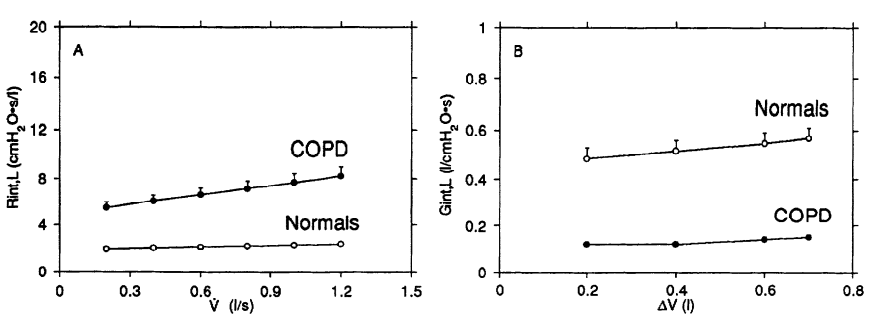


FIG. 4. Average relationships of interrupter resistance of lung (Rint,L) to V̇ at constant ΔV of 0.73 liter (*A*) and of interrupter conductance of lung (Gint,L) to ΔV at constant V̇ of 0.8 l/s (*B*) of 10 COPD patients and 18 normal subjects (11). Bars, SE when larger than symbols.

TABLE 2. *Values of $K_1$ and $K_2$ and of a′ and b′ of 10 COPD patients and 18 normal subjects*

| | COPD | Normal Subjects |
|---|---|---|
| $K_1$, $cmH_2O \cdot l^{-1} \cdot s$ | 5.03±0.45 | 1.85±0.13* |
| $K_2$, $cmH_2O \cdot l^{-2} \cdot s^2$ | 2.69±0.63 | 0.43±0.03* |
| $a'$, $l \cdot s^{-1} \cdot cmH_2O^{-1}$ | 0.11±0.01 | 0.46±0.04* |
| $b'$, $s^{-1} \cdot cmH_2O^{-1}$ | 0.06±0.02 | 0.15±0.02† |

Values are means ± SE. $K_1$ and $K_2$, constants from *Eq. 5*; $a'$ and $b'$, constants from *Eq. 6*. Values for normal subjects from D'Angelo et al. (11). * $P < 0.001$, † $P < 0.01$ between COPD and normal subjects.

in normal subjects (Fig. 6). At constant ΔV, in both groups ΔRL decreased with increasing V̇, whereas at constant V̇, ΔRL increased with increasing ΔV. In both COPD patients and normal subjects, the changes of RL (=ΔRL + Rint,L) with increasing V̇ or ΔV (Fig. 5) were less than the concomitant changes in ΔRL because the changes in Rint,L with V̇ and ΔV were in the opposite direction (Fig. 4).

Both under iso-ΔV and iso-V̇ conditions ΔRw was significantly higher in COPD patients than in normal subjects (Fig. 7). At constant ΔV, ΔRw significantly decreased with increasing V̇ in both groups, whereas at constant V̇ it increased with increasing ΔV.

### *Est and Edyn*

The average values of Est,L and Est,W of 10 COPD patients and 18 normal subjects (11) obtained during baseline mechanical ventilation are listed in Table 3. There were no significant differences between the two groups. As in normal subjects (11), in COPD patients neither Est,L nor Est,W correlated significantly with $R_2$, $E_2$, and $\tau_2$ of lung and chest wall. In both groups the values of Est,L and Est,W during the iso-ΔV experiment did not change significantly with V̇ (Fig. 8). By contrast, the values of Edyn,L and Edyn,W significantly increased with increasing V̇ in both groups (Fig. 8). In COPD patients, the relative increase of Edyn,L with increasing V̇ from 0.2 to 1.2 l/s amounted to 70 ± 12 vs. 21 ± 3% in normal subjects ($P < 0.001$), whereas that for Edyn,W was 59 ± 0 vs. 20 ± 2% ($P < 0.001$). The values of Edyn,L were significantly higher in COPD patients, whereas those of Edyn,W were not significantly different between the two groups over the entire experimental range of V̇.

In the iso-V̇ experiments, the values of Est,L and Est,W were not significantly different between COPD patients and normal subjects and did not vary with ΔV in either group (Fig. 9). By contrast, Edyn,L and Edyn,W decreased with increasing ΔV in both groups. The values of Edyn,L were significantly higher in COPD patients than in normal subjects, whereas the values of Edyn,W were not significantly different.

TABLE 3. *Values of Est and "viscoelastic" parameters of lung and chest wall of 10 COPD patients and 18 normal subjects*

| | Lung | | Chest Wall | |
|---|---|---|---|---|
| | COPD | Normal subjects | COPD | Normal subjects |
| Est, $cmH_2O/l$ | 7.69±0.78 | 8.15±0.36 | 5.20±0.68 | 6.26±0.28 |
| $R_2$, $cmH_2O \cdot l^{-1} \cdot s$ | 8.75±1.21 | 3.44±0.23* | 3.25±0.60 | 2.12±0.14† |
| $\tau_2$, s | 1.40±0.19 | 1.11±0.10 | 2.49±0.48 | 1.29±0.08† |
| $E_2$, $cmH_2O/l$ | 6.76±1.03 | 3.21±0.27* | 1.90±0.53 | 1.66±0.09 |

Values are means ± SE. Est, static elastance; $R_2$, $\tau_2$, $E_2$, "viscoelastic" resistance, time constant, and elastance, respectively, according to model in Fig. 2. Values for normal subjects from D'Angelo et al. (11). Values of Est pertain to baseline ΔV of present study (0.73 liter). * $P < 0.001$, † $P < 0.05$ between COPD and normal subjects.

