Measurement of pulmonary resistance and dynamic compliance with airway obstruction

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Officer, Todd M., Riccardo Pellegrino, Vito Brusasco, and Joseph R. Rodarte. Measurement of pulmonary resistance and dynamic compliance with airway obstruction. J. Appl. Physiol. 85(5): 1982–1988, 1998.—We compared four algorithms by using least squares regression for determination of pulmonary resistance and dynamic elastance in subjects with emphysema, normal subjects, and subjects with asthma before and after bronchoconstriction. The four methods evaluated include 1) a single resistance and elastance, 2) separate resistances and elastances for each half breath, 3) separate inspiratory and expiratory resistances with a single elastance, and 4) separate inspiratory and expiratory resistances, an expiratory volume interaction term, and a single elastance. All methods gave comparable results in normal and asthmatic subjects. We found expiratory resistance was larger than inspiratory resistance in normal and asthmatic subjects during control conditions, but inspiratory resistance was higher than expiratory resistance in subjects who experienced severe bronchoconstriction in response to methacholine. In subjects who are flow limited, method 2 gives a higher inspiratory resistance than would be computed by assuming that the elastic pressure-volume curve passes through the zero-flow points. Methods 1 and 3 overestimate dynamic elastance and inspiratory resistance. Method 4 appears to identify flow limitation and dynamic hyperinflation and gives a good measure of inspiratory resistance and dynamic elastance.

least squares; lung mechanics; asthma; chronic obstructive pulmonary disease; flow limitation

INTEREST IN THE MECHANISMS by which airway inflammation produces airflow limitation in asthma (11) and the role of intrinsic airflow disease vs. loss of recoil as a predictor of surgical response in emphysema (17) has contributed to a recent renewal of interest in lung mechanics. The concept of pulmonary resistance (RL) and dynamic compliance (Cdyn) or its reciprocal elastance (Edyn) implies that the pressure loss across the lung can be divided into a dissipative component and a convective component in phase with the flow and into an elastic component in phase with the volume (6, 15). Classically, the dissipative component, or resistance, is considered to occur between the airway opening and the alveoli due to frictional pressure losses in the flow and convective acceleration, and the elastic component is considered to occur between the alveoli and the pleural surface (3, 8, 15, 20). It is known that this model is an approximation and that the pressure losses in the airways are different on inspiration and expiration, are dependent on lung volume, and are nonlinear functions of flow. Pulmonary compliance is also a function of volume, and a substantial part of total pressure difference occurs between the alveolar and pleural pressures and is caused by lung viscoelastic and viscoplastic behavior (5, 11). Nevertheless, measurements of RL and pulmonary compliance during spontaneous breathing are sensitive indexes of lung mechanics. However, with severe airway obstruction, maximal expiratory flow (V˙E) in the normal tidal breathing volumes is inadequate for the subjects' ventilatory needs, and subjects develop dynamic hyperinflation (9) and intrinsic positive end-expiratory pressure (PEEP) (1). When this occurs, fitting RL and Cdyn by least squares from an entire breath produces a falsely low Cdyn. If separate inspiratory and expiratory RL (RLi and RLe, respectively) are determined, RLi is overestimated and RLe is underestimated. In this study, we present a new algorithm for analyzing quiet breathing that computes compliance and RLi values which are not significantly different from these obtained from analyzing only the inspiratory portion of the breath and that detects a volume dependence of RLe which is highly correlated with V˙E limitation.

METHODS

Seven asthmatic subjects, seven healthy subjects, and 19 subjects with chronic obstructive pulmonary disease (COPD) caused by emphysema were studied. The asthmatic and COPD subjects were currently smoking: 1/6, 1/6, and 0/19, respectively. Anthropometric characteristics of subjects are given in Table 1.

