Work of Breathing in Patients with Chronic Obstructive Pulmonary Disease in Acute Respiratory Failure[1-3]

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SUMMARY In 11 spontaneously breathing patients with chronic obstructive pulmonary disease (COPD) in acute ventilatory failure, we measured the total inspiratory ($\dot{W}$itot) and total resistive ($\dot{W}$I + Eres) work rate of breathing, together with lung mechanics (dynamic pulmonary elastance and inspiratory and expiratory pulmonary flow resistance). All variables were markedly increased compared with those in normal subjects. No significant correlation was found between $\dot{W}$itot and $\dot{W}$I + Eres with lung mechanics data. However, when $\dot{W}$itot and $\dot{W}$I + Eres were expressed per liter of ventilation, a significant positive correlation was found with all lung mechanics data. These results indicate that although in patients acutely ill with COPD, work rate and work per liter of ventilation are increased, only the latter is related to the severity of pulmonary mechanical impairment, and it could be used as one of the criteria for extubation. In addition, our results indicate that at end-expiration the alveolar pressure was positive (range, 6 to 13 cm H_2O) in all patients (intrinsic PEEP), a fact that must necessarily affect hemodynamics; furthermore, it imposes an extra burden on the inspiratory muscles.

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Introduction

In a study on critically ill patients with chronic obstructive pulmonary disease (COPD), Henning and coworkers (1) concluded that the measurement of the respiratory flow-resistive work rate is a "useful objective variable for determining the capability of independent ventilation." Dependence on mechanical ventilation was observed when the respiratory resistive work rate was greater than 1.7 $kg \cdot min^{-1}$, whereas patients were ordinarily capable of spontaneous ventilation when the corresponding values were lower than 1.0 $kg \cdot min^{-1}$. In a recent study on patients with COPD in acute respiratory failure (2), we observed (but not reported) that in the patients with the highest values of pulmonary flow resistance, the minute ventilation ($\dot{V}$I) tended to be lower than in the patients with lesser airways obstruction. Because the resistive work rate ($\dot{W}$res) depends not only on the magnitude of the flow resistance (R) but, more importantly, on the magnitude of minute ventilation ($\dot{W}res = 0.5 \pi^2 R \dot{V}I^2$, according to a simplified equation from reference 3), it follows that $\dot{W}$res may actually be lower in patients with COPD with very severe airway obstruction than in patients with lesser increase in airway resistance. This possibility needs to be assessed before accepting the criteria for determining capability of independent ventilation postulated by Henning and coworkers (1). Accordingly, in the present investigation we have determined the respiratory mechanical work rate in 11 with COPD in acute respiratory failure, and we have related these results to concomitant measurements of dynamic pulmonary elastance and flow resistance as well as to minute ventilation.

Methods

Eleven patients with COPD (6 women and 5 men) admitted to the intensive care unit of the Hôpital Beaujon, Paris, for management of acute ventilatory failure were studied. Their average (± SD) age, weight, and height were, respectively, 67 ± 11 yr, 57 ± 14 kg, and 162 ± 10 cm. Chronic obstructive pulmonary disease was confirmed by medical history and clinical examination. The apparent cause of acute ventilatory failure was airway infection in all patients. They were intubated or tracheostomized with the cuff of the tube inflated and, prior to our study, they were being mechanically ventilated. They were not sedated nor did they receive any drugs that are said to affect the respiratory drive or the contractile properties of the respiratory muscles. The study was approved by the institutional ethics committee. Patients or their relatives gave informed consent.

Air flow ($\dot{V}$) was measured with a Fleisch no. 3 pneumotachygraph (Fleisch, Lausanne, Switzerland) connected to a MP-45 Validyne differential pressure transducer (Validyne Corp., Northridge, CA). Changes in volume (V) were measured by electronic integration of the flow signal. Esophageal pressure (Pes) was measured with a balloon 10 cm long and with a perimeter of 3.6 cm (4). The catheter had an internal diameter of 1.4 mm and a length of 100 cm and was connected to a DP-15 Validyne differential pressure transducer. Pressure at the airway opening (Pao) was measured with another DP-15 Validyne differential pressure transducer. Transpulmonary pressure was obtained as the difference between Pao and Pes.