## DISCUSSION

We analyzed our results in terms of the viscoelastic model in Fig. 2. Although this model has been found to provide a useful representation of the dynamic behavior of the respiratory system in normal humans (10, 11), it clearly should not be regarded as a complete and perfect representation of respiratory mechanics. This is particularly true in COPD patients in whom time constant inequality within the lung probably significantly contributes to the time dependency of pulmonary elastance and resistance. Obviously, more complicated models would describe respiratory dynamics more accurately but at the expense of more parameters, the values of which would have to be estimated and then interpreted. Such interpretation is difficult because the precise anatomic or functional components of the elements pertaining to the lung and chest wall tissues in Fig. 2 are poorly understood. Nevertheless, the model has served as a useful conceptual aid to understanding the effects of a flow interruption. Furthermore, although the precise nature of the constants $R_2$, $E_2$, and $\tau_2$ is not known, these constants together with *Eqs. 1–4* provide a good description of the TI dependency of the resistance and elastance of the lung and chest wall. In this connection it should be noted that when Rohrer introduced *Eq. 5*, he attributed specific physical meaning to the constants $K_1$ and $K_2$ (27). Although Rohrer's interpretation of the constants is now disregarded, *Eq. 5* is still applied as a useful descriptive tool. Similarly, *Eqs. 1–4* appear to be useful for

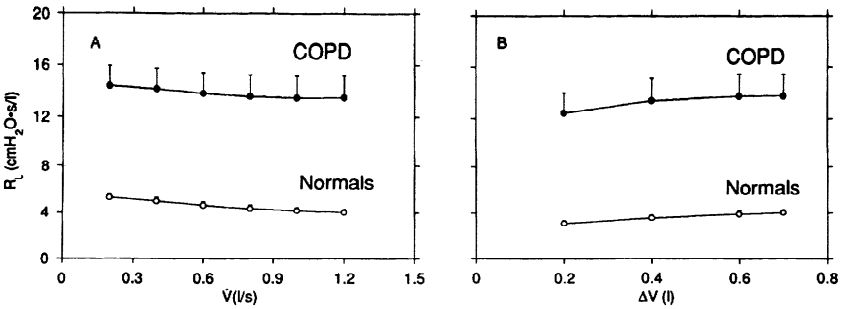


FIG. 5. Average relationships of total pulmonary resistance (RL) to V̇ at constant ΔV of 0.73 liter (*A*) and to ΔV at constant V̇ of 0.8 l/s (*B*) of 10 COPD patients and 18 normal subjects (11). Bars, SE when larger than symbols.

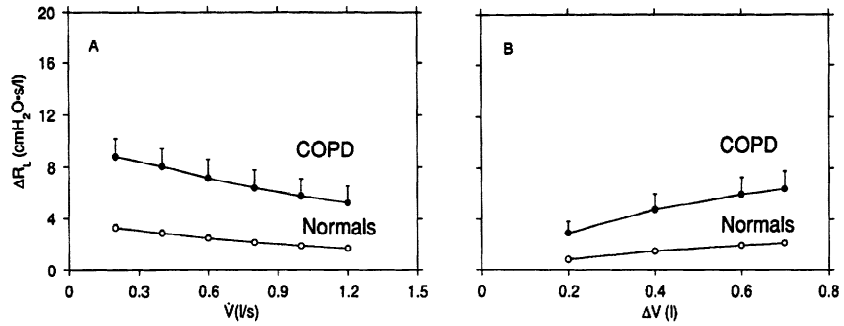


FIG. 6. Average relationships of additional resistance of lung (ΔRL) to $\dot{V}$ at constant ΔV of 0.73 liter (*A*) and to ΔV at constant $\dot{V}$ of 0.8 l/s (*B*) of 10 COPD patients and 18 normal subjects (11). Bars, SE when larger than symbols.

descriptive purposes despite the limitations inherent to our simplistic model analysis. A full discussion of the limitations and advantages of the flow interruption method can be found in a recent review (3).

*Chest Wall*

*Rint.* In cats (30) and dogs (31), the chest wall exhibits a substantial Rint. By contrast, in normal anesthetized paralyzed humans (11), there is no appreciable change in Pes immediately after airway occlusion, indicating that the tissues of the chest wall do not offer any appreciable velocity-dependent dissipative forces (11). Similar to normal subjects, the COPD patients of the present study did not exhibit any appreciable immediate drop in Pes after airway occlusion, except for *patient 3*. We have no explanation for this discrepant result. In patients with ischemic and valvular heart disease, Auler et al. (1) found a small but consistent Rint,W averaging ~1 $cmH_2O \cdot l^{-1} \cdot s$.

*ΔR.* Because Rint,W was absent in COPD patients, ΔRW represents the total resistance of the chest wall (ΔRW = RW). As in normal subjects (11), in our patients the iso-ΔV and iso-$\dot{V}$ values of ΔRW fitted *Eq. 1* (Fig. 7). Because of higher values of $R_2$,W, the values of ΔRW were higher in COPD patients than in normal subjects. The nature of this discrepancy is not clear. It should be noted, however, that the COPD patients were much older than the normal subjects.

*Est.* In the COPD patients the values of Est,W were similar to those of the normal subjects of D'Angelo et al. (11) (Table 3). During anesthesia paralysis in the supine position, Van Lith et al. (33) found that Est,W averaged 4.9 ± 0.1 $cmH_2O/l$ in five stable COPD patients. The latter value is similar to the results obtained in the present study in COPD patients mechanically ventilated for acute respiratory failure (5.2 ± 0.7 $cmH_2O/l$).

*ΔE and Edyn.* As in normal subjects, in COPD patients Edyn,W (=Est,W + ΔEW) was higher than Est,W (Figs. 8 and 9). As predicted by *Eq. 4*, at constant ΔV, Edyn,W increased with $\dot{V}$ (Fig. 8), whereas at constant $\dot{V}$, it decreased with ΔV (Fig. 9). ΔEW implies that under dynamic conditions the effective elastic recoil pressures of the chest wall are not fixed but exceed Pst,W by $P_1 - P_2$, the latter representing the additional elastic pressure stored in the viscoelastic units of the chest wall tissues (i.e., in springs $E_2$,W of the model in Fig. 2) (11). ΔEW was slightly but significantly ($P < 0.01$) higher in COPD patients than in normal subjects over the entire experimental ranges of $\dot{V}$ and ΔV.