Table 1. Anthropometric characteristics of subjects

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Normal Subjects</th>
<th>Asthmatic Subjects</th>
<th>COPD Subjects</th>
</tr>
</thead>
<tbody>
<tr>
<td>n</td>
<td>7</td>
<td>7</td>
<td>19</td>
</tr>
<tr>
<td>Age, yr</td>
<td>39 ± 5</td>
<td>30 ± 2</td>
<td>61 ± 2</td>
</tr>
<tr>
<td>Gender (M/F)</td>
<td>7/0</td>
<td>6/1</td>
<td>14/5</td>
</tr>
<tr>
<td>FEV₁, %predicted</td>
<td>99 ± 5</td>
<td>80 ± 6</td>
<td>25 ± 8</td>
</tr>
<tr>
<td>Height, cm</td>
<td>180 ± 2</td>
<td>174 ± 3</td>
<td>172 ± 2</td>
</tr>
<tr>
<td>Current smoker (yes/no)</td>
<td>1/6</td>
<td>1/6</td>
<td>0/19</td>
</tr>
</tbody>
</table>

Values are means ± SE. COPD, chronic obstructive pulmonary disease; M, male; F, female. FEV₁, forced expiratory volume in 1 s.
normal subjects were included in a previous study (12). The subjects' anthropometric data are shown in Table 1. One normal subject and one asthmatic subject were moderate smokers. The illnesses of asthmatic and COPD subjects were diagnosed on the basis of the criteria of the American Thoracic Society (2). All subjects were clinically stable at the time of the study, and the asthmatic subjects had stopped use of bronchodilators for $\geq 24$ h before tests were conducted. The protocol for normal and asthmatic subjects was approved by the Institutional Review Board, and each subject gave written consent. All COPD subjects had ceased smoking $\geq 6$ mo before the study, and all were being evaluated for lung volume reduction or lung transplantation.

Fig. 1. Pressure-volume relationship in normal subject. A: baseline; B: after maximal dose of methacholine (MCh). For each plot, $y$-axis is transpulmonary pressure (Ptp; in cmH₂O) and $x$-axis is volume (in liters) relative to functional residual capacity (FRC). RL, pulmonary resistance; RLi, RL, inspiratory and expiratory RL, respectively; RLe, volume interaction term. Top left: whole-breath method (method 1); top right: half-breath method (method 2). Bottom left: whole-breath method $RL + RLe$ method (method 3); bottom right: whole-breath $RLi + RLe + RLei$ method (method 4). $\circ$, Recorded data; solid line through the $\circ$, estimated pressure fit; $\ast$, zero-flow points; dashed line, connects zero-flow points at start of inspiration to end of inspiration. Thick solid line, estimated elastance from each method, as described above. For the half-breath method, thick solid line represents elastance of inspiration; dotted line represents elastance of expiration. In this normal individual, all methods fit the data well, and elastic pressure computed from dynamic elastance does not differ greatly from line connecting zero-flow points. After MCh (B), amplitude of pressure-volume loop doubles. Two elastances determined from half-breath method are quite different. Inspiratory pressure-volume relationship from single-resistance method 1 but passes through zero-flow points in method 3 from which RLe is greater than RLi. Method 4 fits data well.

Fig. 2. Pressure-volume relationship in asthmatic subject. A: baseline; B: after maximal dose of MCh. Symbols are same as in Fig. 1. A: dynamic elastance during inspiration in method 2 and methods 1, 3, and 4 is very similar to dashed line connecting zero-flow points. Computed elastic pressure-volume relationship is displaced toward expiratory side of loop in single-resistance method 1 but passes through zero-flow points in method 3 from which RL is greater than RLi. B: computed elastic pressures are quite different during inspiration and expiration with the half-breath method 2. Elastic pressure with method 3 is significantly different from line connecting zero-flow points, causing a higher RLi and lower RLe. Method 4 fits data well. Elastic pressure computed from method 4 differs slightly in this breath from line connecting points of zero flow, but it was not different when averaged across several breaths. Ptp at FRC is increased, because this subject had substantial increase in FRC during MCh-induced bronchoconstriction.
Fig. 3. Pressure-volume relationship in patient with emphysema. Symbols are same as in Fig. 1. Methods 1 and 3, while fitting to the pressure-volume data reasonably well, overestimate width of loop at high lung volumes and underestimate it at low lung volumes. Elastance is much greater than slope of dashed line connecting zero-flow points because of reduced estimate of elastic recoil at FRC.