All signals were conditioned and displayed on an ALLCO En 68 recorder using a paper speed of 25 or 50 $mm \cdot s^{-1}$ during the analyzed periods. The inspiratory and expiratory lines were separated by a Mauve and Legarde valve. The dead space of the circuit was 75 ml. The flow resistances of the inspiratory and expiratory lines were, respectively, 2.1 and 3.6 $cmH_2O \cdot L^{-1} \cdot s$ at a flow of 1 $L \cdot s^{-1}$. The flow resistances of the tracheal and tracheostomy tubes amounted, respectively, to 1.92 and 0.75 $cmH_2O \cdot L^{-1} \cdot s$, at a flow of 1 $L \cdot s^{-1}$. Airway occlusions were performed by inflating a rubber balloon with a syringe on the inspiratory line during a preceding expiration so that the occlusion became effective from the onset of the next inspiration. Immediately after the onset of the inspiratory effort against the closed airways, the expiratory line was closed with a tap so that complete occlusion pressure waves were obtained at functional residual capacity.

Arterial blood gases were measured with an IL 213 (Instrumentation Laboratories; Lexington, MA) or a BMS 3 Radiometer analyzer (Radiometer; Copenhagen, Denmark).

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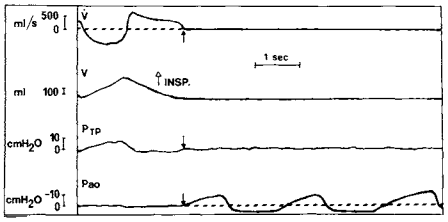


Fig. 1. Record of flow (V̇), volume (V), transpulmonary pressure (PL), and pressure at the airway opening (Pao) in a representative patient. Arrows indicate onset of airway occlusion at end-expiration. During the 3 occluded efforts, PL is virtually constant (apart from the small changes reflecting cardiac artifact), indicating that Δ Pes is a valid measure of the changes in pleural pressure ("occlusion test"). During the latter part of occluded expiration, there is a plateau in Pao that presumably reflects the end-expiratory elastic recoil pressure of the total respiratory system. The end-expiratory elastic recoil of the chest wall is obtained as difference between end-expiratory Pao and PL.

Procedure

All patients were studied in semirecumbent posture. The studies were made in an intensive care unit. A physician was present in order to take care of the patient. The balloon was introduced via the nose into the esophagus and placed at a distance varying between 40 and 45 cm from the nostril to the tip of the balloon depending on the size of the subject. The validity of the esophageal balloon technique as a measure of pleural surface pressure was assessed with the "occlusion test" (2, 5). In all patients the ratio of ΔPes/ΔPao was close to unity (range, 0.97 to 1.11), indicating that the measurements of ΔPes were a satisfactory index of the changes in pleural surface pressure.

Patients were disconnected from the ventilator and allowed to breathe room air spontaneously for 15 to 30 min. When minute ventilation, respiratory frequency, and tidal volume (VT) were stable, a series of tracheal occlusions at end-expiration were performed randomly and maintained for 3 to 4 breaths. This allowed us to estimate the elastic recoil pressure of the total respiratory system and of the chest wall at end-expiration, as previously described in detail (2). Briefly, during the terminal part of the occluded expirations all subjects exhibited a plateau (lasting between 0.2 and 0.6 s) in both Pao and Pes, representing the elastic recoil of the total respiratory system and of the chest wall, respectively (2). A representative record is shown in figure 1.

Total resistive work done on the lungs per breath (WI+ERES) was obtained by integration of the area subtended by the dynamic change in Pes and lung volume during the breathing cycle (figure 2) (6, 7). This was partitioned into inspiratory (WRES) and expiratory (WERES) components by drawing a line between the values of Pes at points of zero flow, the slope of the line representing the dynamic pulmonary compliance (CLdyn). The resistive work thus measured included work done in overcoming the flow resistance of the lungs, of the endotracheal or tracheostomy tube, and of the equipment. The total inspiratory elastic work per breath (WEL) was obtained using Campbell's diagram (6). In this analysis, we used measured values of the elastic recoil pressure of the chest wall at functional residual capacity (open circle in figure 2A) and assumed that the compliance of the chest wall (Cw) in patients with COPD is within normal limits, as described by Sharp and coworkers (8). According to Agostoni and Mead (9), in normal subjects, Cw amounts to about 4% of vital capacity per cmH_2O. In our computations of Cw, we used predicted normal values of vital capacity (10). The Cw line was then fitted on the volume-pressure diagram, by passing it through the end-expiratory elastic recoil pressure point of the chest wall (see previous discussion), and WEL was measured as the area of the volume-pressure curve subtended by the CLdyn and Cw lines (figure 2A).

