Evaluation of pulmonary resistance and maximal expiratory flow measurements during exercise in humans

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Beck, Kenneth C., Robert E. Hyatt, Panagiotis Mpougas, and Paul D. Scanlon. Evaluation of pulmonary resistance and maximal expiratory flow measurements during exercise in humans. J. Appl. Physiol. 86(4): 1388-1395, 1999.—To evaluate methods used to document changes in airway function during and after exercise, we studied nine subjects with exercise-induced asthma and five subjects without asthma. Airway function was assessed from measurements of pulmonary resistance (Rl) and forced expiratory vital capacity maneuvers. In the asthmatic subjects, forced expiratory volume in 1 s (FEV1) fell 24 ± 14% and Rl increased 176 ± 153% after exercise, whereas normal subjects experienced no change in airway function (Rl -3 ± 8% and FEV1 -4 ± 5%). During exercise, there was a tendency for FEV1 to increase in the asthmatic subjects but not in the normal subjects. Rl, however, showed a slight increase during exercise in both groups. Changes in lung volumes encountered during exercise were small and had no consistent effect on Rl. The small increases in Rl during exercise could be explained by the nonlinearity of the pressure-flow relationship and the increased tidal breathing flows associated with exercise. In the asthmatic subjects, a deep inspiration (DI) caused a small, significant, transient decrease in Rl 15 min after exercise. There was no change in Rl in response to DI during exercise in either asthmatic or nonasthmatic subjects. When percent changes in Rl and FEV1 during and after exercise were compared, there was close agreement between the two measurements of change in airway function. In the groups of normal and mildly asthmatic subjects, we conclude that changes in lung volume and DI's had no influence on Rl during exercise. Increases in tidal breathing flows had only minor influence on measurements of Rl during exercise. Furthermore, changes in Rl and in FEV1 produce equivalent indexes of the variations in airway function during and after exercise.

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taking inhaled or oral corticosteroid medications and were asked to withhold inhaled β-agonists for 12 h before each study. Subjects in the asthma group were screened for exercise-induced asthma by using an incremental exercise protocol on a stationary cycle ergometer while breathing dry room air as described previously (3). All subjects completed the two additional exercise studies on separate days within a 2-wk period. The subjects with asthma were asymptomatic at the time of study.

Spirometry

Spirometry was performed with the subject wearing a noseclip and connected directly by a mouthpiece to a screen-type pneumotachograph with a \( \pm 2 \) cmH\(_2\)O differential pressure transducer. The transducer signal was digitized at a rate of \( 100 \) s\(^{-1}\), and the flow data were digitally linearized (34) and then integrated to produce the volume signal. The pneumotachograph was calibrated before each study by using a 3-liter air-filled syringe. Integrated volumes were required to be within \( \pm 3\% \) of the syringe volume across a range of flows from \( \sim 0.5 \) to \( \sim 6.0 \) l/s. To correct flow and volume measurements to BTPS conditions, expired temperature was assumed to be 28–32°C, saturated (18), the actual value being adjusted to be within \( \pm 3\% \) of the syringe volume across a range of flows. Before data analysis, data for each breath were inspected on a plot of volume vs. Ptp, and breath volumes that did not match at end expiration compared with the volume to Ptp between points of zero flow at end inspiration and end expiration. RL,MW was obtained by linear regression of flow vs.

\[
\Delta P_{\text{tp}} = \frac{\Delta V_L}{C_L,dyn} + V \cdot C_L,MW
\]

where \( \Delta V_L \) and \( \Delta P_{\text{tp}} \) indicate the change in lung volume and Ptp during the breath, respectively, and \( V \) indicates mouth flow. \( C_L,dyn \) was obtained by taking the ratio of the tidal volume to \( \Delta P_{\text{tp}} \) between points of zero flow at end inspiration and end expiration. RL,MW was obtained by linear regression of flow vs.

\[
R_{L,\text{iso}} = \frac{P_{\text{tp},E} - P_{\text{tp},I}}{V_{E} - V_{I}}
\]

where \( P_{\text{tp},E} - P_{\text{tp},I} \) and \( V_{E} - V_{I} \) refer to the differences in Ptp and V between inspiration and expiration at a given volume below TLC. Because these points were picked according to the volume, the flow was unconstrained and likely increased with exercise. To assess the effects of increasing tidal breathing flows on \( R_{L,\text{iso}} \), we used isovolume pressure-flow (IVPF) curves to model changes in \( R_{L,\text{iso}} \) that would be expected because of the increase in airflows during exercise, as described in the Appendix.