Table 2. Summary data

<table>
<thead>
<tr>
<th>Condition</th>
<th>Method 1</th>
<th>Method 2</th>
<th>Method 3</th>
<th>Method 4</th>
<th>Zero Elastance Method</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>( R_L )</td>
<td>( E_{dyn} )</td>
<td>( R_{Li} )</td>
<td>( E_{dyni} )</td>
<td>( R_{Le} )</td>
</tr>
<tr>
<td>Normal</td>
<td>1.59</td>
<td>3.05</td>
<td>1.43</td>
<td>3.46</td>
<td>2.11</td>
</tr>
<tr>
<td>Normal +</td>
<td>±0.24</td>
<td>±0.44</td>
<td>±0.22</td>
<td>±0.43</td>
<td>±0.38</td>
</tr>
<tr>
<td>MCh</td>
<td>6.56</td>
<td>6.9</td>
<td>7.38</td>
<td>6.47</td>
<td>8.28</td>
</tr>
<tr>
<td>Asthmatic</td>
<td>±0.94</td>
<td>±1.28</td>
<td>±3.17</td>
<td>±1.13</td>
<td>±2.3</td>
</tr>
<tr>
<td>Asthmatic +</td>
<td>3.39</td>
<td>5.13</td>
<td>3.49</td>
<td>5.14</td>
<td>4.66</td>
</tr>
<tr>
<td>COPD</td>
<td>±0.77</td>
<td>±0.63</td>
<td>±0.78</td>
<td>±0.67</td>
<td>±0.95</td>
</tr>
</tbody>
</table>

Values are means ± SE. \( R_L \), lung resistance (in cmH\(_2\)O l\(^{-1}\) s\(^{-1}\)); \( R_{Li} \), inspiratory and \( R_{Le} \), expiratory \( R_L \), respectively; \( E_{dyn} \), dynamic elastance (in cmH\(_2\)O l\(^{-1}\) s\(^{-1}\)); \( E_{dyni} \), inspiratory and \( E_{dyn} \), expiratory elastance, respectively; MCh, methacholine; \( E_{dyn} \), volume interaction term.
forced to zero during expiration, the \( \dot{V}_E \) is forced to zero during inspiration, and the data are fitted to the equation

\[
P_{tp} = P_{L\text{FRC}} + Edyn \cdot V + R_{L_i} \cdot \dot{V}_i + R_{L_e} \cdot \dot{V}_E
\]

Method 4. Whole-breath \( R_{L_i} + R_{L_e} + R_{L_e} \). This method examines the whole breath, as in method 3, with the addition of a \( R_{L_e} \) term. This additional term will account for the increasing resistance during expiration in subjects with dynamic hyperinflation. The \( R_{L_e} \) term measures an interaction between volume and resistance during expiration. After determining the zero-flow points, the data are fit to the equation

\[
P_{tp} = P_{L\text{FRC}} + Edyn \cdot V + R_{L_i} \cdot \dot{V}_i + (R_{L_e} + R_{L_e} \cdot V) \cdot \dot{V}_E
\]

(5)

For comparison, a zero-elastance method is also included. This method looks only at the inspiratory portion of the breath. A pressure-volume (PV) relationship is determined between the points of zero flow at the beginning of inspiration and end of inspiration. This elastance volume is then subtracted from the inspiratory pressure to give a pressure-flow curve. This leads to the equation

\[
P_{tp} - Edyn \cdot V = R_{L_i} \cdot \dot{V}_i
\]

Again, the least squares method is used to determine the \( R_{L_i} \) and the intercept term is forced to zero by reflecting the data around the intercept.

Inhalation challenge. Subjects from both the normal and asthmatic groups were requested to undergo bronchial challenges with methacholine (MCh). After diluent, MCh was delivered in doubling concentrations through a dosimeter (Rosenthal) with a manually triggered solenoid valve that was electronically controlled to deliver compressed air at 20 psi for 1 s. Each dose of aerosol was delivered during five breaths taken from FRC to total lung capacity. The starting concentrations of agents were 0.125–0.5 mg/ml for asthmatic subjects and 1–5 mg/ml for normal subjects. The challenge ended when maximal flow at 50% vital capacity (VC) was decreased by 60% or at a concentration of MCh of 320 mg/ml.

After breaths were recorded for \( R_L \) and \( Edyn \) data in normal and asthmatic subjects, a partial forced expiration was performed from ~70% of VC to determine whether subjects were flow limited at end expiration. In COPD patients, a moderate increase in expiratory effort was initiated at start of expiration to determine whether subjects were flow limited. Increased effort with constant \( \dot{V}_E \) was determined by an increased \( P_{tp} \).