Work per minute (W) was obtained by multiplying work per breath by the corresponding respiratory frequency. Work per liter of ventilation (W/V̇I) was obtained dividing Ẇ by minute ventilation (V̇I). The latter was obtained by multiplying the tidal volume and respiratory frequency measured on the same breaths used to compute the work of breathing. In the same patients we also measured mean inspiratory, $\overline{R}_L$ insp, and expiratory, $\overline{R}_L$ exp, pulmonary flow resistance. This was obtained by measuring RL at 0.1-s intervals throughout inspiration and expiration and averaging the data points (11).

Immediately preceding the measurements of work of breathing, the arterial P_{O_2} and P_{CO_2} were determined.

Regression analysis was done using the least squares method.

Results

While spontaneously breathing room air, our patients were hypoxemic and hypercapnic, the average values (± SD) of Pa_{O_2} and Pa_{CO_2} amounting, respectively, to 45 ± 9.7 and 63 ± 10 mmHg. This is in line with previous reports (2, 12).

In table 1, our results of respiratory mechanics and work of breathing are compared with those obtained in 8 apparently normal elderly subjects (4 women and 4 men) by Delhez and coworkers (13). Although the age of the normal subjects was somewhat greater than that of our patients, the data of Delhez and associates were chosen because of lack of other comparable results for elderly subjects. The average minute ventilation of the patients was within normal limits but, as previously reported (2, 12), their tidal volume (mean ± SD, 0.285 ± 0.097 L) was decreased and their respiratory frequency (30 ± 7.5 breaths/min) increased as compared with normal subjects.

Dynamic lung elastance (ELdyn), and pulmonary flow-resistance (both inspiratory and expiratory) were significantly ($r = 0.81$; $p < 0.001$) greater in the patients with COPD than in the normal elderly subjects (table 1). It should be noted that our values of pulmonary flow resistance in table 1 include the equipment resistance plus that of the endotracheal or tracheostomy tubes. Our equipment resistance was somewhat higher than that in the study of Delhez

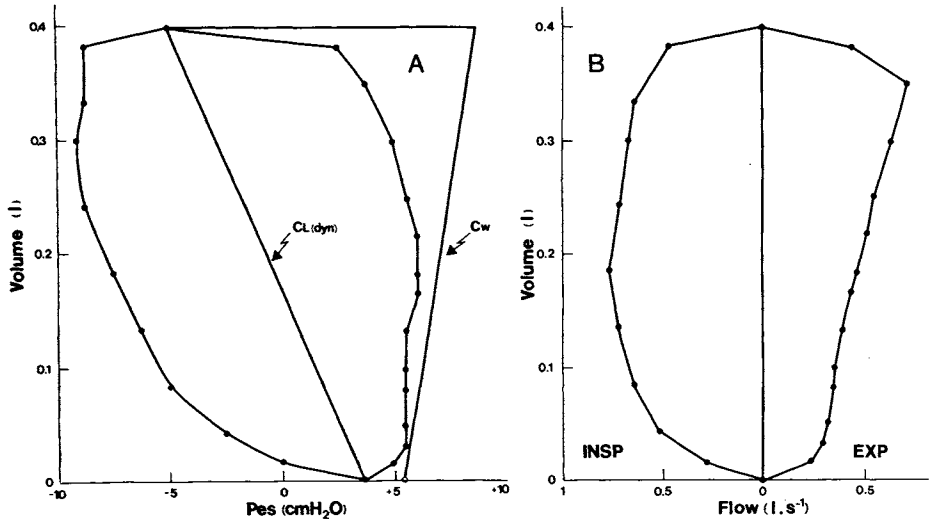


Fig. 2. A. Esophageal pressure (Pes) on the abscissa plotted against volume on the ordinate. Filled circles represent measurements made at 0.1-s intervals during a breathing cycle of a patient. CLdyn indicates the dynamic pulmonary compliance, and Cw is the static chest wall compliance. The open circle represents the elastic recoil pressure of the chest wall at end-expiration. B. Volume-flow curve corresponding to the same breathing cycle in A. For further explanation see text.

