Inspiratory lung impedance in COPD: effects of PEEP and immediate impact of lung volume reduction surgery

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There are major limitations in quantifying the degree of functional impairment in patients with COPD, with most techniques relying on spirometric indexes or measurements of dynamic lung resistance (Rt) and elastance (Et) at a single frequency. Such information can be misleading in patients with COPD. For example, reduced forced expiratory flows may result from either bronchitic airway obstruction or premature airway collapse due to emphysematous tissue destruction. In addition, alterations in dynamic Rt and Et may reflect changes in airway caliber, alterations in parenchymal tissue integrity, or serial and parallel time-constant heterogeneity. Thus these traditional measurement indexes lack specificity in localizing disease processes or gauging the effectiveness of medical or surgical interventions.

CHRONIC OBSTRUCTIVE PULMONARY DISEASE (COPD) is characterized by both intrinsic airway obstruction (bronchitis) and parenchymal tissue destruction (emphysema). The compromise in lung function in this disease is often slow and progressive. Traditional therapeutic measures for both early- and late-stage COPD consist of beta agonists and anticholinergics for the relief of bronchospasm, corticosteroids for controlling airway inflammation, antibiotics for treatment of infectious exacerbations, and supplemental oxygen to improve hypoxemia. Usually these approaches offer only mild improvement in symptoms and clinical outcomes.

Recently, several investigators have advocated the use of low-level positive end-expiratory pressure (PEEP) in patients suffering from acute exacerbations of COPD, with the goal of prevention of atelectasis and/or small airway closure. Extrinsic PEEP may also counterbalance intrinsic PEEP and unload the inspiratory muscles during assisted modes of ventilation. Even more recently, there has been a resurgence of interest in the use of lung volume reduction surgery (LVRS) for the treatment of severe emphysema. Although different approaches to LVRS have been developed, their common goal is the removal of the most diseased portions of the lung, allowing less diseased areas to expand and develop greater elastic recoil pressures. In addition to an improvement in driving pressure, the decompression of healthier lung tissues results in increased radial traction on the airways, which helps maintain their caliber during expiration. As a result, LVRS can potentially increase expiratory airflow.

There are major limitations in quantifying the degree of functional impairment in patients with COPD, with most techniques relying on spirometric indexes or measurements of dynamic lung resistance (Rt) and elastance (Et) at a single frequency. Such information can be misleading in patients with COPD. For example, reduced forced expiratory flows may result from either bronchitic airway obstruction or premature airway collapse due to emphysematous tissue destruction. In addition, alterations in dynamic Rt and Et may reflect changes in airway caliber, alterations in parenchymal tissue integrity, or serial and parallel time-constant heterogeneity. Thus these traditional measurement indexes lack specificity in localizing disease processes or gauging the effectiveness of medical or surgical interventions.

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Several studies from our group have shown that the frequency-dependent features of $R_L$ and $E_L$ over low frequencies (0.1–10 Hz) are specific to particular patterns of airway obstruction (20, 22–24). For example, when there is large and homogeneous peripheral airway obstruction, $R_L$ will be increased uniformly throughout this bandwidth. The $E_L$ will be unaffected below 1 Hz but will demonstrate positive frequency dependence above 1 Hz because of the shunting of air flow into the central airway walls (27). Thus $E_L$ at higher frequencies will reflect the mechanical properties of the airway walls (23, 24, 27, 31). With mild heterogeneous airway obstruction in which a few closed airways occur randomly throughout the lung periphery, both $R_L$ and $E_L$ will demonstrate substantial elevations in frequency dependence below 1 Hz (23).

The most direct way to determine such $R_L$ and $E_L$ spectra is through measures of pulmonary impedance ($Z_L$), the complex ratio of transpulmonary pressure to flow at the airway opening. However, the measurement of $Z_L$ in ventilated patients is difficult, especially in patients with severe airway obstruction. For example, the measurement of $Z_L$ using forced oscillations or random noise near breathing frequencies requires the suspension of ventilatory support (30). Moreover, its physiological interpretation is difficult in the presence of highly nonlinear phenomena such as dynamic airway compression and flow limitation (34). Whereas expiratory flow limitation is a central feature of the pathophysiology in COPD and a major contributor to the functional compromise in such patients, it is nonetheless a highly nonlinear phenomenon in which flow is no longer related to the pressure drop across the airways (17, 18, 28, 34). Thus any linear description of lung mechanics in these patients (i.e., transfer function approximation) must be restricted to pressure and flow data in which such nonlinearities are known to be minimal, such as inspiration (1, 21, 28).