Exercise Evaluations

Exercise studies were performed on an electrically braked stationary cycle ergometer. The inspiratory port of the breathing valve was connected to a large gas bag (weather balloon) that was kept inflated by dry gas from a compressed-air cylinder. Dry air at room temperature has been shown to be nearly as effective as cold, dry air in inducing bronchospasm after exercise (1, 8, 14, 29). All subjects completed an initial screening evaluation as described previously (3), followed on different days by a submaximal exercise study (see below).

Submaximal Exercise

Six-minute periods of constant-load exercise of moderate intensity (60–65% of the subject’s maximal capacity, from the initial evaluation) were utilized. After preexercise spirometry, IVPF curve generation, and baseline RL measurements, the external power output was set to a low value for a 3-min warm-up period, followed by 6 min at the target exercise intensity and finally 3 more min at low intensity for a cool-down period. Two 3-min continuous recordings of mouth flow, integrated volume, and pressures were obtained, starting 1.5 min before power output was increased to the target level and starting 1.5 min before cool-down. A full inflation to TLC followed by an FVC maneuver was performed at the beginning and end of these recordings to obtain the reference volumes at full inflation used for drift correction and for spirometry data. Thus each 3-min recording interval spanned a change in exercise intensity and allowed determination of spirometry and RL late in warm-up, early and late in exercise, and early in the postexercise period. Spirometry and 2-min
Table 1. Physiological characteristics of subjects

<table>
<thead>
<tr>
<th></th>
<th>Asthmatic Subjects</th>
<th>Nonasthmatic Subjects</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>(n=9)</td>
<td>(n=5)</td>
</tr>
<tr>
<td>FVC, liters</td>
<td>4.74±1.01</td>
<td>5.19±0.51</td>
</tr>
<tr>
<td>%Pred</td>
<td>97±11%*</td>
<td>104±11%</td>
</tr>
<tr>
<td>PEF, l/s</td>
<td>7.71±1.75</td>
<td>11.79±1.74</td>
</tr>
<tr>
<td>%Pred</td>
<td>93±15%*</td>
<td>135±15%</td>
</tr>
<tr>
<td>FEV1, liters</td>
<td>3.10±0.74</td>
<td>4.36±0.57</td>
</tr>
<tr>
<td>%Pred</td>
<td>77±12%*</td>
<td>107±12%</td>
</tr>
<tr>
<td>FEF50, l/s</td>
<td>2.37±0.85</td>
<td>5.07±1.21</td>
</tr>
<tr>
<td>%Pred</td>
<td>48±13%*</td>
<td>101±13%</td>
</tr>
<tr>
<td>RL, iso, cmH2O·l⁻¹·s</td>
<td>3.50±1.87</td>
<td>2.01±0.40</td>
</tr>
<tr>
<td>RL, iso, cmH2O·l⁻¹·s</td>
<td>3.72±2.40</td>
<td>2.11±0.38</td>
</tr>
<tr>
<td>IC, liters</td>
<td>3.17±0.80</td>
<td>3.39±0.24</td>
</tr>
</tbody>
</table>

Values are means ± SD. n, No. of subjects. FVC, forced vital capacity; PEF, peak expiratory flow; FEV1, forced expiratory volume in 1 s; FEF50, forced expiratory flows at 50% of expired FVC; RL, MW and RL, iso: pulmonary resistance by Mead and Whittenberger (25) and isovolume technique, respectively; IC, inspiratory capacity. Predicted (Pred) values from Miller et al. (26) and Knudson et al. (17).