*Lung*

*Rint.* In open-chest dogs in which alveolar pressure was measured directly with the alveolar capsule technique, Bates et al. (2) found that Rint,L was due essentially entirely to Raw. Moreover, even after histamine-induced intrapulmonary heterogeneities in dogs, Rint,L was still found to reflect Raw almost entirely (18). According to Liistro et al. (17), in humans Rint,L also probably reflects Raw, as originally proposed by Neegaard and Wirz (25). As in normal subjects (11), Rint,L of COPD patients exhibited $\dot{V}$ and ΔV dependence (Fig. 4): at fixed ΔV, Rint,L increased with increasing $\dot{V}$ according to Rohrer's equation; and, at constant $\dot{V}$, it decreased with increasing ΔV, as originally described by Briscoe and Dubois (8).

In previous studies in mechanically ventilated COPD patients (7, 9, 32), Rint,rs was studied only at a single inflation $\dot{V}$ and ΔV (i.e., solely under the baseline ventilatory settings). These results are summarized in Table 4 together with the data obtained in the present study at baseline ventilatory settings. The values of Rint,rs and Rrs of the present study were close to those of Bernasconi et al. (7) and of Tantucci et al. (32) but lower than those reported by Broseghini et al. (9). This discrepancy can probably be explained by the fact that in the latter investigation the patients were studied during the first day of mechanical ventilation. Indeed, in COPD patients the impairment of respiratory mechanics is in general

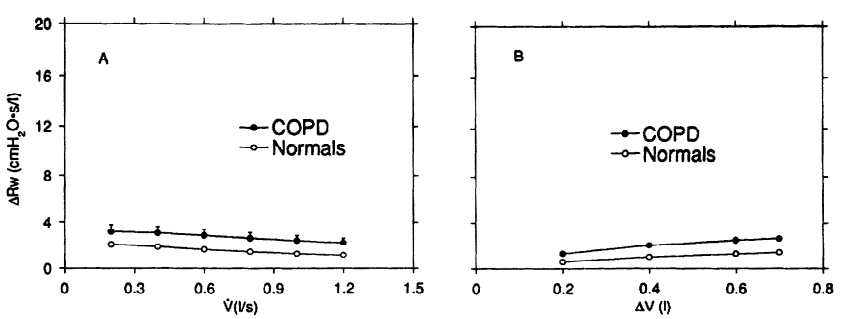


FIG. 7. Average relationships of additional resistance of chest wall (ΔRW) to $\dot{V}$ at constant ΔV of 0.73 liter (*A*) and to ΔV at constant $\dot{V}$ of 0.8 l/s (*B*) of 10 COPD patients and 18 normal subjects (11). Bars, SE when larger than symbols.

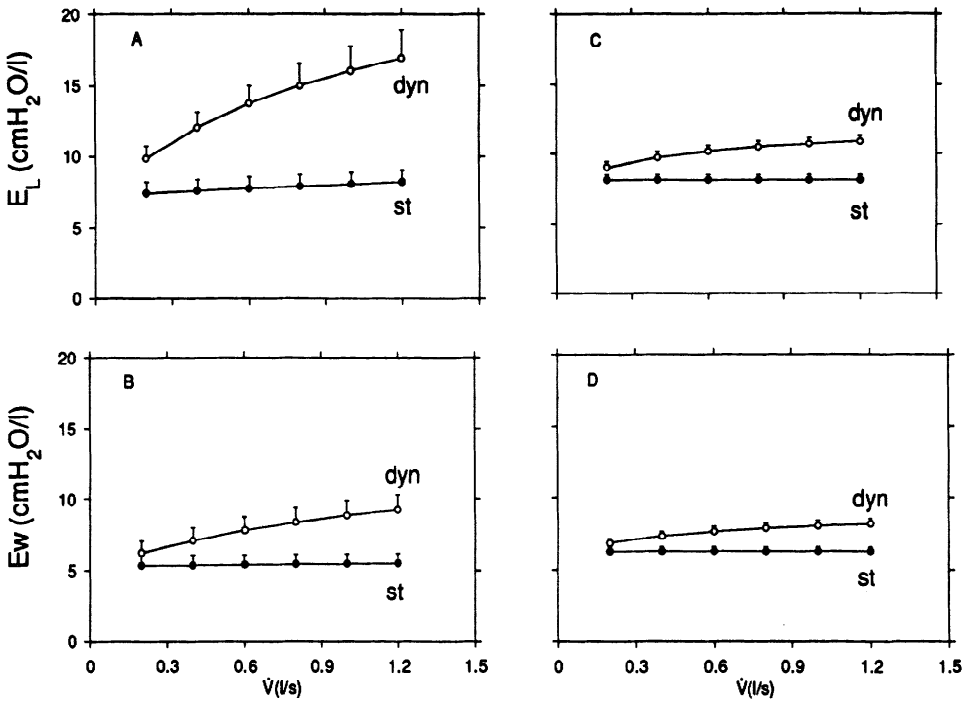


FIG. 8. Average relationships of static (st) and dynamic (dyn) elastance of lung (EL; *A* and *C*) and chest wall (Ew; *B* and *D*) to V̇ at constant ΔV of 0.73 liter of 10 COPD patients (*A* and *B*) and 18 normal subjects (*C* and *D*) (11). Bars, SE when larger than symbols.

more severe on the first day of mechanical ventilation than later on (24). The values of PEEPi were also higher in the study of Broseghini et al. compared with the other studies. This probably not only reflects the earlier investigation of the patients but also the shorter duration of mechanical expiration (Table 4). Our values of $K_1$ and $K_2$ were 2.7 and 6.3 times higher than those of normal subjects, respectively (Table 2). An increase of $K_1$ and $K_2$ has been previously reported in stable COPD patients (13, 15).

*ΔR.* An increase of ΔRrs has been previously reported at fixed inflation V̇ and ΔV in mechanically ventilated COPD patients (7, 9, 32). The values obtained by Tantucci et al. (32) were essentially the same as in the present study and were obtained at similar baseline ventilatory settings (Table 4). The values of Bernasconi et al. (7) were slightly higher, probably reflecting the longer TI (see *Eq. 1*). The highest values of ΔRrs were exhibited by the patients studied on the first day of mechanical ventilation by Broseghini et al. (9). Although this probably mostly reflected greater severity of lung disease, a relatively long TI may also have contributed to it.