In a recent study (21), we introduced an enhanced ventilator waveform (EVW) to measure inspiratory lung impedance ($Z_L^{\text{insp}}$), a linear and theoretically valid description of lung mechanics that avoids the confounding influence of expiratory flow limitation. The EVW excites the respiratory system with an inspiratory flow pattern consisting of multiple sinusoids while allowing for a patient-driven exhalation to the atmosphere or against an externally applied PEEP. The EVW’s ability to measure $Z_L^{\text{insp}}$ while simultaneously sustaining ventilation makes it ideal for probing low-frequency inspiratory mechanics in ventilated patients and patients with severe lung obstruction.

In the present study, we applied the EVW to anesthetized, paralyzed patients to obtain accurate measurements of $Z_L^{\text{insp}}$. The goals of this study were: 1) to provide additional insight into the nature and distribution of airway obstruction during inspiration in COPD patients, 2) to assess the impact of PEEP on dynamic inspiratory mechanics, and 3) to investigate the effects of LVRS on inspiratory mechanics in the immediate postoperative period. More specifically, we investigated the effects of low-level PEEP (0–6 cmH2O) on $Z_L^{\text{insp}}$ in patients with mild and severe airway obstruction, as well as the immediate postoperative effects of LVRS on $Z_L^{\text{insp}}$ in patients with COPD.

**METHODS**

**Patients.** Measurements were made on 14 patients undergoing elective thoracic surgery (Table 1). Patients consisted of a control group of six patients with mild obstruction or normal lung function [forced expiratory volume in 1 s (FEV1) = 86 ± 18% predicted] undergoing thoracoscopic surgery and eight patients with severe COPD (FEV1 = 26 ± 9% predicted) undergoing LVRS. The protocol was approved by the appropriate institutional research committees, and informed consent was obtained from each patient.

**Experimental measurements.** The details of the EVW measurements have been previously described (21). Briefly, the flow pattern of the EVW inspiration consists of a rectified sine wave at a frequency of 0.156 Hz with superimposed lower amplitude sinusoids at frequencies of 0.391, 0.859, 1.484, 2.422, 4.609, and 8.047 Hz. The frequencies of these sinusoids are selected to minimize the effects of harmonic distortion on estimates of $Z_L^{\text{insp}}$ (32), and their phases are optimized to ensure that a physiologically appropriate tidal volume is delivered to the patient (25).

Each discretized EVW volume signal was generated from a digital-to-analog board (Data Translations DT-2811, Marlboro, MA) at a rate of 40 Hz, low-pass filtered at 10 Hz (Frequency Devices, Haverhill, MA), and presented to a servo-amplifier that drove a linear motor (Infomag 7315–1, Goleta, CA) connected to a piston-cylinder arrangement. Precisely at the end of each inspiration, an exhalation valve was triggered open by a separate digital-to-analog channel to allow the patient to passively exhale against a spring-loaded PEEP valve while fresh air from the atmosphere was brought into the cylinder through a separate intake valve. Airway flow (V) was measured with a pneumotachograph (Hans & amp; Amp; Co, Goleta, CA) connected to a piston-cylinder arrangement. Pre-exposure to the appropriate institutional research committees, and informed consent was obtained from each patient.