*Significant difference between groups, unpaired t-test, P < 0.01.

RESULTS

Physiological Characteristics of Subjects (Table 1)

Compared with the nonasthmatic subjects, the asymptomatic asthmatic subjects had lower expiratory flows (P < 0.01), particularly FEF50, and there was a nonsignificant tendency for the asthmatic subjects to have higher RL, MW and RL, iso (P > 0.1). The asthmatic subjects experienced a drop in FEV1 averaging −24 ± 14% (P < 0.01) and an increase in RL, MW of 176 ± 153% after exercise at 60%–65% of their maximal work rate. Normal subjects showed no significant change in either FEV1 (−4 ± 5%) or RL, MW 1(−3 ± 8%).

Effects of Lung Volume on RL

The effects of lung volume on RL were evaluated by plotting the inverse slope of the preexercise IVPF curves (1/K, Eq. A1 in the APPENDIX, which has units of resistance) against lung volume below total lung capacity (TLC) in asthmatic (A) and nonasthmatic subjects (B). With exception of 1 person with asthma, IVPF curve slopes were not strongly dependent on lung volume (Vl) within range investigated here. Dotted lines, predicted changes in pulmonary resistance (RL) with lung volume (Vl) with lung volume (15); arrows on volume axes, average lung volumes, where RL was measured by isovolume method (RL, iso) at rest (R) and with exercise (Ex).

Effect of Changing Airflows on RL

Figure 2 compares mean values for RL, iso (○), RL, MW (■), and the modeled change in RL, iso (dotted lines; based on IVPF curves, APPENDIX) during exercise and in the postexercise period. In both asthmatic and nonasthmatic subjects, RL, iso increased slightly during exercise compared with preexercise, but the increase in RL, iso did not attain significance in either group (P > 0.10). RL, MW stayed constant in the asthmatic subjects but fell slightly (P < 0.05) in the normal subjects. RL, iso was expected to increase slightly with increasing tidal breathing flows, on the basis of the shape of the IVPF curve (dashed curve). Note that RL, MW is determined in a constant range of flow (±1 l/s) and is therefore not expected to be affected as much by changes in tidal breathing flows. After exercise, the marked increase in...
RL,iso and RL,MW in the asthma group demonstrates induced bronchoconstriction. In the normal subjects, RL,iso followed the pattern predicted by the IVPF curve model after exercise, indicating no overall change in airway function, and RL,MW returned to preexercise values.

Effects of DI on RL

The average RL,MW and RL,iso before and 30–60 s after DI at rest and during and after exercise are shown for each group in Fig. 3. In eight of the nine asthmatic subjects, DI caused a slight increase in RL,MW and RL,iso before exercise, although both changes just failed to reach significance by paired t-test (P > 0.05).

DI caused a transient but statistically significant decrease in RL,iso and RL,MW when measured 15 min after exercise in the asthmatic subjects.

Changes in Forced Expiratory Flows and RL During and After Exercise

Mean data for spirometric variables are shown in Fig. 4. In the asthma group, there was a nonsignificant trend for forced expiratory flows to increase during exercise but a significant decrease in flows (FEV1, −24 ± 14%) occurred after exercise. A possible mechanism for an increase in forced expiratory flows would be a slightly reduced effort by the subjects, leading to paradoxical increase in flows (19). The
average Ptp generated by the asthmatic subjects at PEF were the same during exercise (−114 ± 50 cmH2O) compared with preexercise (−115 ± 48 cmH2O), indicating a similar degree of effort in the early part of the forced expiratory maneuver in both conditions. The normal subjects showed a transient decline in FEV1 at one point during exercise (P < 0.05) not reflected in the PEF or FEF50, but no significant changes were seen after exercise.

Mean data for RL are shown in Figs. 2 and 3. The changes in RL,iso and RL,MW in the asthma group were small and not statistically significant during exercise, similar to the spirometry data. The asthmatic subjects experienced a considerable increase in both RL,iso and RL,MW after exercise (RL,MW 176 ± 153%), also consistent with the decline in spirometric flows. There was good agreement between the two indexes of changes in airway function during and after exercise (r² = 0.58, P < 0.01) (Fig. 5).