The increase of ΔRrs found in the COPD patients was mainly due to increased ΔRL (Fig. 6), which probably mainly reflects increased dynamic dissipations due to time constant inhomogeneity within the lungs (26). Increased pressure losses of viscoelastic units within the lung could also contribute to increased ΔRL in COPD.

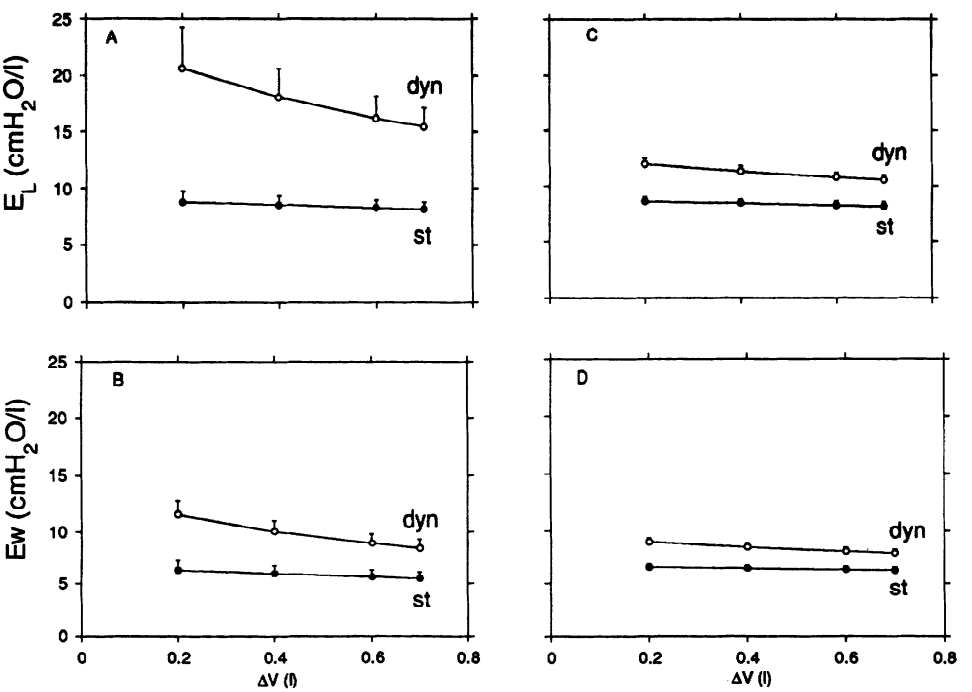


FIG. 9. Average relationships of static (st) and dynamic (dyn) EL (*A* and *C*) and Ew (*B* and *D*) to ΔV at constant V̇ of 0.8 l/s of 10 COPD patients (*A* and *B*) and 18 normal subjects (*C* and *D*). Bars, SE when larger than symbols.

TABLE 4. *Values of respiratory mechanics in mechanically ventilated COPD patients*

| Reference | $n$ | Time, days | ΔV, liter | $\dot{V}$, l/s | TI, s | TE, s | PEEPi, $cmH_2O$ | ΔFRC, liter | Est,rs, $cmH_2O/l$ | Rint,rs, $cmH_2O \cdot l^{-1} \cdot s$ | ΔRrs, $cmH_2O \cdot l^{-1} \cdot s$ | Rrs, $cmH_2O \cdot l^{-1} \cdot s$ |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Bernasconi et al. (7) | 11 | 1–9 | 0.68±0.05 | 0.61±0.04 | 1.30±0.06 | 2.60±0.18 | 5.1±0.3 | | 22.2±0.01 | 8.1±1.3 | 7.2±0.3 | 15.8±0.6 |
| Broseghini et al. (9) | 8 | 1 | 0.69±0.03 | 0.62±0.01 | 1.20±0.05 | 2.14±0.05 | 13.6±0.8 | 0.66±0.10 | 17.9±0.01 | 15.6±3.1 | 10.8±2.0 | 26.4±4.7 |
| Tantucci et al. (32) | 6 | 1–4 | 0.80±0.04 | 1.01±0.03 | 0.93±0.04 | 3.35±0.04 | 4.6±0.9 | 0.42±0.18 | 11.1±0.01 | 8.0±1.8 | 5.5±1.0 | 13.5±1.0 |
| Present study | 10 | 1–16 | 0.73±0.02 | 0.80±0.03 | 0.92±0.01 | 3.98±0.20 | 5.7±0.9 | 0.34±0.06 | 12.6±0.7 | 7.2±0.6 | 5.6±0.5 | 12.8±1.1 |

Values are means ± SE; $n$, no. of patients studied. Time, range of days between orotracheal intubation and experiment; ΔV, baseline tidal volume; $\dot{V}$, baseline inspiratory flow; TI, inspiratory time; TE, expiratory time; PEEPi, intrinsic end-expiratory positive pressure; ΔFRC, difference between end-expiratory lung volume during mechanical ventilation and relaxation volume; Est,rs, Rrs, Rint,rs, and ΔRrs, static elastance, total resistance, interrupter resistance, and additional resistance, respectively, of the respiratory system.

Indeed, derecruitment of lung units due to airway closure and loss of pulmonary tissue due to emphysema could be expected to result in an increase of both ΔRL and ΔEL.

As in normal subjects (11), ΔRL fitted *Eq. 1* in our patients. Because of higher values of $R_2$,L, the values of ΔRL were higher in COPD patients than in normal subjects. In contrast, the values of $\tau_2$,L were not significantly different between COPD patients and normal subjects (Table 3), reflecting equivalent changes in $R_2$,L and $E_2$,L in the COPD patients. The nature of this phenomenon is not clear. Loss of pulmonary tissue, whether anatomic (resection, emphysema) or functional (derecruitment), in the absence of rheologic changes of the remaining tissue should result in a proportional increase of $R_2$ and $E_2$ without a change in $\tau_2$ (e.g., resection of one lung should result in approximately doubling of both $R_2$,L and $E_2$,L but no change in $\tau_2$,L). This explanation, however, does not take into account the complex structural changes in the lungs of COPD patients nor the increased regional time constant inhomogeneity within their lungs. In normal lungs, the regional time constants are small relative to the time constant of the viscoelastic units. Accordingly, in normal subjects $\tau_2$,L, which amounts to 1.11 ± 0.10 s, mainly reflects viscoelastic behavior (11). In patients with COPD the regional differences in the time constant should increase substantially. Nevertheless, the slow viscoelastic behavior is probably still predominant, such that $\tau_2$,L does not increase significantly in COPD patients (Table 3). However, this hypothesis must be taken with reservations because our analysis does not allow us to assess separately the contribution of pendelluft and viscoelastic behavior to ΔRL, ΔEL, and "viscoelastic" constants. Nevertheless, independent of the underlying mechanisms, the increase of ΔRL and ΔEL observed in the COPD patients implies increased work of breathing.