**Table 1. Patient characteristics**

<table>
<thead>
<tr>
<th>Subject</th>
<th>Gender</th>
<th>Age, yr</th>
<th>FEV1, % pred</th>
<th>Diagnosis</th>
<th>Surgical Procedure</th>
</tr>
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<tbody>
<tr>
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<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>F</td>
<td>66</td>
<td>73</td>
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<td>RLL</td>
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<td>2</td>
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<td>RTR</td>
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<tr>
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<td>M</td>
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<tr>
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<td>F</td>
<td>28</td>
<td>72</td>
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<td>RLL</td>
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<tr>
<td>5</td>
<td>F</td>
<td>27</td>
<td>81</td>
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<td>LTB</td>
</tr>
<tr>
<td>6</td>
<td>M</td>
<td>67</td>
<td>89</td>
<td>Interstitial fibrosis</td>
<td>LTB</td>
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<td></td>
</tr>
<tr>
<td>7</td>
<td>F</td>
<td>58</td>
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<td>LLVR</td>
</tr>
<tr>
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<td>BLVR</td>
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<td>14</td>
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<td>RLV</td>
</tr>
<tr>
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<tr>
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<tr>
<td>14</td>
<td>M</td>
<td>62</td>
<td>23</td>
<td>COPD</td>
<td>LLVR</td>
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</tbody>
</table>

FEV1, forced expiratory volume in 1 s; F, female; M, male; CA, carcinoma; OS, osteosarcoma; COPD, chronic obstructive pulmonary disease; RLL, right lower lobectomy; RTR, right thoracoscopic resection; LTB, left thoracoscopic biopsy; LLVR, left lung volume reduction; RLV, right lung volume reduction; BLVR, bilateral lung volume reduction.
Rudolph 4700A, Kansas City, MO) placed at the proximal end of a single lumen endotracheal tube (ETT) and connected to a 0 to 2 cmH2O variable-reluctance pressure transducer (Celesco LCVR-0002, Canoga Park, CA). Esophageal pressure was obtained with a balloon catheter inserted orally, the distal tip of which was positioned 35–40 cm from the incisors. Tracheal pressure was obtained with a small polyethylene catheter placed into the ETT and allowed to extend ~2 cm into the trachea. Transpulmonary pressure (Ptp) was estimated as the difference between tracheal and esophageal pressures across a single 0 to 50 cmH2O variable-reluctance pressure transducer (Celesco LCVR-0050). The flow and pressure signals were demodulated (Celesco LCCD-110), low-pass filtered at 10 Hz (Frequency Devices), and sampled at 40 Hz by an analog-to-digital board (Data Translations DT-2811).

Protocol. After induction of anesthesia and muscle paralysis, all patients were intubated with a single-lumen ETT. The EVW measurements were made before any surgical manipulation. After an inspiratory sigh and passive expiration to resting lung volume, patients were switched from conventional ventilatory support and connected to the EVW system as shown in Fig. 1. Each patient received at least six EVW breaths with PEEPs of 0, 3, and 6 cmH2O in random order. Each run lasted ~40–50 s, during which time arterial oxygen saturation, systemic arterial pressure, central venous pressure, and electrocardiogram were continuously monitored. At no time during the EVW forcings did the arterial oxygen saturation of any patient drop below 98%.

In the LVRS patients, the single-lumen ETT was removed and replaced with a double-lumen ETT for single lung ventilation during the surgical procedure. Lung volume was reduced by using sequential unilateral or bilateral thoracoscopic plication (33). Incisions were made in the fifth intercostal space in the midaxillary line anterior to the latissimus dorsi, and the auscultatory triangle. On thoracoscopic visual inspection, the most distended and emphysematous lung areas were plicated with a knifeless, thick-tissue endoscopic stapler (33). When the surgical procedure was complete, the double-lumen ETT was removed and replaced with a single-lumen ETT.

In four of the COPD patients who did not have an appreciable air leak after LVRS (patients 11–14), postoperative EVW measurements were made just before emergence and reversal of muscle relaxation. Each of these patients required a chest drainage system postoperatively. After endotracheal suctioning, postoperative EVW measurements were made with two to four chest tubes in place to drainage systems with an underwater seal. Any applied suction was turned off just before the measurement.