TABLE 1

ANTHROPOMETRIC, VENTILATORY, WORK OF BREATHING, AND PULMONARY MECHANICS DATA OF 11 PATIENTS WITH COPD BREATHING AIR TOGETHER WITH CORRESPONDING VALUES OF 8 ELDERLY NORMAL SUBJECTS FROM DELHEZ AND COWORKERS (13)*

	Patients with COPD	Normal Elderly Subjects	p Value
Age, yr	67 ± 11	77 ± 8	< 0.02
Height, cm	162 ± 10	155 ± 8	NS
Weight, kg	58 ± 15	67 ± 11	< 0.05
$\dot{V}_I$, L·min^{-1}	8.1 ± 2.2	8.7 ± 3.1	NS
E_{Ldyn}, cmH$_2$O·L^{-1}	36 ± 11.6	6.8 ± 2.3	< 0.0001
$\bar{R}_{Linsp}$, cmH$_2$O·L^{-1}·s	16.9 ± 7.0	3.7 ± 1.2	< 0.0001
$\bar{R}_{Lexp}$, cmH$_2$O·L^{-1}·s	23.9 ± 13.5	5.0 ± 1.7	< 0.0001
Ew, cmH$_2$O·L^{-1}	7.1 ± 1.7	7.6 ± 1.9	NS
$\dot{W}_{Itot}$, kg·min^{-1}	1.52 ± 0.36	0.76 ± 0.54	< 0.002
$\dot{W}_{Itot}/\dot{V}_I$, kg·L^{-1}	0.19 ± 0.05	0.09 ± 0.02	< 0.0001
$\dot{W}_{Ires}$, kg·min^{-1}	0.71 ± 0.20	—	
$\dot{W}_{Eres}$, kg·min^{-1}	0.57 ± 0.14	—	
$\dot{W}_I$ + Eres, kg·min^{-1}	1.27 ± 0.29	0.45 ± 0.31	< 0.0001
$\dot{W}_I$ + Eres/$\dot{V}_I$, kg·L^{-1}	0.16 ± 0.05	0.05 ± 0.02	< 0.0001
$\dot{W}_{Iel}$, kg·min^{-1}	0.82 ± 0.10	—	

* Values are mean ± SD. Statistical analysis was done using unpaired *t* test.

Definition of abbreviations: $\dot{V}_I$ = minute ventilation; E_{Ldyn} = dynamic pulmonary elastance; $\bar{R}_L$ insp = mean inspiratory pulmonary flow resistance; $\bar{R}_{Lexp}$ = mean expiratory pulmonary flow resistance; $\dot{W}_{Itot}$ = total inspiratory work per minute; $\dot{W}_{Itot}/\dot{V}_I$ = total inspiratory work per liter of ventilation; $\dot{W}_{Ires}$ = inspiratory resistive work per minute; $\dot{W}_{Eres}$ = expiratory resistive work per minute; $\dot{W}_I$ + Eres = total resistive work per minute; $\dot{W}_I$ + Eres/$\dot{V}_I$ = total resistive work per liter of ventilation; $\dot{W}_{Iel}$ = inspiratory elastic work per minute.

and coworkers (13), which amounted to about 1 cmH$_2$O·L^{-1}·s. On the other hand, in comparing our pulmonary resistance values with those of Delhez and coworkers, it should also be noted that in our patients the upper airways were bypassed, and this should have resulted in a decrease in pulmonary flow resistance of approximately 1 cmH$_2$O·L^{-1}·s. When allowance is made for these differences in equipment resistance and for bypass of the upper airways, the differences of inspiratory and expiratory $\bar{R}_L$ values between our patients with COPD and the normal subjects are reduced by only 20% approximately.

