Correlation of Changes in Quality of Life After Lung Volume Reduction Surgery With Changes in Lung Function, Exercise, and Gas Exchange*

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**Study objectives:** To evaluate correlations between improvement in quality of life (QOL) in patients with severe COPD before and after they undergo lung volume reduction surgery (LVRS) with changes in pulmonary function tests, gas exchange, exercise performance, and alterations in medical management.

**Design:** Case-series analysis.

**Setting:** University hospital.

**Patients:** Forty-two patients (mean [± SD] age, 56 ± 8 years; 53% women) with severe airflow obstruction (FEV₁, 0.62 ± 0.2 L), and moderate to severe hyperinflation (total lung capacity [TLC], 6.9 ± 1.7 L).

**Intervention and measurements:** All patients underwent bilateral LVRS via median sternotomy. Measurements of lung function, symptom-limited cardiopulmonary exercise testing, the total distance the patient was able to walk in 6 min in a corridor, and sickness impact profile (SIP) scores were made before and 3 months after LVRS. SIP scores are inversely proportional to the level of function and QOL.

**Results:** Compared to baseline, FEV₁ increased (0.87 ± 0.3 vs 0.62 ± 0.2 L, respectively; p < 0.01) while residual volume significantly decreased (3.2 ± 1.8 vs 6.3 ± 1.2 L, respectively; p < 0.004) at 3 months post-LVRS. On cardiopulmonary exercise testing, values increased from baseline to post-LVRS for total exercise time (9.0 ± 2.2 vs 6.0 ± 1.5 min, respectively; p = 0.045), maximum oxygen uptake (VO₂) (16 ± 3 vs 11 ± 2 mL/kg/min, respectively; p = 0.01), and maximum minute ventilation (VE) (33 ± 5 vs 28 ± 5 L/min, respectively; p = 0.03). The percentage change in the oxygen cost of breathing (VO₂/VE ratio) from low to high workloads during exercise was significantly lower after LVRS (p = 0.002). There was no significant change in oxygenation after LVRS (PaO₂/fraction of inspired oxygen, 331 ± 57 vs 337 ± 39, respectively; p = 0.76), but PaCO₂ tended to be lower (41 ± 9 vs 48 ± 6 mm Hg, respectively; p = 0.07). Overall SIP scores were significantly lower after LVRS than before (8 ± 4 vs 15 ± 2, respectively; p = 0.002). Changes in SIP scores correlated with the change in VO₂/VE ratio from low to high workloads, with patients having the smallest changes in VO₂/VE ratio having the smallest changes in SIP scores after LVRS (r = 0.6; p = 0.01). Improved or lower SIP scores also tended to correlate with a reduction in residual volume/TLC ratio (r = 0.45; p = 0.09), and there was a linear correlation with a statistically significant Pearson r value with decreased steroid requirements (r = 0.7; p = 0.001). Moreover, changes in psychological SIP subscore tended to correlate with diminished oxygen requirements post-LVRS (r = 0.45; p = 0.09). However, there was no significant correlation between changes in SIP scores and routine measurements of lung function, exercise performance, or gas exchange.

**Conclusion:** There is an association between an improvement in QOL and reduced hyperinflation after LVRS. Reduced hyperinflation may lead to more efficient work of breathing during exercise and, therefore, to an increased ability to perform daily activities. Changes in QOL scores correlate best with behaviorally based variables that directly affect the patient’s well-being, such as systemic steroid administration.

**Key words:** cardiopulmonary exercise testing; COPD; emphysema; lung volume reduction surgery; quality of life

**Abbreviations:** DLCO = diffusing capacity of the lung for carbon monoxide; f = breathing frequency; FRC = functional residual capacity; LVRS = lung volume reduction surgery; mph = miles per hour; MVV = maximum voluntary ventilation; 6MWD = 6-min walk distance; QOL = quality of life; RV = residual volume; SIP = sickness impact profile; TLC = total lung capacity; VA = alveolar volume; VO₂ = oxygen uptake; VO₂max = maximum oxygen uptake; VE = minute ventilation; Vf = tidal volume; WOB = work of breathing

(CHEST 2000; 118:728–735)
Emphysema is a major cause of pulmonary disability, causing patients to experience significant dyspnea at rest and during exercise, which limits their ability to perform the activities of daily living. Because of these physical constraints, patients with advanced emphysema have a markedly impaired quality of life (QOL).1-4

Lung volume reduction surgery (LVRS) has been reported to improve spirometry,5 exercise performance,6 gas exchange,7 and QOL8 in selected patients with severe COPD. However, these changes in physiologic outcomes have not been correlated with changes in QOL. Since the ultimate goal of any therapy is to improve the patient’s QOL, knowledge of the physiologic factors that are most responsible for improving the patient’s functional status may be the most important in identifying the best patient candidates for LVRS.