Data analysis and statistics. In flow-limited patients, data analysis must be restricted to the inspiratory segments of V˙ and Ptp if any linearity assumptions are to remain valid (28). Because the frequency content of the EVW is exactly specified during each inspiratory period T1, our approach was to model both the V˙ and Ptp inspiratory segments with trigonometric approximations

\[ V(t) = a_0 + \sum_{k=1}^{K} a_k \cos(2\pi f_k t) + \sum_{k=1}^{K} b_k \sin(2\pi f_k t) \]  

\[ Ptp(t) = c_0 + \sum_{k=1}^{K} c_k \cos(2\pi f_k t) + \sum_{k=1}^{K} d_k \sin(2\pi f_k t) \]

where the scaling coefficients \( a_k \), \( b_k \), \( c_k \), and \( d_k \) are real numbers that determine the steady-state magnitude and phase information for V and Ptp at each specified frequency \( f_k \). Note that Eqs. 1 and 2 are not true Fourier expansions of the inspiratory flow and pressure segments, because each \( f_k \) is not constrained to be an integer multiple of 1/T1 (21). The trigonometric coefficients were estimated by using a least squares approach with error weighting (i.e., time-domain windowing) to minimize the effects of Ptp transient responses due to stress-relaxation, pendulluft, and alveolar recruitment (21). The \( Z_{L,\text{insp}}^{\text{true}} \) at each \( f_k \) was then obtained from these coefficients as

\[ Z_{L,\text{insp}}^{\text{true}}(f_k) = \frac{c_k - jd_k}{a_k - jb_k} \]
where $j$ is the unit imaginary number. The corresponding inspiratory lung resistance ($R_{L_{insp}}^{\text{insp}}$) and elastance ($E_{L_{insp}}^{\text{insp}}$) were then obtained from the real ($\text{Re}$) and imaginary ($\text{Im}$) parts, respectively, of $Z_{L_{insp}}^{\text{insp}}$

$$R_{L_{insp}}^{\text{insp}}(f_b) = \text{Re}[Z_{L_{insp}}^{\text{insp}}(f_b)]$$

$$E_{L_{insp}}^{\text{insp}}(f_b) = -2\pi f_b \text{Im}[Z_{L_{insp}}^{\text{insp}}(f_b)]$$

Previous studies based on anatomically consistent models have demonstrated that $R_{L_{insp}}^{\text{insp}}$ at 0.156 Hz reflects lung tissue resistance as well as the mean level and spread (i.e., heterogeneity) of airway resistance, whereas at 8.047 Hz, it is more indicative of mean airway resistance alone (23, 24). The $E_{L_{insp}}^{\text{insp}}$ at 0.156 Hz is most representative of static lung elasticity, whereas at 8.047 Hz it is indicative of airway wall properties due to the shunting of flow into the central airway walls that may occur in the presence of increased peripheral airway resistance (27). Between-group comparisons of $R_{L_{insp}}^{\text{insp}}$ and $E_{L_{insp}}^{\text{insp}}$ for a given frequency and PEEP level were made by use of both one- and two-tailed unpaired Student's $t$-tests. Within-subject dependencies of $R_{L_{insp}}^{\text{insp}}$ and $E_{L_{insp}}^{\text{insp}}$ on PEEP level were assessed by using a paired Student's $t$-test. $P < 0.05$ was considered statistically significant.

RESULTS

Between-group comparisons of the $R_{L_{insp}}^{\text{insp}}$ and $E_{L_{insp}}^{\text{insp}}$ spectra at the three PEEP levels are shown in Fig. 2. Despite marked differences in spirometry between the groups, the values and frequency dependence of $R_{L_{insp}}^{\text{insp}}$ were only slightly higher for the COPD patients, with statistically significant differences noted only at 2.42 Hz with 3 cmH$_2$O PEEP and at 4.61 Hz at 6 cmH$_2$O PEEP. The COPD patients demonstrated a significantly lower $E_{L_{insp}}^{\text{insp}}$ at 0.156 Hz with all PEEP levels. No significant differences in $E_{L_{insp}}^{\text{insp}}$ were found between the groups between 0.156 and 2.422 Hz. Above 2.422 Hz, COPD patients displayed a more rapid rise with frequency compared with the control group, with significantly higher $E_{L_{insp}}^{\text{insp}}$ at 4.609 Hz and above for 6 cmH$_2$O PEEP and at 8.047 Hz for 0 and 3 cmH$_2$O PEEP.