The values of total inspiratory work of breathing per minute ($\dot{W}_{Itot}$) and per liter of ventilation ($\dot{W}_{Itot}/\dot{V}_I$) were markedly increased in the patients. Both were approximately twice as large as in normal subjects. The total resistive work per minute ($\dot{W}_I$ + Eres) was approximately 3 times greater in patients than in normal subjects, and a similar increase was also found in terms of the total resistive work per liter of ventilation. Unfortunately, Delhez and coworkers (13) did not provide the separate values of inspiratory and expiratory resistive work nor of inspiratory elastic work of their normal elderly subjects, and, accordingly, a comparison with our patients is not possible. In the patients with COPD, the inspiratory elastic work represented, on the average, 54% of the total inspiratory work. Although in the patients, $\bar{R}_{Lexp}$ was substantially greater than $\bar{R}_{Linsp}$, the expiratory resistive work per minute was smaller than the inspiratory one (0.71 versus 0.57 kg·min^{-1}). This was due to the smaller expiratory flows, as shown by the representative example in figure 2B. The smaller expiratory flows reflected a longer duration of expiration (1.38 ± 0.41 s) relative to inspiration (0.74 ± 0.13 s) as well as dynamic airway compression (14, 15). Indeed, expiratory flow limitation prevented all patients from reaching the elastic equilibrium point of the respiratory system during expiration, as indicated by the fact that the elastic recoil pressure of the total respiratory system at end-expiration (i.e., relaxed tracheal pressure during occlusion at end-expiration) was not zero but positive in all patients, amounting to 8.8 ± 2.3 cmH$_2$O. This is also reflected by the fact that at end-expiration the C_{Ldyn} and Cw lines did not intercept (figure 2A) (6, 9). The positive elastic recoil of the total respiratory system at end-expiration can be defined auto-PEEP (16) or *intrinsic* PEEP (15, 17). Not surprisingly, a positive correlation ($r = 0.60$; $p < 0.05$) was found between intrinsic PEEP and $\bar{R}_{Lexp}$, indicating that the higher the latter is, the more overinflated is the patient at end-expiration.

In all of our patients, Pes during expiration was lower than the static elastic recoil pressure of the chest wall, as shown by the example in figure 2A. This suggests that expiratory muscle activity was absent (6), and is in line with a previous report on patients with COPD in acute respiratory failure (2). Furthermore, the difference between Pes during expiration and the static pressure-volume relationship of the chest wall, which was more pronounced during early expiration (figure 2A), indicates that in addition to the pressure used to overcome chest wall flow resistance, some of the elastic energy stored during inspiration was expended as negative (pliometric) work of the in-

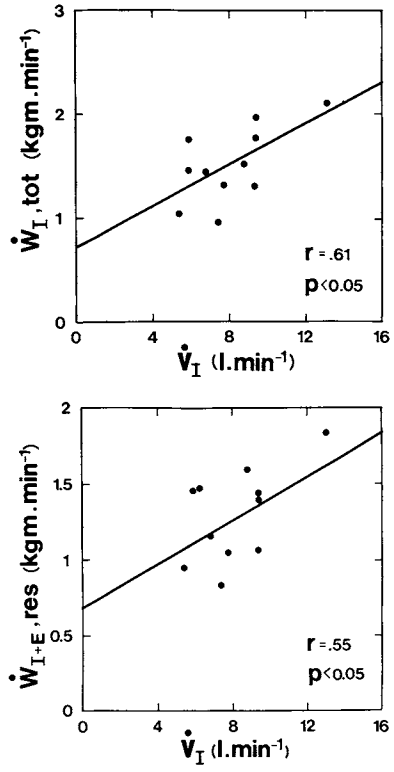


Fig. 3. *Top*. Total inspiratory work per minute ($\dot{W}_{Itot}$) plotted against minute ventilation ($\dot{V}_I$). *Bottom*. Total resistive work per minute ($\dot{W}_I$ + Eres) plotted against minute ventilation. Circles represent individual values in 11 patients with COPD. Regression lines are also shown.

spiratory muscles during expiration (6). The negative work per minute done by the inspiratory muscles during expiration, computed as the difference between $\dot{W}_{El}$ and $\dot{W}_{Eres}$ (6), amounted in the patients to 0.25 ± 0.14 kg·min^{-1} as compared with 0.34 ± 0.19 kg·min^{-1} in the subjects of Delhez and coworkers (13). It should be noted that both our data and those of Delhez and coworkers included in the negative work a small component of work required to overcome the flow resistance of the chest wall during expiration (6).

A positive correlation was found between $\dot{W}_{Itot}$ and $\dot{V}_I$ (figure 3, *top panel*), $\dot{W}_{El}$ and $\dot{V}_I$ ($r = 0.77$, $p < 0.01$), $\dot{W}_{Eres}$ and $\dot{V}_I$ ($r = 0.82$, $p < 0.001$), and $\dot{W}_I + E_{res}$ and $\dot{V}_I$ (figure 3, *bottom panel*). However, when work was expressed per liter of ventilation and plotted against $\dot{V}_I$, a significant *negative* correlation was found between $\dot{W}_{Ires}/\dot{V}_I$ and $\dot{V}_I$ ($r = -0.57$, $p < 0.05$) and between $\dot{W}_{I+E,res}/\dot{V}_I$ and $\dot{V}_I$ (figure 4, *bottom panel*). The relationships of $\dot{W}_{Itot}/\dot{V}_I$ (figure 4, *top panel*), $\dot{W}_{El}/\dot{V}_I$, and $\dot{W}_{Eres}/\dot{V}_I$ with $\dot{V}_I$ also tended to be negative, although not at a significant level.

