Increased Effective Lung Volume Following Lung Volume Reduction Surgery in Emphysema*

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Study objectives: Lung volume reduction surgery (LVRS) for emphysema has a variable effect on spirometry with improvement linked to increases in lung elastic recoil. The mechanism by which recoil increases following LVRS has not been described completely. This study examines preoperative and postoperative pulmonary function to describe a mechanism for changes in airflow obstruction.

Design: Change in pulmonary function following LVRS.

Setting: Public teaching hospital in Australia.

Patients: Patients with severe emphysema and pulmonary function measurements made before and after LVRS.

Measurements: Routine pulmonary function testing performed with ventilated lung alveolar volume (VA) derived from the gas transfer measurement used as a proxy for the effective lung volume.

Results: Pulmonary function tests from 36 consecutive patients with measurements made at the same laboratory were analyzed. The mean FEV1 was 29.1% predicted presurgery and increased following LVRS from 0.900 L (SD, 0.427 L) to 1.283 L (SD, 0.511 L; p < 0.0001) and TLC (143% predicted) decreased from 8.19 L (SD, 1.492 L) to 7.07 L (SD, 1.52 L; p < 0.0001; n = 35). The mean VA increased by 0.674 L (SD, 0.733 L) from 4.04 to 4.72 L (p < 0.0001; n = 34). The change in FEV1 correlated well with the change in VA (r = 0.63). The change in FEV1 in those patients whose VAs did not increase (n = 7) was not significant.

Conclusions: The increase in VA reflects an increase of functional or ventilating lung volume and is associated with an improvement in spirometry following LVRS.

Key words: emphysema; lung volume reduction surgery; pulmonary function

Abbreviations: DLCO = diffusing capacity of the lung for carbon monoxide; ELV = effective lung volume; KCO = lung diffusion capacity corrected for alveolar ventilation; LVRS = lung volume reduction surgery; Pel = elastic recoil of the alveoli; RV = residual volume; TLC = total lung capacity; VA = alveolar volume; VC = vital capacity; Vmax = maximal flow

There has been a resurgence in the use of lung volume reduction surgery (LVRS) for the treatment of patients with breathlessness due to severe emphysema. In general, the outcomes have been positive, but those for individuals have been variable and unpredictable. The benefits to quality of life and exercise tolerance, respiratory muscle effectiveness, dyspnea and disability, decreased respiratory drive, and increased airway and ventilatory function have been reported.

The LVRS procedure targets selected regions of emphysematous lung for resection in order to reduce lung capacity to less than the thoracic cavity volume. This results in the rearrangement of the chest wall and diaphragm geometry and of lung mechanics. Improved pulmonary function follows because of the increased lung recoil that contributes to airway patency and stability. Successful surgery will not improve oxygenation in all patients, and pulmonary artery pressures are changed little, suggesting that the net perfusion level and match with ventilation are not factors in the success of LVRS.
The role and interpretation of estimations of the diffusing capacity of the lung for carbon monoxide (DL\textsubscript{CO}) made using the single-breath technique is well-established in healthy individuals and in patients with interstitial lung disease in whom the impairment of diffusion is the major functional defect. In airways disease, the interpretation of DL\textsubscript{CO} and its derivatives, lung diffusion capacity corrected for alveolar ventilation (KCO), and alveolar volume (VA) are less clear.\textsuperscript{16} The reduced values of DL\textsubscript{CO} and KCO that are characteristic of emphysema are due for the most part to the loss of alveolar tissue. However, they also may be, in part, a consequence of technical factors such as poor mixing and prolonged inspiratory and expiratory times. The VA is calculated from the dilution of an inert component of the DL\textsubscript{CO} test gas. Because DL\textsubscript{CO} is estimated at total lung capacity (TLC), VA is a measure of the communicating volume of the lung at TLC, that is, the volume of air inspired plus the component of residual volume (RV) able to dilute the inspired air effectively within 10 s. In subjects with a normal or high FEV\textsubscript{1}/FVC ratio, VA correlates strongly with and approximates TLC measured plethysmographically. Typically in our laboratory, the VA/TLC ratio lies between 0.74 and 1.02 in the absence of airway disease (mean, 0.88; SD, 0.07) (based on 184 consecutive patients with FEV\textsubscript{1}/FVC ratios of > 80%) and decreases with airway obstruction.