**DISCUSSION**

Our results showed 1) there was no consistent effect of changes in lung volume on measurements of RL during exercise in subjects either with or without mild asthma; 2) with exercise, the slight increase in RL,iso was consistent with the increase in tidal breathing flows and the nonlinearity of the pressure vs. flow relationship, indicating no actual change in airway

**Fig. 5.** Percent changes compared with preexercise in FEV1 compared with percent changes in RL,MW during and after exercise in asthmatic subjects. Each data point represents 1 observation in 1 subject. Data for nonasthmatic subjects, which would form a cluster of points around (0,0), are not shown for clarity. Heavy diagonal line, linear regression (r² = 0.57).
function; 3) DI caused a small transient decrease in $R_L$ after exercise in the asthmatic subjects but had little immediate effect on $R_L$ during exercise in either group of subjects; 4) $R_{L,iso}$ and $R_{L,MW}$ gave similar results; and 5) changes in $R_L$ and FEV$_1$ indicated similar changes in airway function during and after exercise.

Effects of Lung Volume on $R_L$

Because of the mechanical interdependence of airways and lung parenchyma, increasing lung volume increases the tethering forces on intraparenchymal airways, resulting in an expected decrease in $R_L$ as lung volume increases (15). We found little effect of increasing lung volume on $R_L$ in the limited volume range encountered during exercise. The resistance vs. volume relationship in our study was derived from IVPF curves constructed from near-vital capacity breaths with varying flows rather than from tidal breathing. To our knowledge, no one has reported effects of lung volume on $R_L$ by using this technique. Whether upper airway effects or other technique differences account for the generally smaller effect of lung volume in our study compared with previous studies remains to be determined.

Effects of Increasing Flows on $R_{L,iso}$

Several studies have demonstrated the nonlinear relationship of Ptp to flow at any given lung volume (11, 24, 25). The increasing flows of exercise would be expected to increase $R_L$, although the amount of this increase has not been previously measured. By referring to IVPF curves generated before exercise, we documented the degree to which the increasing flows of exercise should increase $R_{L,iso}$. The increase in $R_{L,iso}$ found was small in our subjects and of a magnitude predicted by the nonlinearity of the pressure-flow relationship. In subjects with more advanced lung disease, the effect of increasing flow is likely to be larger because of the increased curvature of the IVPF curve in the lower flow range (11, 32).

In studies using $R_L$ measurements where substantial increases in flow are encountered, either of two approaches can be used. Measurements of $R_L$ can be restricted to low inspiratory and expiratory flows, as in the Mead and Whittenberger technique (25). Alternatively, the IVPF curve technique described in this study can be employed to document the effect of increasing flows.

Effects of DI on Lung Function During Exercise

A potential problem in assessing airway function by spirometry is that the DI required for the maneuver may induce either transient bronchodilation or bronchoconstriction (7, 10, 12, 22). We investigated the effect of DI on assessment of airway function by measuring $R_L$ before and after each DI associated with the FVC maneuvers. DI decreased $R_L$ 15 min after exercise in the asthma group. However, there was no consistent change in $R_L$ in the 30- to 60-s period after each DI during any other phase of the study in either group of subjects. We have no information on whether our results apply to subjects with more severe asthma or other forms of obstructive lung disease.

In an additional separate study in the same nine asthmatic subjects, we compared the pattern of $R_{L,MW}$ change before, during, and after exercise when no FVC maneuvers were performed. The pattern of changes was not statistically different from that in Figs. 2 and 3 (data not shown).