In order to determine whether changes in objective physiologic measurements and alterations in medical management (ie, decreased use of oxygen and systemic steroids) affect patients’ estimates of changes in QOL post-LVRS, we evaluated the correlation between changes in QOL and gas exchange, exercise capacity, pulmonary function tests, and medical management before and after LVRS.

**Materials and Methods**

**Patient Selection**

Fifty-three patients with severe COPD were enrolled into the study after fulfilling the inclusion/exclusion criteria (Table 1). Forty-two patients with complete data before and 3 months after LVRS were analyzed. Three patients died before enrollment into the study. Eight patients did not complete either preoperative or postoperative testing for different reasons and, therefore, were not included in the final analysis. All patients were nonsmokers, as determined by self-report and the measurement of carboxyhemoglobin levels on the results of arterial blood gas analysis performed for at least 6 months. All patients signed written informed consent approved by our institution’s Human Research Committee. Baseline data were measured 8 weeks after intensive outpatient pulmonary rehabilitation. Pulmonary rehabilitation was performed in a supervised outpatient setting and consisted of arm and leg cycling, treadmill exercise, weight training of the extremities, and pulmonary education given in three 1.5-h sessions per week for 8 weeks. Following LVRS, each patient underwent outpatient rehabilitation for another 3 months. Follow-up data were obtained 3 months after LVRS. There was no loss to follow-up or death within the study period among the analyzed patients.

**Physiologic Measurements**

**Pulmonary Function Tests:** Pulmonary function testing was performed (System 6200 Autobox DL Plethysmograph; SensorMedics Corporation; Yorba Linda, CA) following American Thoracic Society guidelines.9 FEV1, FVC, and FEV1/FVC ratio were measured. Only postbronchodilator results are reported. Thoracic gas volumes were determined by plethysmography. Functional residual capacity (FRC) also was measured using the helium dilution technique. Trapped gas is reported as the difference between FRC values measured by plethysmography and helium dilution.

The diffusing capacity of the lung for carbon monoxide (DLCO) was measured by the single-breath technique. Maximum voluntary ventilation (MVV) was determined by measuring the expired volume during 12 s of rapid and deep breathing. All pulmonary function data are presented in absolute numbers and as percentages of normal reference values. Normal reference values from the studies by Crapo et al10,11 were used for spirometry, lung volumes, and DLCO.

**Exercise Testing:** All patients underwent incremental maximum treadmill exercise (Precor 9.4 sp; Precor Inc; Bothell, WA), starting at a speed of 1.0 miles per hour (mph) and an inclination of 0% and increasing by 0.5 mph with every 3% increase in inclination every 180 s to the symptom-limited maximum following American Heart Association guidelines.12 During the test, oxygen saturation and multiple-lead ECG (Maxi; SensorMedics) were recorded continuously. The need for supplemental oxygen was individually determined for each patient to prevent oxygen desaturation, and the same supplemental oxygen concentration that was given at baseline was used in follow-up testing. During the test, oxygen uptake (VΩO2), carbon dioxide production, minute

**Table 1—Criteria for LVRS**

<table>
<thead>
<tr>
<th>Inclusion criteria</th>
</tr>
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<tbody>
<tr>
<td>New York Heart Association class III–IV</td>
</tr>
<tr>
<td>Evidence of airflow obstruction and hyperinflation by pulmonary function studies (ie, FEV1 &lt; 30% of predicted, postbronchodilator administration, and RV &gt; 150% of predicted)</td>
</tr>
<tr>
<td>Hyperinflation documented by chest radiograph and emphysema documented by high-resolution CT scan</td>
</tr>
<tr>
<td>Severe reduction in perfusion and significant gas trapping documented in planned resected lung tissue by quantitative ventilation-perfusion lung scan</td>
</tr>
</tbody>
</table>

**Exclusion criteria**

- Patients with severe and refractory hypoxemia (PaO2/FIO2 ratio, < 150)
- Severe hypercapnic respiratory failure requiring mechanical ventilation
- The presence of significant cardiovascular disease
- The presence of severe pulmonary hypertension (mean pulmonary artery pressure, > 25 mm Hg)
- Severe debilitated state with total body weight < 70% of ideal body weight
- Presence of significant extrapulmonary end-stage organ dysfunction expected to limit survival time
- Psychosocial dysfunction
- Continued smoking

*FIO2 = fraction of inspired oxygen.