Because little change was observed between 0 and 3 cmH$_2$O PEEP for most patients, we performed within-group comparisons of $R_{L_{insp}}^{\text{insp}}$ and $E_{L_{insp}}^{\text{insp}}$ at PEEPs of 0 and 6 cmH$_2$O (Fig. 3). For the control group, significant decreases in $R_{L_{insp}}^{\text{insp}}$ were noted only at the very lowest frequencies: 0.156, 0.391, and 0.859 Hz ($P < 0.05$), and no significant changes in $E_{L_{insp}}^{\text{insp}}$ with PEEP were observed at any frequency. However, in the COPD group, $R_{L_{insp}}^{\text{insp}}$ decreased significantly at almost all frequencies with PEEP, and significant decreases in $E_{L_{insp}}^{\text{insp}}$ were noted at frequencies of 4.609 and 8.047 Hz. The average drop in $R_{L_{insp}}^{\text{insp}}$ with 6 cmH$_2$O PEEP was similar for both groups.

The impact of LVRS on $R_{L_{insp}}^{\text{insp}}$ and $E_{L_{insp}}^{\text{insp}}$ for four of the COPD patients is shown in Fig. 4. Pre-LVRS, all patients demonstrated pronounced frequency depen-
Dence in E_{insp}^L, which from modeling studies suggest the presence of substantial peripheral obstruction with flow shunting into the central airway walls (20, 23). After LVRS, there was a substantial increase in R_{insp}^L at all frequencies regardless of PEEP level. The E_{insp}^L demonstrated increases at all frequencies and PEEP levels, which was most notable at the highest frequencies.

A summary of the impact of PEEP on R_{insp}^L and E_{insp}^L at the lowest (0.156 Hz) and highest (8.047 Hz) fre-

![Fig. 3. Comparison of preoperative R_{insp}^L and E_{insp}^L spectra at 0 (●) and 6 (●) cmH_2O PEEP for control (left) and COPD (right) patients. *Significant difference between PEEP levels (P < 0.05) via paired t-test.]

![Fig. 4. R_{insp}^L and E_{insp}^L spectra in four COPD patients measured immediately before (open symbols; Pre-Op) and immediately after (filled symbols; Post-Op) lung volume reduction surgery (LVRS) at PEEP levels of 0 (circles), 3 (inverted triangles), and 6 (squares) cmH_2O. Preoperative data at 0 cmH_2O PEEP were not obtained for patient 12.]

Recall that $R_L^{\text{insp}}$ at 0.156 Hz reflects both lung tissue resistance and the heterogeneity of airway resistance, whereas at 8.047 Hz it is more indicative of mean airway resistance alone (23, 24). The $E_L^{\text{insp}}$ at 0.156 Hz most closely reflects static lung elasticity, whereas at 8.047 Hz it is indicative of central airway wall properties (27). Regardless of PEEP level, $R_L^{\text{insp}}$ significantly increased at 0.156 and 8.047 Hz after LVRS. Significant increases in $E_L^{\text{insp}}$ after LVRS were detected at 3 and 6 cmH$_2$O PEEP for 0.156 Hz but only at 3 cmH$_2$O for 8.047 Hz.

DISCUSSION

Several techniques are available to provide clinical assessments of pulmonary mechanics in patients maintained on artificial ventilation. Measures of peak inspiratory pressure, work of breathing, and effective dynamic resistance and elastance for a particular breathing pattern are simple indexes that can provide a rough estimate of the relative ease with which air is brought into and out of the lungs. However, none of these permit inference on the distribution or nature of obstruction in the airways. As such, they are limited in their ability to enhance our understanding of the physiological effects of interventions such as PEEP or LVRS. Although the airway occlusion technique has been used to analyze pulmonary mechanics in ventilated patients (6, 9, 13), such an approach provides only an indirect and model-based prediction of the frequency dependence in $R_L$ and $E_L$. Moreover, the accuracy of the airway occlusion is questionable in COPD patients because of its limited bandwidth of excitation (9).