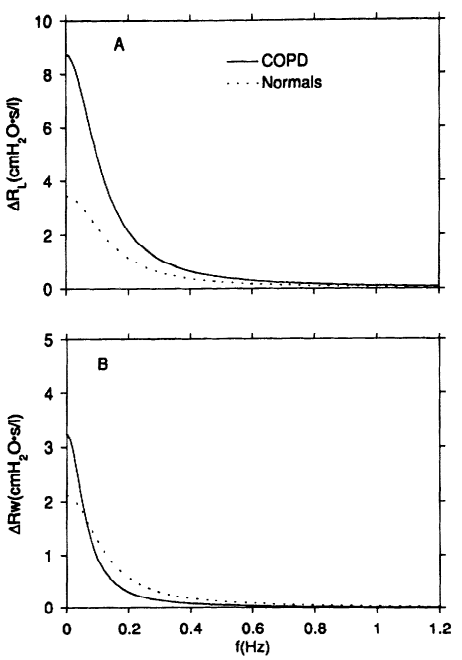


FIG. 10. Average relationships of ΔRL (*A*) and ΔRW (*B*) to frequency ($f$) of 10 COPD patients and 18 normal subjects (11) computed according to *Eq. 7* using constants in Table 3. Intercepts of curves at $f$ = 0 correspond to $R_2$.

*Est.* The values of Est,L of the COPD patients of the present study were similar to those of the normal subjects of D'Angelo et al. (11) (Table 3). During anesthesia paralysis in the supine position, Van Lith et al. (33) found that in five stable COPD patients Est,L averaged 3.8 ± 0.8 $cmH_2O/l$. This value is substantially lower than that in the COPD patients of the present study, possibly reflecting the fact that the patients of Van Lith et al. had a greater degree of pulmonary emphysema or that Est,L increases in acute failure due to dynamic pulmonary hyperinflation, small airway closure, atelectasis, etc. In fact the value of Est,rs of our COPD patients was similar to that of the COPD patients in acute respiratory failure studied by Tantucci et al. (32) (Table 4). In contrast, a higher value of Est,rs was found by Broseghini et al. (9) in COPD patients studied during the first day of mechanical ventilation (Table 4). This is probably because of the fact that the latter patients exhibited a more marked degree of dynamic hyperinflation, as reflected by a higher change in functional residual capacity (Table 4), and hence were operating on a flatter part of the static V-P curve of the lungs.

*ΔE and Edyn.* As a result of ΔEL, Edyn,L was higher than Est,L. As predicted by *Eq. 4*, at constant ΔV, Edyn,L increased with $\dot{V}$ (Fig. 8), whereas at constant $\dot{V}$, it decreased with ΔV (Fig. 9). ΔEL implies that under dynamic conditions the effective elastic recoil pressure of the lung exceeds Pst,L by $P_1 - P_2$. $P_1 - P_2$ reflects the additional elastic pressure stored in the viscoelastic units of the pulmonary tissues (i.e., in springs $E_2$,L in Fig. 2) (11) and contributions due to time constant inhomogen-

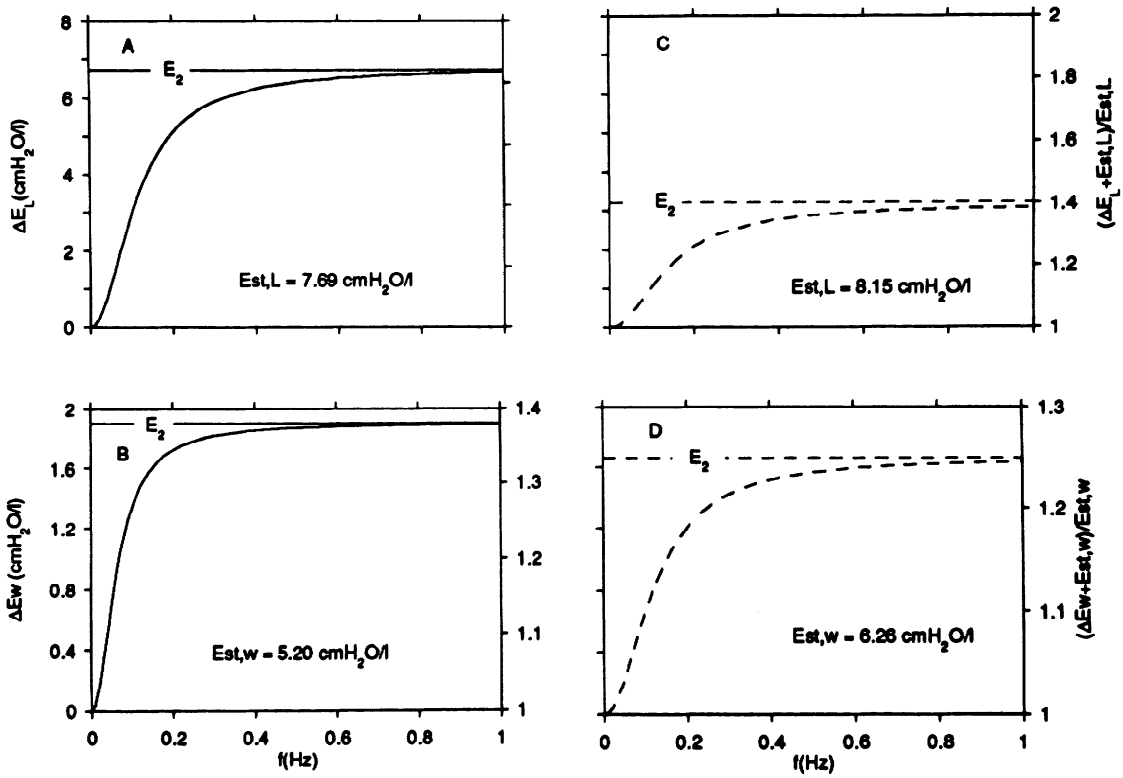


FIG. 11. Average relationships of ΔEL (*A* and *C*) and ΔEW (*B* and *D*) to *f* of 10 COPD patients (*A* and *B*) and 18 normal subjects (*C* and *D*) (11) computed according to *Eq. 8* using constants in Table 3. Curves asymptote toward $E_2$. Also shown on right-hand ordinates are changes in dynamic elastance (=ΔE + Est) expressed as a fraction of Est.