No significant correlation was found between any of the respiratory work rate data in table 1, with E_{Ldyn}, $\bar{R}_L$ insp, and $\bar{R}_{Lexp}$. However, as shown in table 2 and figures 5 and 6, when work was expressed per liter of ventilation, significant positive correlations were found between all work per liter values and all pulmonary mechanics data in table 1, except for $\dot{W}_{El}/\dot{V}_I$, which was significantly correlated with only $\bar{R}_{Lexp}$. Because (*1*) $\dot{W}_{El}/\dot{V}_I$ has the dimensions of pressure and should reflect the elastic recoil of the total respiratory system and (*2*) because increased $\bar{R}_{Lexp}$ tends to cause pulmonary overinflation (see previous discussion), the significant correlation between $\dot{W}_{El}/\dot{V}_I$ and $\bar{R}_{Lexp}$ is not surprising. The other correlations in table 2 are readily explainable because with increased respiratory mechanical impedance (increased pulmonary elastance and flow resistance), the work per liter of ventilation would be expected to increase. In this connection, it should be noted that in our patients there was a strong, significant ($p < 0.001$), positive correlation between E_{Ldyn} and R_{Linsp}.

TABLE 2

CORRELATION COEFFICIENTS BETWEEN WORK OF BREATHING PER LITER OF VENTILATION AND PULMONARY MECHANICS DATA IN ELEVEN PATIENTS WITH COPD

	$\dot{W}_{Itot}/\dot{V}_I$ (kg·L^{-1})	$\dot{W}_{Ires}/\dot{V}_I$ (kg·L^{-1})	$\dot{W}_{Eres}/\dot{V}_I$ (kg·L^{-1})	$\dot{W}_I \times E_{res}/\dot{V}_I$ (kg·L^{-1})	$\dot{W}_{El}/\dot{V}_I$ (kg·L^{-1})
E_{Ldyn},	$r = 0.64$	$r = 0.58$	$r = 0.63$	$r = 0.72$	$r = 0.51$
$cmH_2O \cdot L^{-1}$	$p < 0.05$	$p < 0.05$	$p < 0.05$	$p < 0.01$	NS
$\bar{R}_{Linsp}$,	$r = 0.71$	$r = 0.81$	$r = 0.75$	$r = 0.88$	$r = 0.29$
$cmH_2O \cdot L^{-1} \cdot s$	$p < 0.01$	$p < 0.001$	$p < 0.01$	$p < 0.001$	NS
$\bar{R}_{Lexp}$,	$r = 0.88$	$r = 0.77$	$r = 0.81$	$r = 0.82$	$r = 0.77$
$cmH_2O \cdot L^{-1} \cdot s$	$p < 0.001$	$p < 0.01$	$p < 0.001$	$p < 0.001$	$p < 0.01$

For definition of abbreviations, see table 1.

Discussion

The rationale for using the resistive work rate as a "useful objective variable for determining the capability of independent ventilation" (1) in patients with COPD should presumably be based on the assumptions (*1*) that it reflects the severity of abnormalities in pulmonary mechanics and (*2*) that it is closely related to the energy demands (oxygen cost) of breathing. Clearly, a high O_2 cost of breathing involves susceptibility to respiratory muscle fatigue (18, 19) and leads to ventilator dependence. Accordingly, this will be discussed first.