In obstructive diseases such as asthma, there may be substantial and widespread peripheral airway constriction. Previous morphometric modeling studies have demonstrated that if this obstruction is not inclusive of peripheral airway closure, $R_L$ will be elevated at all frequencies, whereas $E_L$ will show mild frequency dependence below 1 Hz (23, 24). Above 1 Hz, $E_L$ will demonstrate pronounced positive frequency dependence due to the shunting of flow into the central airway walls (23, 27). When the obstruction is heterogeneous and includes a few closed or nearly closed peripheral airways, both $R_L$ and $E_L$ will be elevated for frequencies below 1 Hz, and $E_L$ will show sharp frequency dependence above 2 Hz. In patients with severe COPD, additional mechanisms may also contribute to frequency dependence in $R_L^{\text{insp}}$ and $E_L^{\text{insp}}$, such as collateral ventilation (26) or parallel time constant discrepancies arising from heterogeneous tissue destruction (16). Nevertheless, the frequency dependence of $R_L^{\text{insp}}$ and $E_L^{\text{insp}}$ can still provide far more insight into the mechanisms contributing to compromised breathing function compared with most current assessments of lung mechanics.

Our data demonstrate that despite large differences in forced expiratory flows, both the values and frequency dependence of $R_L^{\text{insp}}$ are similar for patients with mild obstruction and severe COPD. However, it should be noted that $R_L^{\text{insp}}$ is measured in the absence of dynamic airway compression and expiratory flow limitation and as such is more reflective of the level of bronchitic airway disease rather than functional compromise (19). Our values of $R_L^{\text{insp}}$ at low frequencies are similar to previously reported values of $R_L^{\text{insp}}$ in awake COPD patients during spontaneous breathing (19). Thus the low FEV$_1$ in the COPD group appears to be primarily due to the loss of recoil (driving) pressure and premature airway compression from reduced airway tethering. The $E_L^{\text{insp}}$ at 0.156 Hz was significantly lower for the COPD patients regardless of PEEP level. This is consistent with their diagnosis of emphysema, because $E_L^{\text{insp}}$ at this frequency would be the closest to the value of static elastance of the lung.

**Effects of PEEP.** Recently, several studies have advocated the use of low-level PEEP in patients suffering from acute exacerbation of COPD (5, 11, 14, 35) to
prevent atelectasis, counterbalance intrinsic PEEP, and unload the inspiratory muscles during assisted modes of ventilation. The pattern of reduced $R_{L}^{\text{insp}}$ at all frequencies and reduced $E_{L}^{\text{insp}}$ at high frequencies can be interpreted as if PEEP causes a reduction in airway wall shunting by lowering peripheral airway resistance. This is demonstrated in our data by decreases in both $R_{L}^{\text{insp}}$ and $E_{L}^{\text{insp}}$ at 8.047 Hz (Fig. 3). Thus PEEP appears to have an additional benefit to COPD patients by increasing peripheral airway caliber. The $E_{L}^{\text{insp}}$ at 8.047 Hz, which is most reflective of airway wall properties (20, 23, 24), was significantly lower in the control patients compared with the COPD patients at all PEEP levels, suggesting the presence of less peripheral airway obstruction in this group. The fact that increasing PEEP in the control group produced no significant changes in $E_{L}^{\text{insp}}$ at 8.047 Hz implies that there was not a significant reduction in peripheral airway obstruction in these patients.

Small airway opening with PEEP could result in substantial decreases in $R_{L}$ and $E_{L}$ at low frequencies by the recruitment of more lung tissue (23). The fact that $E_{L}^{\text{insp}}$ at 0.156 Hz showed virtually no change with PEEP for the majority of COPD patients would argue against significant airway opening or alveolar recruitment, at least with low-level PEEP during inspiratory maneuvers. Four of the six control patients did exhibit decreases $R_{L}^{\text{insp}}$ and $E_{L}^{\text{insp}}$ at 0.156 Hz with PEEP, suggesting that some of their airways may have been opened by the application of PEEP.

Effects of LVRS. There has been a resurgence of interest in the use of LVRS for the treatment of severe emphysema. Although many different approaches of LVRS have been developed, their common goal is the surgical removal of the most diseased portions of the lung, allowing healthier portions to expand and develop greater elastic recoil pressures. In addition to an improvement in driving pressure, the decompression of healthier lung tissue can result in increased radial traction on the airways, which helps maintain their caliber during expiration. As a result, LVRS can often increase expiratory airflow. Although the size of our group is small, our data are consistent with those of Barnas et al. (1), who reported significant increases in inspiratory $R_{L}$ and $E_{L}$ from 0.16 to 0.50 Hz immediately after LVRS. The increases we observed in $R_{L}^{\text{insp}}$ and $E_{L}^{\text{insp}}$ after LVRS may seem paradoxical, considering the reported improvements in FEV$_{1}$ with this procedure. We point out that our data reflect the mechanical properties of lungs during inspiratory maneuvers immediately after surgical resection of emphysematous tissue and thus do not speak directly to the mechanism of improved forced expiratory flows measured several weeks postoperatively. Indeed, several mechanisms probably contribute to the acute changes we observed.