Maximal expiratory flow is dependent on recoil pressure and, therefore, on lung volume, as illustrated by the maximal expiratory flow-volume curve. Because VA is a measure of lung inflation, it too also should be a determinant of recoil and, therefore, of maximal flow (V\textsubscript{max}) and FEV\textsubscript{1}. The aim of this study was to examine the effect of LVRS on VA and its association with dynamic lung function. The hypothesis examined is that improvement in airway function depends on an increase in VA.

**Materials and Methods**

**Patient Selection**

Patients were referred for assessment for LVRS from private practitioners or hospital clinics. Patients were accepted for LVRS if their baseline screening showed that heterogeneous emphysema was the major lung abnormality, that the emphysema caused severe functional impairment and hyperinflation (ie, TLC, > 120% predicted), and that the patient had gas trapping with a residual volume > 150% predicted. Quantitative radionuclide perfusion scanning was used to demonstrate localized areas of poor perfusion. Patients were excluded if they were > 75 years of age, had a recent history of smoking, had significant pulmonary hypertension (systolic pulmonary artery pressure > 55 mm Hg), had significant heart disease, or if they required a maintenance prednisolone dose of ≥ 12.5 mg daily.

**LVRS**

The LVRS was performed at The Queen Elizabeth Hospital, a tertiary-care referral center and teaching hospital in Adelaide, South Australia, by bilateral videoscopic surgery.\textsuperscript{17}

**Pulmonary Function Assessment**

Pulmonary function was performed prior to and at intervals following the LVRS. The test protocol for each visit required, in order, the following: a 6-min walk test; spirometry testing with salbutamol response; measurement of the DL\textsubscript{CO}; measurement of lung volumes (Boyle’s law); arterial blood gas measurements; and a repeat 6-min walk test.

Spirometry, lung volumes, and DL\textsubscript{CO} were measured using a rolling seal spirometer and whole-body plethysmograph incorporating gas diffusion (6200 Autobox DL; SensorMedics Corporation; Yorba Linda, CA). From the DL\textsubscript{CO} maneuver, the VA was derived and KCO was calculated (DL\textsubscript{CO}/VA ratio). The presurgical mean differences in intratracheal gas transfer estimates were the following: DL\textsubscript{CO}, 0.13 mL/mm/mm Hg (SD, 0.76 mL/mm/mm Hg) [1.2%; SD, 9.5%]; KCO, 0.11 mL/mm/mm Hg (SD, 0.23 mL/mm/mm Hg) [4.5%; SD, 10.9%]; and VA, 0.16 L (SD, 0.29 L) [3.5%; SD, 7.3%]. All gas transfer measurements were corrected for hemoglobin concentrations. The equipment used to measure DL\textsubscript{CO} used a fast gas analyzer and real-time measurement of expired gas concentrations,\textsuperscript{18} which allowed washout and sample volumes to be selected post hoc. The change from the washout to the alveolar phase was obvious on the gas concentration tracings of the maneuver in all tests, and the washout volume was adjusted when necessary to ensure that only alveolar sample concentrations were included in the DL\textsubscript{CO} calculations.

The 6-min walk test (ie, the distance covered in 6 min of free walking) was measured in a 30-m corridor. The protocol, which included written instructions that were read verbatim to the patient, was designed to minimize the influence of the technician on test performance.