Our results show that in patients with COPD in acute respiratory failure, the rate of mechanical work of breathing (power) is increased relative to normal subjects. However, the power output is not correlated with the severity of abnormalities in pulmonary mechanics. Indeed, in the present study, the highest value of $\dot{W}_I + E_{res}$ (1.85 kg·min^{-1}) and $\dot{W}_{Itot}$ (2.1 kg·min^{-1}) was exhibited by a patient in whom $\bar{R}_{Linsp}$ and $\bar{R}_{Lexp}$ were among the lowest. His minute ventilation, however, was the highest (13.1 L·min^{-1}). Because as a useful approximation $\dot{W}_I + E_{res} = 0.5\ \pi\ ^2[\bar{R}_{Linsp} + \bar{R}_{Lexp}]\dot{V}_I^2$ (3), it is evident that the magnitude of resistive power output depends more on minute ventilation than

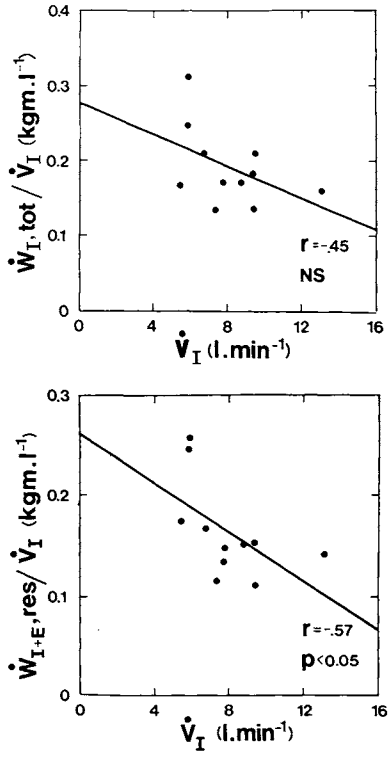


Fig. 4. *Top.* Total inspiratory work per liter of ventilation ($\dot{W}_{Itot}/\dot{V}_I$) plotted against minute ventilation ($\dot{V}_I$). *Bottom.* Total resistive work per liter of ventilation ($\dot{W}_I + E_{res}/\dot{V}_I$) plotted against minute ventilation. Circles represent individual values in 11 patients with COPD. Regression lines are also shown.

Fig. 5. Total inspiratory work per liter of ventilation ($\dot{W}_{Itot}/\dot{V}_I$) plotted against dynamic pulmonary elastance (E_{Ldyn}) (*left panel*), mean inspiratory pulmonary flow resistance, ($\bar{R}_{Linsp}$) (*middle panel*), and mean expiratory pulmonary flow resistance ($\bar{R}_{Lexp}$) (*right panel*). Circles represent individual values of 11 patients. Regression lines are also shown.

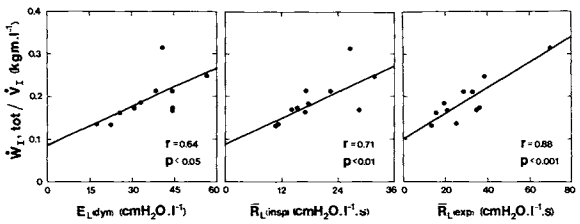
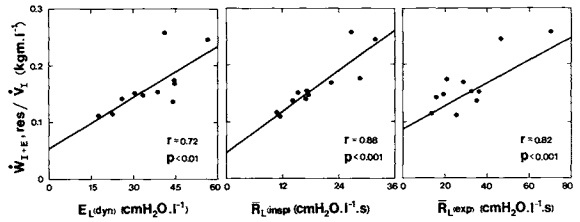


Fig. 6. Total resistive work per liter of ventilation ($\dot{W}_I + E_{res}/\dot{V}_I$) plotted against dynamic pulmonary elastance (E_{Ldyn}) (*left panel*), mean inspiratory pulmonary flow resistance ($\bar{R}_{Linsp}$) (*middle panel*), and mean expiratory flow resistance ($\bar{R}_{Lexp}$) (*right panel*). Circles represent individual values of 11 patients. Regression lines are also shown.



on resistance. On the other hand, the data of work per liter of ventilation were significantly correlated with the lung mechanics data, except for $\dot{W}_{EL}/\dot{V}_I$. Because the elastic work per liter is proportional to V_T^2 (3), the lack of a positive correlation between $\dot{W}_{EL}/\dot{V}_I$ and E_{LDYN} is not surprising in view of the fact that in our patients V_T tended to decrease with increasing E_{LDYN} ($r = -0.65$, $p < 0.05$).