It may be argued that prolonged anesthesia and paralysis had an influence on our postoperative measurements. Several studies have reported conflicting results on the effect of anesthesia and paralysis on lung mechanics compared with the awake state (7, 15, 29, 36). However, Fahy et al. (8) have demonstrated that the duration of anesthesia and paralysis has only minimal effects on both lung and chest wall mechanics as measured by ventilatory forcings, at least during 4 h of laparoscopic surgery. Because our postoperative measurements were made under similar conditions of anesthesia and paralysis and within a similar time period, we feel that the duration of anesthesia and paralysis had little effect on $Z_{L}^{\text{insp}}$.

Some of the increases in $R_{L}^{\text{insp}}$ and $E_{L}^{\text{insp}}$ we observed may be secondary to an accumulation of secretions and pulmonary edema. In our patients, the operated lung was collapsed while the contralateral lung was ventilated. Barnas et al. (3) have reported increases in lung resistance and elastance after prolonged cardiopulmonary bypass for which both lungs were collapsed, consistent with data obtained in dogs with experimentally induced pulmonary edema (2). In addition to decreasing the number of lung units in communication with the airway opening, such edema may also contribute to mechanical inhomogeneity in the lungs, further increasing the levels and frequency dependence in $R_{L}^{\text{insp}}$ and $E_{L}^{\text{insp}}$ (23, 24).

After the LVRS procedure, two to four drainage tubes were placed into the pleural space of our COPD patients. We feel that this had little impact on our measurements, because it has been reported that such tubes, whether opened to the atmosphere, clamped off, or connected to a vacuum source, cause little change in $R_{L}$ and $E_{L}$ as measured during mechanical ventilation (1, 3).

The removal of lung tissue by itself will certainly cause increases in both $R_{L}^{\text{insp}}$ and $E_{L}^{\text{insp}}$ at low frequencies, because less lung is available to communicate with the airway opening. In this case, both $R_{L}^{\text{insp}}$ and $E_{L}^{\text{insp}}$ should increase by the same amount. Increases in $E_{L}^{\text{insp}}$ at low frequencies (<1 Hz) may also reflect an improvement in overall lung elasticity, because previously compressed lung regions can now better expand and possibly impinge on the nonlinear region of their pressure-volume relationship. Such increases in $E_{L}^{\text{insp}}$ would cause an obligate increase in the tissue component of $R_{L}^{\text{insp}}$, by virtue of the structural damping hypothesis (10).

Although not entirely intuitive, some of the postoperative increases in high-frequency $R_{L}^{\text{insp}}$ and $E_{L}^{\text{insp}}$ may reflect an improvement in airway tethering. By removing portions of diseased lung tissue and allowing healthier portions to expand, there is enhanced radial traction on the airways and an increase in their caliber (12). Because of the nonlinear relationship between airway cross-sectional area and transmural pressure (17), this results in a stiffening of their walls. This increase in airway wall elastance would be reflected as an increase in high-frequency $E_{L}^{\text{insp}}$ (i.e., >2–3 Hz), because this portion of the elastance spectrum is most reflective of airway wall properties in lungs with severe peripheral airway obstruction (23, 27, 31). The shunting of high-frequency flows into airway walls would therefore decrease in this situation, because the total impedance of the airway walls has increased. A greater
portion of the flow will now encounter the serial resistance of the peripheral airways leading into the alveoli, and the overall energy dissipation and resistive pressure losses will be increased at high frequencies. A model-based interpretation of this phenomenon is presented in the APPENDIX.