**Results**

From February 1996 to November 1998, 54 patients underwent LVRS. Twenty-three men and 13 women (mean age, 64.3 years [SD, 7.6 years]; body mass index, 24.0 kg/m\textsuperscript{2} [SD, 3.0 kg/m\textsuperscript{2}]) had pulmonary function measured before and after surgery at the same laboratory. All patients had severe disability as a consequence of severe airflow obstruction. One patient could not perform plethysmographic lung volume maneuvers prior to surgery, and two patients could not perform DL\textsubscript{CO} measurements, either before or after surgery.

The mean time between the presurgery and post-surgery measurements was 173 days (SD, 63 days). Postbronchodilator measurements of spirometry, lung volumes, DL\textsubscript{CO}, and the best value from the two 6-min walk tests on each visit are reported.

Presurgery pulmonary function results (Table 1) showed severe airflow obstruction, gas trapping, hyperinflation, and reduced gas transfer. Patients were mildly hypoxic at rest (PO\textsubscript{2}, 68.3 mm Hg;
SD, 8.2 mm Hg), and the 6-min walk test distance demonstrated their severe disability (mean distance, 305 m; SD, 135 m).

The LVRS reduced all static lung volume measurements (TLC reduction, 1.12 L; RV, 1.68 L). Overall spirometric function improved with a mean increase in FEV₁ of 0.383 L. Twenty-three subjects increased FEV₁ significantly (p < 0.0001). FVC increased significantly in 27 subjects. DLCO increase, KCO decrease, and VA increase were significant (p < 0.0001) (Table 1).

There was good correlation between the change in VA and the change in FEV₁ (r = 0.63), the change in FVC (r = 0.51; Fig 1), and the change in the results of the 6-min walk test (r = 0.5; Fig 2). PaO₂ increased by 5.5 mm Hg (SD, 9.1 mm Hg; p = 0.006), and PaCO₂ decreased by 1.8 mm Hg (SD, 3.7 mm Hg; p = 0.023).

**DISCUSSION**

This analysis of the pulmonary function measurements of 36 consecutive patients made prior to and following LVRS showed the procedure to be effective for the group as a whole, with reductions in static lung volumes and increases in FEV₁ that were similar to those in other reports.1–15 Associated with this was improvement in physical function that was assessed by the 6-min walk test.

The decrease in static lung volumes occurred in all patients, but the response of FEV₁ and VA was variable with decreases in some patients. The change in FEV₁ correlated with the change in VA, giving support to the hypothesis that improvement in airway function in emphysema requires increased expansion of the lung with relatively normal elastic recoil characteristics.

Central to the interpretation of the data are the measurement and interpretation of VA. The routine measurement of gas transfer, DLCO, includes a measure of lung volume, the VA, so called because in subjects without airways disease it provides a reasonably accurate estimate of alveolar volume. The measurement principle is inert gas dilution, which is analogous to the helium dilution technique for measuring lung volumes but differs in that the time for dilution is just 10 s (by convention). These tech-