Thus, the present results indicate that in patients acutely ill with COPD, both total inspiratory work per liter and resistive work per liter provide a good index of the severity of abnormalities in pulmonary mechanics, and, accordingly, these indexes could be used as one of the criteria for extubation. In this connection, it should be noted that the measurement of $\dot{W}_I + E_{RES}$ is more accurate and easier to perform than is that of $\dot{W}_{ITOT}$ (6, 7). Furthermore, in our patients the values of $\dot{W}_{ITOT}$ and $\dot{W}_I + E_{RES}$ were close and highly correlated ($r = 0.93$, $p < 0.001$). Indeed, the difference between these 2 variables is represented by the negative work done by the inspiratory muscles during expiration (including flow-resistive work done on the chest wall). This negative work was relatively small; expressed as a percentage fraction of $\dot{W}_{ITOT}$, it averaged (± SD) 17 ± 7%. Thus, in practice, the measurement of $\dot{W}_I + E_{RES}/\dot{V}_I$ appears a more simple and reliable index of abnormalities in respiratory mechanics than that of $\dot{W}_{ITOT}/\dot{V}_I$.

McGregor and Becklake (20) and, more recently, Rochester and Bettini (21) and Field and coworkers (22) have shown that the O_2 cost of breathing is more closely related to the mean pressure developed by the inspiratory muscles than to the mechanical work rate. Because $\dot{W}_{ITOT}/\dot{V}_I$ represents *the mean pressure developed by the inspiratory muscles*, this variable should more closely reflect the O_2 cost of breathing than the variable $\dot{W}_{ITOT}$. Thus, because $\dot{W}_{ITOT}/\dot{V}_I$ (and $\dot{W}_I + E_{RES}/\dot{V}_I$) more closely reflect the severity in pulmonary mechanics and the O_2 cost of breathing, the mechanical work output per liter of ventilation appears to provide a more useful index of ventilator dependence than does mechanical work rate *per se*.

Hyperinflation is typically present in patients with COPD, reflecting loss of lung recoil. During acute respiratory failure, as a result of increased respiratory frequency (2, 12), the time available to breathe out during expiration decreases, and, consequently, there must be a further increase in lung volume (23). In fact, in our patients, the respiratory frequency averaged (± SD) 30 ± 7.5 breaths/min, whereas the corresponding values of expiratory duration were 1.38 ± 0.42 s. This rapid breathing pattern, associated with expiratory flow limitation (15), resulted in the presence of intrinsic PEEP at the end of spontaneous expirations in all of our patients. This is in line with previous reports on both spontaneously breathing (2, 14) and mechanically ventilated (14–16) patients with COPD in acute respiratory failure.

It should be stressed that in the present study we made no specific attempt to assess the usefulness of $\dot{W}_{ITOT}/\dot{V}_I$ (or of other variables) in terms of ventilator-dependence. Clearly, however, variables other than abnormalities of pulmonary mechanics must also be taken into account (e.g., maximal inspiratory pressures available, respiratory timing, etc.) (24, 25). To these, intrinsic PEEP should be added. In fact, the presence of intrinsic PEEP in our 11 patients implies that in addition to the pressure required to produce the actual breathing movements, their inspiratory muscles had to develop a pressure ranging between 6 and 13 cmH_2O in order to overcome the intrinsic PEEP. In this respect, the latter can be considered as an inspiratory threshold load (26, 27). This additional pressure requirement implies a substantial burden on the inspiratory muscles whose performance as pressure generators is already impaired by pulmonary hyperinflation (14, 23, 28, 29) and by the relatively old age (67 ± 11 yr).

Martin and associates (30) and Muller and coworkers (31) were able to induce hyperinflation in normal subjects and asthmatics by histamine inhalation. Surprisingly, they found that this was not due merely to the increase in airways resistance and respiratory frequency but was caused in part by persistent tonic activity of the inspiratory muscles. In our patients, tonic inspiratory muscle activity was probably not present, as indicated by the fact that during late expiration dynamic Pes closely corresponded to the predicted static volume-pressure relationships of the chest wall (figure 2A), the small discrepancy between dynamic and static Pes probably reflecting the resistive pressure of the chest wall (6). Although plausible, this conclusion has to be accepted with some reservations in view of the fact that our static volume-pressure relationships for the chest wall were assumed and not measured.

Finally, it should also be noted that intrinsic PEEP can lead to decreased cardiac output (16), and hence failure to recognize the hemodynamic consequence of intrinsic PEEP can lead to inappropriate fluid restriction or unnecessary vasopressor therapy. The intrinsic PEEP, however, can be detected and quantified by a simple bedside maneuver, namely, end-expiratory occlusion during spontaneous expiration (figure 1) (2) or at the end of the exhalation period set by the ventilator (16).

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