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Table 2—Baseline Patient Characteristics (n = 42)

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, yr*</td>
<td>56 ± 8</td>
</tr>
<tr>
<td>Gender, %</td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td>53</td>
</tr>
<tr>
<td>Male</td>
<td>47</td>
</tr>
<tr>
<td>Oxygen dependence</td>
<td>70%</td>
</tr>
<tr>
<td>Steroid requirements &gt; 10 mg</td>
<td>32%</td>
</tr>
<tr>
<td>Smoking history, pack-yr*</td>
<td>59 ± 21</td>
</tr>
<tr>
<td>New York Heart Association class</td>
<td>III-IV</td>
</tr>
</tbody>
</table>

*Values given as mean ± SD.

was to remove 20 to 40% of the volume of each lung. High-resolution chest CT and quantitative ventilation-perfusion lung scanning were used preoperatively to target lung regions with the worst emphysema for resection. At the conclusion of the operation, chest tubes were placed and were managed in conventional manner.

Data Analysis

Data are expressed as mean ± SD, except where otherwise noted. Statistical significance between data obtained at baseline and those at 3 months following LVRS was determined by two-tailed t test. A p value < 0.05 was considered statistically significant. Bivariate associations between variables were assessed using the Pearson correlation and linear regression. All statistical analyses were conducted using a commercially available computer software program (Sigmastat, version 10; Jandel Corporation; San Rafael, CA).

RESULTS

Patient Characteristics

Patient characteristics are represented in Table 2. The mean age of patients was 56 ± 8 years. Women and men were equally represented. The majority of patients required oxygen supplementation during their daily activities, as determined by either oximetry during ambulation or arterial blood gas levels obtained on room air. About one third of patients required > 10 mg prednisone per day. All patients had a significant smoking history and functional impairment. All patients were on a maximum bronchodilator regimen prior to enrollment into the study.

Physiologic Data Before and 3 Months After LVRS

Spirometry and Lung Volumes: Table 3 shows the results of spirometry and measurement of lung volumes and DLCO at baseline and 3 months after LVRS. At baseline, all patients had severe airflow limitation.
obstruction (FEV$_1$, 0.62 ± 0.2 L), hyperinflation (total lung capacity [TLC], 6.3 ± 1.2 L), air trapping (residual volume [RV]/TLC ratio, 78 ± 17%), and decreased DLCO/alveolar volume (VA) (1.9 ± 0.3 L/min/mm Hg). After LVRS, FEV$_1$ significantly decreased (p = 0.01), TLC and RV significantly decreased (p = 0.03 and 0.004, respectively), and there was no significant change in the DLCO/VA ratio (p = 0.25).

**Gas Exchange, 6MWD, and Exercise Performance:**

Table 4 shows gas exchange, 6MWD and symptom-limited maximum cardiopulmonary exercise at baseline and 3 months after surgery. All patients had significant exercise limitation at baseline as evidenced by significantly reduced 6MWD, total exercise time, and maximum V˙$\text{e}$. All patients had limited maximum cardiopulmonary exercise at baseline as evidenced by significantly reduced 6MWD, total exercise time, and maximum V˙$\text{e}$. The pattern of breathing changed after LVRS, and patients were less dyspneic, which was reflected by a reduction in dyspnea score (p = 0.04). Oxygenation did not change significantly after LVRS (p = 0.8). PaCO$_2$ showed a trend to be lower after surgery (p = 0.07).

Oxygen cost of breathing (V˙$\text{o}_2$/Ve ratio)$^{37,38}$ was measured at similar workloads during exercise, before and 3 months after LVRS. The V˙$\text{o}_2$/Ve slope of a representative patient is shown in Figure 1. As shown, pre-LVRS there is a steeper increase in the V˙$\text{o}_2$/Ve slope than post-LVRS, reflecting a reduction in energy expenditure at an equivalent exercise level. The mean percentage changes in V˙$\text{o}_2$/Ve ratio from baseline to the highest workloads were significantly lower after LVRS, as shown in Figure 2.