**Table 1—Lung Function Prior to and Following LVRS**

<table>
<thead>
<tr>
<th>Variables</th>
<th>Pre-LVRS</th>
<th>SD</th>
<th>% predicted</th>
<th>Post-LVRS</th>
<th>SD</th>
<th>Change</th>
<th>SD</th>
<th>p value*</th>
</tr>
</thead>
<tbody>
<tr>
<td>FEV₁, L (n = 36)</td>
<td>0.900</td>
<td>0.427</td>
<td>29.1</td>
<td>1.283</td>
<td>0.511</td>
<td>0.383</td>
<td>0.333</td>
<td>&lt; 0.0001</td>
</tr>
<tr>
<td>FVC, L (n = 36)</td>
<td>2.827</td>
<td>0.956</td>
<td>71.5</td>
<td>3.409</td>
<td>0.940</td>
<td>0.582</td>
<td>0.611</td>
<td>&lt; 0.0001</td>
</tr>
<tr>
<td>TLC, L (n = 35)</td>
<td>8.190</td>
<td>1.492</td>
<td>143.1</td>
<td>7.074</td>
<td>1.515</td>
<td>-1.116</td>
<td>0.730</td>
<td>&lt; 0.0001</td>
</tr>
<tr>
<td>RV, L (n = 35)</td>
<td>5.309</td>
<td>1.180</td>
<td>252.9</td>
<td>3.631</td>
<td>0.837</td>
<td>-1.678</td>
<td>0.859</td>
<td>&lt; 0.0001</td>
</tr>
<tr>
<td>FRC, L (n = 35)</td>
<td>6.177</td>
<td>1.291</td>
<td>193.4</td>
<td>4.700</td>
<td>1.058</td>
<td>-1.478</td>
<td>0.893</td>
<td>&lt; 0.0001</td>
</tr>
<tr>
<td>TLC, L (n = 35)</td>
<td>9.403</td>
<td>3.640</td>
<td>56.0</td>
<td>10.462</td>
<td>3.810</td>
<td>0.956</td>
<td>1.381</td>
<td>&lt; 0.0001</td>
</tr>
<tr>
<td>DLCO, mL/min/mm Hg (n = 34)</td>
<td>2.418</td>
<td>0.630</td>
<td>5.07</td>
<td>2.242</td>
<td>0.507</td>
<td>-0.176</td>
<td>0.361</td>
<td>0.0046</td>
</tr>
<tr>
<td>KCO, mL/min/mm Hg/L (n = 34)</td>
<td>4.042</td>
<td>1.369</td>
<td>1.438</td>
<td>4.716</td>
<td>1.674</td>
<td>0.674</td>
<td>0.733</td>
<td>0.0001</td>
</tr>
<tr>
<td>VA, L (n = 34)</td>
<td>11.166</td>
<td>1.678</td>
<td>56.0</td>
<td>10.462</td>
<td>3.810</td>
<td>-0.176</td>
<td>0.361</td>
<td>0.0046</td>
</tr>
</tbody>
</table>

*p Paired t test.
Techniques include in their estimate the physiologic dead space component, which, along withVA, is increased in patients with emphysema. All communicating lung volume regions accessible to and therefore able to dilute inhaled gas will have some impact on the estimate of VA, depending on their size and dynamic function. The greatest effect will be from rapidly emptying regions, whereas those regions that are relatively static because of poor elastic recoil will have little diluting effect on the tracer gas. Thus, VA may be more accurately considered to represent the effective lung volume (ELV) able to participate in lung ventilation.

In the present work, the method of measuring DLCO (and therefore VA) differed from the classic approach in that the washout volume was selected post hoc. This ensured that DLCO was not underestimated by including expire from conducting airways in the alveolar sample. Methane was used as the tracer gas.

The average VA increase was 674 mL (16.8%). This result is compatible with the quantitative CT scan findings of Becker et al who used the total functional lung volume index, which was defined at TLC, as a measure of the “volume of lung that is relatively less destroyed and therefore responsible for respiratory function.” They found that the index was increased by an average of 9% in lungs following LVRS. Reports of the effect of LVRS on VA are isolated. However, the effects of LVRS on DLCO have been reported widely and small changes similar to the present series are typical, although substantial increases also have been reported.

The determination of VA is linked to vital capacity (VC). The American Thoracic Society recommendation for the measurement of VA requires an inspiration of the test gas to a TLC that is at least 90% of VC. The volume inspired is used in the calculation of VA (ie, VA = volume inspired × concentration of inert gas inspired/concentration of expired inert gas).

The accuracy of the estimate of VA depends on the breath-holding taking place at TLC, but theoretically it would be unaffected by inspiration from volumes above RV if gas mixing were perfect. The difference would be accounted for by the expired gas concentration. Therefore, the VA and VC reflect different facets of lung function.

Conceptually, an increased VC could be caused by a greater inspiration (ie, increased TLC), but in patients with airways disease gas trapping is the reason for the termination of an expiratory VC maneuver, and it is assumed that an increase following an intervention is due to a reduction in gas trapping and to more complete emptying. If VC is increased because of a reduced RV following an intervention, there will be no effect on FEV1. Because VA is a static measurement at TLC, it will not be sensitive to the changes in gas trapping that affect VC, which are a feature of low volume and dynamic maneuvers.