eities within the lungs, which in COPD should be substantial (26).

*Frequency Dependence of Elastance and Resistance in COPD Patients*

During steady-state sinusoidal breathing, ΔRL and ΔRW should decrease with increasing frequency (*f*) according to the following function (11)

$$\Delta R = R_2/(1 + \omega^2\tau_2^2) \quad (7)$$

where $\omega$ is angular frequency (= $2\pi f$).

Figure 10 illustrates the relationships of ΔRL and ΔRW with *f*, computed according to *Eq. 7* using the average values of $R_2$ and $\tau_2$ in Table 3. At low *f*, the values of ΔR were higher in COPD patients than in normal subjects for both lung and chest wall, reflecting the higher values of $R_2$. With increasing *f*, ΔRW and ΔRL decreased rapidly in both COPD patients and normal subjects, becoming negligible at $f > 0.6$ Hz. Although the relationship of ΔRL with *f* was markedly different between COPD patients and normal subjects, that of ΔRW with *f* was relatively close.

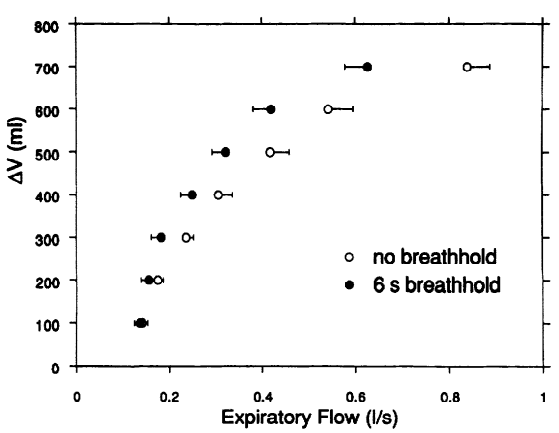


FIG. 12. Average relationships of ΔV to $\dot{V}$ during passive expiration of 10 COPD patients. Results obtained at baseline ventilatory settings (ΔV = 0.73 liter and $\dot{V}$ = 0.8 l/s) without and with 6-s end-inspiratory breathhold. Bars, SE when larger than symbols.

During steady-state sinusoidal breathing, ΔEL and ΔEW should change with *f* according to

$$\Delta E = \omega^2\tau_2^2E_2/(1 + \omega^2\tau_2^2) \quad (8)$$

Figure 11 shows the relationships of ΔEL and ΔEW with *f*, computed according to *Eq. 8* using the average values of $E_2$ and $\tau_2$ in Table 3. Also shown, on the right-hand ordinates, are the corresponding values of dynamic elastance (=Est + ΔE) expressed as a ratio of Est. In contrast to ΔRL and ΔRW, ΔEL and ΔEW increased with increasing *f*, asymptoting toward $E_2$ at $f > 0.6$ Hz. The values of ΔEL were considerably higher in COPD patients than in normal subjects. At $f = 0.6$ Hz, the increase in Edyn,L relative to Est,L was greater in COPD patients than in normal subjects (82 vs. 37%), whereas the corresponding increase for the chest wall was less pronounced (36 vs. 25%). Previous studies on stable awake COPD patients have shown that the magnitude of the changes in pulmonary resistance (15) and elastance (34) with *f* are greater in COPD patients than in normal subjects. Our results (Figs. 10 and 11) are in line with these observations. It should be noted, however, that our analysis was based on results obtained only during inspiration, whereas in the previous studies the measurements were obtained during the whole breathing cycle. Hence our analysis does not

include possible contributions due to plastoelastic phenomena, which may play a role during cycling breathing (3).

The high values of $R_2$,L and $E_2$,L found in the COPD patients imply that at $f < 0.6$ Hz the viscoelastic work is markedly increased relative to normal subjects (11). To a lesser extent, this is also true for the viscoelastic work of the chest wall.

*Implications on Passive Lung Emptying*

Figure 12 shows the relationship between $\Delta V$ and $\dot{V}$ obtained during lung deflation in the 10 COPD patients after baseline mechanical ventilation both without and with an end-inspiratory pause of 6 s. Without the pause, the expiratory flows were higher than with the pause. This could be attributed to the fact that without the end-inspiratory breathhold there is additional energy stored in springs $E_2$,L and $E_2$,W, as reflected by $P_1 - P_2$ (11, 23).

In the iso-$\Delta V$ experiment, $\Delta R$ decreased with flow according to *Eq. 2*. Because $\Delta R = (P_1 - P_2)/\dot{V}$, *Eq. 2* can be rearranged into the following equation, which relates $P_1 - P_2$ to inflation flow for any given $\Delta V$