RESULTS

A typical breath from three subjects is displayed in Figs. 1-3. Each of these figures contains four subplots for the same breath of one subject as determined by using the different methods of estimation for the \( R_L \) and \( Edyn \). Figure 1A shows data from a 58-yr-old normal male, and Fig. 1B shows data from the same subject after a MCh challenge. Figure 2A is a typical breath from a 24-yr-old asthmatic male subject during an asymptomatic period, and Fig. 2B is the same

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**Fig. 4.** Resistance of each subject by other methods compared with inspiratory half-breath method. ○, Normal subjects; *, normal subjects after MCh; □, subjects with chronic obstructive pulmonary disease (COPD); Δ, asthmatic subjects; ○, asthmatic subjects after MCh. Dashed line is line of identity. Both x- and y-axes are in units of cmH₂O·l⁻¹·s⁻¹. A: method 1 (whole-breath \( R_L \)). B: method 3 (whole-breath \( R_{L_i} \) and \( R_{L_e} \)). C: method 4 (whole-breath \( R_{L_i} + R_{L_e} + R_{L_e} \)).
individual after a MCh challenge. Figure 3 shows data from a 52-yr-old female with severe hyperinflation and airway obstruction that were predominantly caused by emphysema.

Summary data are given in Table 2 and Figs. 4 and 5. The R_Li computed by the zero-elastance method is underestimated compared with computation by method 2. The relationships between R_Li from the inspiratory half breath (method 2) to the R_L of method 1 and R_Li of methods 3 and 4 are shown in Fig. 4, A-C, respectively. The relationships between inspiratory elastance from the inspiratory half breath (method 2) and elastance from methods 1, 3, and 4 are shown in Fig. 5, A-C, respectively.

In the normal and the asthmatic subjects before MCh, all methods gave similar results for both resistance and elastance. After MCh, the normal individuals whose resistance increased to >10 cmH_2O·l^{-1}·s and all the asthmatic subjects tended to have a lower total R_L or R_Li by all methods other than the half-breath R_Li. In contrast, in normal and asthmatic subjects, the elastance values, as determined by methods 2 and 3, were fairly comparable, although the fit was best with method 4. Table 3 gives the mean R^2 for the fits obtained by each model in each group of subjects.

The COPD patients tended to have higher R_L and dramatically higher elastance with methods 1 and 3 than with the half-breath method. Method 4 provides good agreement with the half-breath elastance. The R_Li tends to be lower than with the half-breath method. However, R_Li by method 4 agrees much better with the zero-elastance method (Table 2).

None of the normal or asthmatic subjects at baseline was flow limited, as determined by the partial flow-volume curve, and their values for R_L^e were small and variable. Normal subjects whose partial flows after MCh impinged on the control tidal breathing flow-volume relationship increased their FRC, as evidenced by significant decrease in inspiratory capacity, and they had substantial decreases in R_L^e, as shown in Fig. 6. Two of the asthmatic subjects had R_L^e at baseline of less than 5 cmH_2O·l^{-1}·s, and all subjects had decreases in inspiratory capacity (IC) and R_L after MCh. An increasing magnitude of R_L^e is associated with increasing dynamic hyperinflation, as shown by the correlation with decreasing IC.

**DISCUSSION**

The model of a constant R_L and elastance is a useful approximation of the respiratory system properties which are sensitive to changes in lung mechanics (6, 15). Resistive pressure drop is close to the magnitude of cardiogenic oscillation in Ptp; therefore, the R^2 for normal subjects is lower than during bronchoconstriction. The R^2 by all methods was between 0.61 and 0.96 in normal subjects. In all others, the linear regression
models reported in this study give $R^2$ values in excess of 0.80. Method 4, which has the most parameters to fit consistently, gave the highest values of $R^2$ (>0.95) during bronchoconstriction, so it would be difficult to get a substantially better fit by adding additional terms to address the known nonlinearities in the pressure-flow and PV curves (18). The use of regression analysis to fit an elastance for the entire PV in normal individuals yields the same data as the ratio of the difference in pressure and volume at points of zero flow but is less variable than the two-point method, which is more sensitive to cardiogenic oscillations in the pressure.