Airway Function During Exercise

Results from previous studies by using a variety of methods do not provide a consistent picture concerning changes in airway function during exercise in either normal subjects (13, 16, 30, 33) or subjects with asthma (3, 21, 28, 31). A major purpose of this study was to Fig. 6. IVPF curves for asthmatic (A) and nonasthmatic subject (B). In each panel, 2 curves represent 2 volume levels below TLC. Fitted lines were used to derive modeled values for $R_{L,iso}$ described in text.
compare RL and maximal expiratory flows during exercise in normal and mildly asthmatic subjects. Both measurements indicated similar patterns of change in airway function (Figs. 2–4), namely, no consistent change during exercise in either group and bronchoconstriction in the asthmatic subjects after exercise.

The inconsistency in results among the various studies of airway function during exercise may be related, in part, to differences in technique. Three groups reported a dramatic fall in RL during exercise in normal subjects by using techniques that require the subject to increase respiratory rate (16, 21, 33). Two of these reported that the reduction in RL was blocked by treatment with anticholinergic drugs but was not affected by treatment with β-blockers. In contrast, studies reporting RL,iso measured during spontaneous breathing all report no change in RL during exercise in normal subjects (28, 30, 31), results that are similar to ours using the same technique. When taken together, the results from these studies suggest that there may be a vagally induced increase in RL caused together, the results from these studies suggest that similar to ours using the same technique. When taken together, the results from these studies suggest that there may be a vagally induced increase in RL caused.

Furthermore, the FEV1 data were not affected by the possible inability of subjects to perform maximal effort dependence that has been documented in patients with chronic obstructive lung disease (19). Thus, despite the differences in lung mechanics during resistance and maximal expiratory flow measurements, the results were similar with either technique.

APPENDIX

To quantify the effect of increasing flow during exercise, we calculated RL,iso by using preexercise IVPF curves [RL,iso (model)] as follows. We obtained a series of IVPF curves at rest for each subject (Fig. 6). Then we could plot the exercise flows (V) used in the RL,iso measurement on a graph of the preexercise IVPF curve obtained at the same lung volume. If the measured RL,iso increased during exercise but the Ptp vs. V data fell on the control IVPF curve, then the increase in RL,iso would be due to the nonlinearity of the pressure-flow relationship and would not represent bronchoconstriction. Data not falling on the control IVPF curve could reflect either bronchoconstriction or bronchodilation. Thus the method documents the increases in RL secondary to increases in flow. It also controls for increases in lung volume by referring to isopleths of constant volume below TLC. The changes in resistance estimated from the IVPF curves are indicated in Fig. 2 (dotted lines). The slight increase in RL,iso(model) was close to the measured increase in RL,iso, indicating no change in airway function occurred.

Before exercise, subjects generated IVPF curves as described previously (4). With the esophageal balloon in place, the subject performed nearly full vital capacity inspiratory and expiratory maneuvers with increasing effort. This procedure was repeated as many times as needed to cover inspiratory and expiratory flows from < 0.5 to > 4.0 l/s over most of the volume range from ~ 80% TLC to near residual volume. The resulting V and lung volume signals were adjusted to minimize drift in the volume signal as described above. A family of IVPF curves was constructed by plotting Ptp and V against constant volume levels, several of which are shown in Fig. 6. To use these data for calculation of RL,iso(model), we plotted the data for each volume level in each subject by an iterative fitting procedure that minimized the mean square deviation from the equation

\[ Ptp_5 = K_{15} \cdot V_E + K_{55} \cdot V_E^2 \] (expiratory flow)

\[ Ptp_1 = K_{11} \cdot V_I + K_{22} \cdot V_I^2 \] (inspiratory flow)

where \( K_1 \) indicates the inverse slope of the IVPF curve around zero flow. \( K_{2E} \) and \( K_{2I} \) are separate parameters fitted to the expiratory and inspiratory portions (i.e., \( V_E \) and \( V_I \)), respectively, that added curvature. By using Eq. 1, a pair of Ptp,VE,IVPF and Ptp,VI,IVPF points could be determined from the measured VE and VI that had been used to calculate RL,iso. By using these estimated pressures, RL,iso(model) was calculated from

\[ RL_{iso}(model) = \frac{Ptp_{VE,IVPF}(V_E) - Ptp_{VI,IVPF}(V_I)}{V_E - V_I} \] (A2)

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REFERENCES