![Figure 1. Comparison of slopes of oxygen cost of breathing (V˙$\text{o}_2$/Ve) in a representative patient during exercise at the same workloads before (solid line and closed circles) and after LVRS (dashed line and open circles). The V˙$\text{o}_2$/Ve relationship is shifted to the right before LVRS, reflecting a higher energy expenditure during an incremented workload.](http://example.com/figure1)

Figure 3 shows changes in total overall and component SIP scores for patients before and after undergoing LVRS. All scores were statistically lower after LVRS, reflecting an overall mean improvement in QOL assessed 3 months after surgery. About 35% of patients demonstrated a reduction in overall SIP score; close to 50% showed an improvement in the physical score, and nearly 45% had an improvement in the psychological score.

**Correlations of Changes in QOL With Physiologic Variables**

Table 5 shows correlations between changes in SIP scores and changes in physiologic variables before and after LVRS. The only trend for significant

![Figure 2. Comparison of percentage changes in V˙$\text{o}_2$/Ve during exercise testing from baseline to maximum exercise level in patients (n = 42) before and after LVRS. After LVRS, the percentage changes in V˙$\text{o}_2$/Ve are significantly lower (p = 0.02).](http://example.com/figure2)
correlation was observed between reductions in total SIP scores and RV/TLC ratios \((r = 0.45; p = 0.09)\).

Figure 4 shows a significant correlation \((r = 0.6; p = 0.03)\) between changes in total SIP scores and post-LVRS changes in oxygen cost of breathing from low to maximum workloads.

Table 6 demonstrates correlations of changes in total SIP scores with post-LVRS oxygen and steroid requirements and duration of hospitalization. There was a significant correlation between decreased steroid requirement and psychological score \((r = 0.7; p = 0.01)\). There was a trend for correlation between changes in oxygen requirement and changes in psychological score \((r = 0.45; p = 0.09)\).

**Discussion**

This investigation confirms prior reports and demonstrates significant improvements in spirometry, exercise performance, and QOL in patients 3 months after undergoing LVRS. A significant correlation between changes in QOL, assessed by SIP score, and routine measurements of spirometry, maximum exercise testing, gas exchange, and 6MWD were not identified. However, we did find a modest correlation between changes in QOL scores and a reduction in the degree of hyperinflation and air trapping post-LVRS. Patients with the smallest changes in oxygen cost of breathing from low to high workloads during maximum exercise testing after LVRS, and therefore having the most efficient work of breathing (WOB), demonstrated significant improvements in QOL. Significant correlations were also found between

**Figure 3.** Compares total SIP score and component physical and psychosocial scores before and after LVRS (n = 42). The total score and component scores were significantly lower after LVRS \((p < 0.05)\).

**Figure 4.** Correlations of changes in SIP score with post-LVRS changes in oxygen cost of breathing \((\dot{V}O_2/\dot{V}E)\) from low to maximum workloads \((n = 42)\). Subjects with the smallest changes in \(\dot{V}O_2/\dot{V}E\) ratio throughout the exercise period experienced the most significant improvement in total SIP scores \((r = 0.6; p = 0.03)\).

**Table 5—Correlations of Changes in SIP Score and Physiologic Variables Before and After LVRS**

<table>
<thead>
<tr>
<th>Variable</th>
<th>(r) Value</th>
<th>(p) Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>FVC, L</td>
<td>0.2</td>
<td>0.3</td>
</tr>
<tr>
<td>FEV(_1), L</td>
<td>0.15</td>
<td>0.7</td>
</tr>
<tr>
<td>RV</td>
<td>0.4</td>
<td>0.2</td>
</tr>
<tr>
<td>RV/TLC</td>
<td>0.45</td>
<td>0.09</td>
</tr>
<tr>
<td>Pac(_O_2)</td>
<td>0.25</td>
<td>0.3</td>
</tr>
<tr>
<td>Pmax</td>
<td>0.35</td>
<td>0.1</td>
</tr>
<tr>
<td>MVV</td>
<td>0.3</td>
<td>0.8</td>
</tr>
<tr>
<td>VO(_2)max</td>
<td>0.2</td>
<td>1</td>
</tr>
<tr>
<td>VTmax</td>
<td>0.3</td>
<td>0.7</td>
</tr>
<tr>
<td>6MWD</td>
<td>0.1</td>
<td>0.8</td>
</tr>
<tr>
<td>Dyspnea score</td>
<td>0.3</td>
<td>0.9</td>
</tr>
<tr>
<td>Exercise time</td>
<td>0.25</td>
<td>0.5</td>
</tr>
</tbody>
</table>

*Correlations were performed by bivariate regression analysis using changes in SIP score as independent variables.
changes in QOL post-LVRS with a decreased need for systemic corticosteroids. There was also a trend for a correlation between changes in QOL and reductions in daily oxygen requirements.