$$P_1 - P_2 = \dot{V}R_2(1 - e^{-\Delta V/\dot{V}\tau_2}) \qquad (9)$$

According to *Eq. 9*, after rapid lung inflation with a concomitant increase in $P_1 - P_2$ and in absence of an end-inspiratory pause to avoid dissipation of this additional elastic energy into dashpots $R_2$,L and $R_2$,W (Fig. 2), the expiratory flows should be higher than after a slow inflation or an end-inspiratory pause. It should be noted, however, that contrary to normal anesthetized paralyzed subjects (6) the $\Delta V$-$\dot{V}$ relationships of the COPD patients both with and without an end-inspiratory pause exhibited an upward convexity (Fig. 12) that, according to Gottfried et al. (14), should reflect expiratory flow limitation. If expiratory flow limitation was present with the end-inspiratory pause, how could the expiratory flows be higher without the pause? This phenomenon could be attributed to the fact that without the breathhold the overall elastic recoil pressure of the lung was higher than after the breathhold due to the additional elastic recoil pressure stored in spring $E_2$,L ($=P_1$,L $- P_2$,L). Indeed, to the extent that the maximal expiratory flow is modulated by the overall elastic recoil of the lung (20), an increase in expiratory flow should occur when this is increased. According to the model in Fig. 2, an increase in overall lung elastic recoil pressure can result from viscoelastic behavior of the pulmonary tissues. It should be noted, however, that differences in time constants within the lung could also contribute to the observed increase in expiratory flows during expiration without the breathhold. Whatever the nature of this phenomenon, the results in Fig. 12 have important implications in terms of dynamic pulmonary hyperinflation in COPD patients. To reduce dynamic pulmonary hyperinflation in mechanically ventilated COPD patients, low respiratory frequencies associated with low TI/TT ratios (and hence high inspiratory $\dot{V}$) are commonly used. According to the present analysis, this strategy should be beneficial not only because of the prolongation of expiration per se but also because of a concomitant increase in expiratory flows. Both of these mechanisms should contribute to a reduction in end-expiratory lung volume.

In conclusion, the present study is the first systematic investigation of the mechanics of the lung and chest wall in mechanically ventilated COPD patients with acute respiratory failure. Our main results are that in COPD patients *1*) the static elastances of the lung and chest wall are not significantly different from those of normal subjects; *2*) the pressure dissipations due to the viscoelastic properties of the chest wall are slightly increased; *3*) the interrupter resistance is markedly increased; *4*) the pressure dissipations due to the viscoelastic properties of pulmonary tissues and/or time constant inequalities within the lungs are markedly increased; *5*) the magnitude of time dependency of pulmonary flow resistance and elastance is markedly increased; and *6*) for comparative purposes, measurements of pulmonary and chest wall resistance and elastance must be standardized in view of their marked time, flow, and volume dependence.

The authors thank the physicians and nursing staff of the Intensive Care Unit of the Saint-Luc Hospital for their valuable cooperation and Dr. H. Ghezzo for help with the statistical analysis.

This study was supported by the Medical Research Council of Canada, the J. T. Costello Memorial Research Fund, the Royal Victoria Hospital Foundation, the Respiratory Health Network of Centers of Excellence, Canada, and the Fondation de l'Hôpital Saint-Luc.

Address for reprints requests: C. Corbeil, Hôpital Saint-Luc, 1058 Saint-Denis St., Montreal, Quebec H2X 3J4, Canada.

Received 23 December 1991; accepted in final form 6 October 1992.

REFERENCES

1. AULER, J. O. C., W. ZIN, M. P. R. CALDEIRA, W. V. CARDOSO, AND P. H. N. SALDIVA. Pre- and postoperative inspiratory mechanics in ischemic and valvular heart disease. *Chest* 92: 984–990, 1987.
2. BATES, J. H. T., M. S. LUDWIG, P. D. SLY, K. BROWN, J. G. MARTIN, AND J. J. FREDBERG. Interrupter resistance elucidated by alveolar pressure measurement in open-chest normal dogs. *J. Appl. Physiol.* 65: 408–414, 1988.
3. BATES, J. H. T., AND J. MILIC-EMILI. The flow interruption technique for measuring respiratory resistance. *J. Crit. Care* 6: 227–238, 1991.
4. BATES, J. H. T., A. ROSSI, AND J. MILIC-EMILI. Analysis of the behavior of the respiratory system with constant inspiratory flow. *J. Appl. Physiol.* 58: 1840–1848, 1985.
5. BAYDUR, A. P., P. K. BEHRAKIS, W. A. ZIN, M. JAEGER, AND J. MILIC-EMILI. A simple method for assessing the validity of the esophageal balloon technique. *Am. Rev. Respir. Dis.* 126: 788–791, 1983.
6. BEHRAKIS, P. K., B. D. HIGGS, A. BAYDUR, W. A. ZIN, AND J. MILIC-EMILI. Respiratory mechanics during halothane anesthesia and anesthesia-paralysis in humans. *J. Appl. Physiol.* 58: 285–289, 1985.
7. BERNASCONI, M., Y. PLOYSONGSANG, S. B. GOTTFRIED, J. MILIC-EMILI, AND A. ROSSI. Respiratory compliance and resistance in mechanically ventilated patients with acute respiratory failure. *Intensive Care Med.* 14: 547–553, 1988.
8. BRISCOE, W. A., AND A. B. DUBOIS. The relationship between airway resistance, airway conductance and lung volume in subjects of different age and body size. *J. Clin. Invest.* 37: 1279–1285, 1958.
9. BROSEGHINI, C., R. BRANDOLESE, R. POGGI, G. POLESE, E. MANZIN, J. MILIC-EMILI, AND A. ROSSI. Respiratory mechanics during the first day of mechanical ventilation in patients with pulmonary edema and chronic airway obstruction. *Am. Rev. Respir. Dis.* 138: 355–361, 1988.
10. D'ANGELO, E., E. CALDERINI, G. TORRI, F. M. ROBATTO, D. BONO, AND J. MILIC-EMILI. Respiratory mechanics in anesthetized paralyzed humans: effects of flow, volume and time. *J. Appl. Physiol.* 67: 2556–2564, 1989.
11. D'ANGELO, E., F. M. ROBATTO, E. CALDERINI, M. TAVOLA, D.