During airway obstruction, flow limitation causes varying nonlinear pressure-flow relationships which affect the estimate of elastance and the partitioning of $R_L$ and $R_E$ when using least squares curve fitting. We arbitrarily chose to use a regression equation fitted to the inspiratory half-breath as our standard for comparison rather than use the elastic PV relationship from the zero-flow method and fit a resistance to the pressure difference from that PV relationship. In the normal and asthmatic subjects before MCh, the derived elastic PV relationships were essentially the same as the line connecting zero-flow points (Figs. 1A and 2A). However, during severe bronchoconstriction in both the normal subjects and, more dramatically, in the asthmatic subjects, nonlinearities in the pressure-flow relationships (15) are accommodated by an elastance from the half-breath method, which may be similar to that derived by the two-point method, but a PV relationship is consistently displaced toward the expiratory side of the PV loop (Figs. 1B and 2B). Therefore, those normal subjects who had large increases in $R_L$ after MCh (and all asthmatic subjects after MCh) had an overestimate of their $R_L$ when calculated by the half-breath method (Fig. 4).

$V_e$ limitation causes a very nonlinear pressure-flow relationship. One might expect that expiration would be best fit by a resistance like the Rohrer equation, in which pressure drop was proportional to both $V$ and $V$ squared (16). However, in severe airway obstruction, particularly in COPD patients in whom $R_L$ was relatively low and maximal $V$ was very low, the area of the loop which represents flow-resistive work was wider near FRC, when $V$ is low, than near end inspiration, when $V$ is high. These individuals were flow limited during most of their tidal breath. They were dynamically hyperinflated, with substantial intrinsic PEEP. The slope of the expiratory pressure-flow curve near zero flow may be the same as that of the inspiratory pressure-flow curve. However, the positive pleural pressure produced by the passive recoil of their hyperinflated chest wall, plus any expiratory muscle activity, may be 5–7 cmH₂O near end expiration, which exceeds the maximal pressure required to achieve maximal $V$. When this pressure is divided by the maximal $V$ of 0.1–0.2 l/s, the apparent $R_L$ ranges from 25 to 70 cmH₂O·l⁻¹·s⁻¹. The $R_L$ term in the emphysema patients was large and negative, so that $R_L$ ($R_L + R_E$, $V$) was very large near end expiration and decreased dramatically to approximate $R_L$ at the beginning of expiration. Using least squares regression, Peslin and associates (13) found, in subjects who were not flow limited, that adding nonlinear pressure-flow, or PV relationships, or volume dependence of resistance did not materially improve the fit obtained with only resistance and compliance. None of their methods fits data from flow-limited patients, but they did not test a term for volume dependence of only $R_E$.

When the $R_E$ term is not employed, the computed pressure-elastic volume curve is biased toward positive pleural pressure values near end expiration. This produces an overestimate of elastance and $R_L$ and is more marked in the patients with end-stage COPD, who have high levels of intrinsic PEEP, than in asthmatic subjects during MCh challenge who have high resistance but are only encroaching on maximal flow near FRC. Thus asthmatic subjects have lower values of $R_L$ during bronchoconstriction (see Table 2).

In normal and mildly bronchoconstricted individuals, $R_E$ is not significantly different from zero. In a previous study (12) describing the response to MCh in the same asthmatic subjects who participated in the present study, we reported that, during severe bronchoconstriction, asthmatic subjects had higher $R_L$ than $R_E$. We attributed that result to the bronchodilatory effect of tidal inspiration that reduced bronchoconstric-
tion on the subsequent expiration. These individuals also had marked increases in elastance. At that time, we considered the possibility that our computed elastance was biased toward the chest wall PV curve near end expiration, thus artificially increasing both the elastance and the RL. Using method 4 in the present study, we recomputed the RL and RL in those subjects who had RL in excess of 10 cmH2O·l−1·s after MCh. This analysis (Table 2) confirms a dramatic increase in elastance with bronchoconstriction and an RL greater than the RL at midtidal volume (VT)

\[ \text{RL} \times (\frac{\text{RL} \cdot \text{VT}}{2}) \]

In subjects with induced bronchoconstriction, maximal V is very sensitive to end V (4, 11, 21). Standard partial flow-volume curves initiated from 70% VC are usually above end-inspiratory volume, which may result in bronchodilatation that underestimates the amount of flow limitation on the previous tidal respiration (11). Flow limitation can be documented by suddenly applying a negative pressure at the mouth (7) or by inducing a brief voluntary increase in expiratory effort, as we did with the emphysema patients in this study. However, our experience to date suggests that a substantial negative RL term is indicative of VE limitation and intrinsic PEEP. Determination of RL requires no additional manipulation in patients who have an esophageal balloon in place. These data also demonstrate the potential of overestimating the Edyn in the presence of flow limitation if the expiratory portion of the breath is included without adjustment for the volume dependence of RL.

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