Increased VA may lead to increased FEV1. Vmax at a given volume is determined by the driving pressure and airways resistance (Vmax = driving pressure/airways resistance). In the setting of emphysema, in which flow limitation determines Vmax, the driving pressure is effectively the pressure difference across the alveolar walls, that is, the elastic recoil of the alveoli (Pel). Therefore, an increase in Pel will cause Vmax to increase. The relevant airways resistance is that arising in the airways between the alveoli and the point at which the pressure in the airway is insufficient to prevent the airway from narrowing (ie, the equal pressure point). If Pel increases, the equal pressure point will move distally, and resistance will de-
crease and augment the $V_{\text{max}}$. If, as proposed, the increase in $V_A$ is the result of the increased inflation of effective lung tissue, it will cause the Pel to increase. It follows that the Pel will be relatively increased at all lung volumes, that is, there will be a shift to the left of the pressure-volume curve. An increase in the Pel following LVRS was predicted by Fessler and Permutt. Their model of chest wall and lung equilibrium illustrated how Pel at a given volume would be increased and VC would increase, providing that the reduction of RV was greater than the reduction of TLC. Their model concentrated on the forces determining RV at the commencement of inspiration and did not examine ELV beyond what was implied by VC.

Change in the RV/TLC ratio has been advocated as a good measure of LVRS effect. The preoperative TLC in these patients reflects chest size, not potential lung size, which is larger. Therefore the RV/TLC index has a different connotation after LVRS when TLC is more likely to be determined by lung size than chest size. In this series, the FEV$_1$ change correlated more strongly with the change in $V_A$ ($r = 0.63$) than with that in RV/TLC ratio ($r = 0.46$).

Any decrease in chest size and operating lung volume, regardless of the homogeneity of disease, would have benefits for respiratory muscle function through the changed geometry of the chest and diaphragm and the operating length of muscle fibers. The absence of correlation between TLC reduction and the increase in $V_A$ (Fig 3) suggests that these effects may be of secondary importance to the beneficial effects of $V_A$ and recoil increase. The small TLC reduction and the variable effect on $V_A$ in some patients following LVRS may be due to postsurgical inflation of the more diseased lung regions. The mean time between operation and assessment was 173 days; therefore, there may have been additional hyperinflation due to disease progression between the time of surgery and that of the follow-up measurements. With no way of knowing the acute effect of LVRS on TLC, or the volume occupied by the ineffective lung that was removed, conclusions regarding the course of TLC change cannot be made.

Disability was assessed using the 6-min walk test (Fig 2). Overall, there was significant improvement that correlated well with the change in $V_A$ ($r = 0.5$).

The extent to which any improvement in $V_A$ or airway function relates to an improvement in ventilation of the lungs is not clear. Further studies to elucidate this will need to examine the changes in physiologic dead space ventilation and estimations of $P_aO_2$.

Alternative methods for estimating $V_A$, such as the intrabreath technique, may reflect ELV more precisely and may predict LVRS benefit more accurately.

Further prospective investigation is needed to examine how a change in $V_A$ might predict improvement in other indexes of physiologic and perceptual function. The correlation of change in $V_A$ with emphysema type, distribution, and volume of resected tissue may have a place in refining the type and extent of surgical intervention (Fig 4).

In conclusion, $V_A$ is a useful functional measure of outcome in patients who have undergone LVRS.

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FIGURE 4. A schematic of the lungs and of single alveoli at full inspiration before and after LVRS. The alveolus is able to expand to a larger volume following surgery. Benefit depends on the elastic properties of the alveolus. If it is intact, then Pel, ELV, and the results of spirometry testing will all increase. The expansion of severely diseased tissue will have no benefit.
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