BONO, G. TORRI, AND J. MILIC-EMILI. Pulmonary and chest wall mechanics in anesthetized paralyzed humans. *J. Appl. Physiol.* 70: 2602–2610, 1991.
12. EISSA, N. T., V. M. RANIERI, C. CORBEIL, M. CHASSÉ, J. BRAIDY, AND J. MILIC-EMILI. Effects of positive end-expiratory pressure, lung volume, and inspiratory flow on interrupter resistance in patients with adult respiratory distress syndrome. *Am. Rev. Respir. Dis.* 144: 538–543, 1991.
13. FRY, D. L., R. V. EBERT, W. W. STEAD, AND C. C. BROWN. The mechanics of pulmonary ventilation in normal subjects and in patients with emphysema. *Am. J. Med.* 16: 80–96, 1954.
14. GOTTFRIED, S. B., A. ROSSI, B. D. HIGGS, P. M. A. CALVERLEY, L. ZOCCHI, C. BOZIC, AND J. MILIC-EMILI. Noninvasive determination of respiratory system mechanics during mechanical ventilation for acute respiratory failure. *Am. Rev. Respir. Dis.* 131: 414–420, 1985.
15. GRIMBY, G., T. TAKISHIMA, W. GRAHAM, P. T. MACKLEM, AND J. MEAD. Frequency dependence of flow resistance in patients with obstructive lung disease. *J. Clin. Invest.* 47: 1455–1465, 1968.
16. HALUSZKA, J., D. A. CHARTRAND, A. E. GRASSINO, AND J. MILIC-EMILI. Intrinsic PEEP and arterial $P_{CO_2}$ in stable patients with chronic obstructive pulmonary disease. *Am. Rev. Respir. Dis.* 141: 1194–1197, 1990.
17. LIISTRO, G., D. STANESCU, D. RODENSTEIN, AND C. VERITER. Reassessment of the interruption technique for measuring flow resistance in humans. *J. Appl. Physiol.* 67: 933–937, 1989.
18. LUDWIG, M. S., P. V. ROMERO, P. D. SLY, J. J. FREDBERG, AND J. H. T. BATES. Interpretation of interrupter resistance after histamine-induced bronchoconstriction in dogs. *J. Appl. Physiol.* 68: 1651–1656, 1990.
19. MACKLEM, P. T. M., AND J. MEAD. Resistance of central and peripheral airways measured by a retrograde catheter. *J. Appl. Physiol.* 22: 395–401, 1967.
20. MEAD, J., J. M. TURNER, P. T. MACKLEM, AND J. B. LITTLE. Significance of the relationship between lung elastic recoil and maximum expiratory flow. *J. Appl. Physiol.* 22: 95–108, 1967.
21. MILIC-EMILI, J., F. M. ROBATTO, AND J. H. T. BATES. Respiratory mechanics in anaesthesia. *Br. J. Anaesth.* 65: 4–12, 1990.
22. MORRIS, J. F., A. KOSKI, AND L. C. JOHNSON. Spirometric standards for healthy nonsmoking adults. *Am. Rev. Respir. Dis.* 103: 57–67, 1971.
23. MORTOLA, J. P., D. MAGNANTE, AND M. SAETTA. Expiratory pattern of newborn mammals. *J. Appl. Physiol.* 58: 528–533, 1985.
24. MURCIANO, D., J. BOCZKOWSKI, Y. LECOCGUIC, J. MILIC-EMILI, R. PARIENTE, AND M. AUBIER. Tracheal occlusion pressure: a simple index to monitor respiratory muscle fatigue during acute respiratory failure in patients with chronic obstructive pulmonary disease. *Ann. Intern. Med.* 108: 800–805, 1988.
25. NEEGAARD, K. VON, AND K. WIRZ. Die Messung der strömungswiderstände in den Atemwegen des Menschen, insbesondere bei Asthma und Emphysemem. *Z. Klin. Med.* 105: 51–82, 1927.
26. OTIS, A. B., R. A. MCKERROW, R. A. BARTLETT, J. MEAD, N. J. MCILROY, N. J. SELVERSTONE, AND E. P. RADFORD. Mechanical factors in distribution of pulmonary ventilation. *J. Appl. Physiol.* 8: 427–443, 1956.
27. ROHRER, F. Der Strömungswiderstand In Den Menschlichen Atemwegen Und Der Einfluss Der Unregelmässigen Verzweigung Des Bronchialsystems Auf Den Atmungsverlauf In Verschiedenen Lungenbezirken. *Pfluegers Arch. Gesamte Physiol. Menschen Tiere* 162: 225–299, 1915.
28. ROSSI, A., S. B. GOTTFRIED, B. D. HIGGS, L. ZOCCHI, A. GRASSINO, AND J. MILIC-EMILI. Respiratory mechanics in mechanically ventilated patients with respiratory failure. *J. Appl. Physiol.* 58: 1849–1858, 1985.
29. ROSSI, A., S. B. GOTTFRIED, L. ZOCCHI, B. D. HIGGS, S. LENNOX, P. M. A. CALVERLEY, P. BEGIN, A. GRASSINO, AND J. MILIC-EMILI. Measurement of static compliance of the total respiratory system in patients with acute respiratory failure during mechanical ventilation. *Am. Rev. Respir. Dis.* 131: 672–677, 1985.
30. SHARDONOFSKY, F. R., M. SKABURSKIS, J. SATO, W. A. ZIN, AND J. MILIC-EMILI. Effects of volume history and vagotomy on pulmonary and chest wall mechanics in cats. *J. Appl. Physiol.* 71: 498–508, 1991.
31. SIMILOWSKI, T., P. LEVY, C. CORBEIL, M. ALBALA, R. PARIENTE, J.-P. DERENNE, J. H. T. BATES, B. JONSON, AND J. MILIC-EMILI. Viscoelastic behavior of lung and chest wall in dogs determined by flow interruption. *J. Appl. Physiol.* 67: 2219–2229, 1989.
32. TANTUCCI, C., C. CORBEIL, M. CHASSÉ, J. BRAIDY, N. MATAR, AND J. MILIC-EMILI. Flow resistance in patients with chronic obstructive pulmonary disease in acute respiratory failure. *Am. Rev. Respir. Dis.* 144: 384–389, 1991.
33. VAN LITH, P., F. J. JOHNSON, AND J. T. SHARP. Respiratory elastances in relaxed and paralyzed states in normal and abnormal men. *J. Appl. Physiol.* 23: 475–486, 1967.
34. WOOLCOCK, A. J., N. J. VINCENT, AND P. T. MACKLEM. Frequency dependence of compliance as a test for obstruction in the small airways. *J. Clin. Invest.* 48: 1097–1106, 1969.