In summary, we have measured the effective $R_L^{insp}$ and $E_L^{insp}$ spectra from 0.156 to 8.047 Hz in anesthetized and paralyzed patients over varying levels of PEEP and in the immediate postoperative period after LVRS. In patients with severe COPD, low levels of PEEP appear to have beneficial effects by reducing the resistance of the peripheral airways. $R_L^{insp}$ in patients with mild obstruction is similar to that obtained in patients with severe COPD, despite marked differences in spirometry. Thus the combination of both inspiratory impedance and FEV₁ may allow one to quantify the relative roles of bronchitic airway disease vs. premature dynamic airway compression in the pathophysiology of COPD. LVRS appears to increase total $R_L^{insp}$ and $E_L^{insp}$ at all frequencies and PEEP levels immediately after surgery. This may be secondary to loss of diseased lung tissue, increases in tissue resistance or elastance, increases in mechanical heterogeneity, accumulation of pulmonary edema, and/or stiffening of the airway walls secondary to improved radial traction. Regardless of the exact mechanisms contributing to these increases, clinicians must be aware of these changes when evaluating candidates for the LVRS procedure and in managing them in the immediate postoperative period.

APPENDIX

Increases in $E_L^{insp}$ at 8.047 Hz after LVRS seem counterintuitive, because this would imply an increase in peripheral airway obstruction with more flow shunting into airways proximal to the site of obstruction (23, 27). However, under certain conditions, an increase in airway wall elastance after LVRS can actually increase the levels and frequency dependence of both $R_L^{insp}$ and $E_L^{insp}$. To illustrate this point, we simulated $R_L$ and $E_L$ spectra from a simple linear airway wall shunt model often used to describe pulmonary mechanics in COPD patients (27) (Fig. 6A). To make these simulations consistent with our linear $Z_L^{insp}$ construct, the model does not include any nonlinearities to describe expiratory flow limitation (21).

With this model, a central airway compartment consisting of a resistance ($R_1$) and inertance ($I$) is separated from a peripheral resistance ($R_2$) by an airway wall elastance element ($E_{aw}$). The tissues are represented by a single linear elastance element. The $R_L$ and $E_L$ spectra were simulated from the model as described previously (21). We chose model parameter values consistent with emphysematous lungs (27), except that the $E_{aw}$ parameter, representing airway wall elastance, was allowed to vary from 0.5 to 100 times the value expected for healthy lungs. In healthy lungs, airway wall elastance has been estimated to be ~200 cmH₂O/l (27), but in emphysematous lungs it may be lower because of the loss of radial traction on the airways (17).

The three-dimensional surfaces of $R_L$ and $E_L$ as a function of both frequency and $E_{aw}$ are shown in Fig. 6B. Note that there is a range of increasing $E_{aw}$ (100–400 cmH₂O/l) for which $E_L$ actually increases, beyond which $E_L$ progressively decreases. The $R_L$ becomes progressively elevated with increasing $E_{aw}$, even though we did not alter the $R_1$ or $R_2$ parameters. In the limit as $E_{aw}$ approaches infinity (i.e., the airways become rigid), $R_L$ will approach a constant value equal to $R_1 + R_2$. Thus the increase in $R_L$ is not due to an increase in peripheral airway obstruction per se.


**Fig. 6.** A: lumped-element model used to simulate lung resistance and elastance data. Parameter values were selected to be consistent with emphysematous lungs: central airway compartment resistance ($R_1$) = 1.5 cmH₂O·l⁻¹·s, inertance ($I$) = 0.01 cmH₂O·l⁻¹·s, peripheral resistance ($R_2$) = 7.5 cmH₂O·l⁻¹·s, tissue elastance ($E_{ti}$) = 2.5 cmH₂O/l. The $E_{aw}$ parameter, representing airway wall elastance, was allowed to vary from 100 to 1,000 cmH₂O/l. B: 3-dimensional surfaces for lung resistance and elastance as a function of both frequency and $E_{aw}$ simulated from the model.
It should be noted that these simulations are extremely simplified compared with the actual alterations in lung mechanics after LVRS, because they only address the impact of airway wall stiffening on $R_L$ and $E_L$ spectra. Nonetheless, they demonstrate the possibility that increasing airway wall stiffness can in fact increase both $R_L$ and $E_L$ at high frequencies, giving the appearance that peripheral airway resistance has increased.

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