QOL has been used widely both in lay conversations and across fields as diverse as economics, sociology, and medicine, all of which contribute to a level of ambiguity regarding its interpretation. The World Health Organization defines QOL in the following way: “QOL is an individual’s perception of their position in life in the context of the cultural and value systems in which they live, and in relation to their goals, expectations, standards and concerns.”

World Health Organization guidelines provide direction in measuring QOL based on “multidimensional subjective assessment of feelings of wellness and satisfaction, as well as perceptions of impairments, and problems.”

There is abundant literature regarding the methods and role of QOL assessment in patients with end-stage lung disease. Patients with severe COPD experience negative changes in mood and social behavior that are related to a variety of physiologic and psychological factors. Chronic hypoxemia and dyspnea, poor activity tolerance, several different types of medications used in treatment, and frequent hospitalization may all produce detrimental social and emotional changes in a patient’s QOL. Recent data by Seemungal et al support the notion that frequent exacerbations of airflow obstruction in COPD patients provoke significant impairment in their QOL.

Several different methods have been developed to assess QOL, which include the following: the Respiratory Illness Questionnaire, SIP, and St. George’s Chronic Respiratory Disease Questionnaire. All of these tests propose to assess the patient’s subjective evaluation of their functional and behavioral activities. Although it is difficult to identify significant advantages of one test over another, there is some suggestion that the St. George’s questionnaire is more appropriate for assessing small changes in QOL over limited time periods. SIP differs from the Respiratory Disease Questionnaire or the St. George’s Chronic Respiratory Disease Questionnaire in that it is a general measure of health status and can be used not for only the evaluation of a particular disease or symptom, but in variety of situations, therefore providing a great deal of flexibility. SIP provides a measure of health status that is highly sensitive and can be used to detect differences that occur over time or between groups. In our study, we used the SIP to assess QOL because the results of this instrument have been extensively reported.

LVRS has been reported by several investigators to improve QOL. It has been postulated by some authors that improvement in QOL post-LVRS was related to improvements in exercise performance, increases in lung elastic recoil, and reductions in hyperinflation and respiratory muscle function, conditions that result in a decreased sense of dyspnea and an increased range of daily physical activity. However, objective correlations of changes in QOL and physiologic measurements before and after LVRS have not been extensively reported. We are aware of only one study that attempted to evaluate health-related QOL assessment with improvement of functional data. Hajiuro et al found very weak correlations between changes in FEV1 and the domains of social functioning and vitality.

Our data are consistent with those in prior studies that document an improvement in QOL after LVRS. However, we extend those findings by demonstrating for the first time that an improvement in QOL post-LVRS may be associated with a decrease in hyperinflation and gas trapping. Significant hyperinflation and air trapping cause an unfavorable length-tension relationship of respiratory muscles, increased dead space, and, therefore, increased ventilatory demands during activity. Increased ventilatory requirements cannot be met in patients with advanced emphysema because of a reduced ventilatory capacity, which leads to an increased sense of dyspnea and a limitation in physical activity. A reduction in hyperinflation and air trapping post-LVRS favorably affects respiratory mechanics, both at rest and during exercise, and thereby reduces the patient’s sense of dyspnea, optimizes functional capacity, and, therefore, positively affects QOL.

Oxygen cost of breathing has been reported previously as a measure of energy utilization by the respiratory muscles. Henry et al demonstrated that LVRS correlates with a decrease in oxygen cost of breathing.

| Table 6—Correlations of Changes in SIP Scores With Post-LVRS Oxygen and Steroid Requirements and Length of Hospital Stay* |
|-------------------|-------------------|-------------------|
| SIP Scores        | Oxygen Requirements | Steroid Requirements |
|                   | During Activity    | At Rest            | Requirements |
| Overall           |                   |                   |               |
| r value           | 0.2               | 0.4               | 0.01          |
| p value           | 0.01              |                   |               |
| Psychological score |                   |                   |               |
| r value           | 0.45              | 0.4               | 0.7           |
| p value           | 0.09              | 0.1               | 0.01          |
| Physical score    |                   |                   |               |
| r value           | 0.2               | 0.6               | 0.08          |
| p value           |                   |                   |               |

*Correlations were performed by bivariate regression analysis using changes in total SIP score and component scores as independent variables.
that an elevated oxygen cost of breathing represents an increase in the WOB, as well as a decrease in the efficiency of respiratory muscle contraction. Patients with underlying lung disease present with an increased respiratory load that demands greater ventilation. As ventilatory workload increases, a greater amount of \( V_{O_2} \) is diverted to the respiratory muscles. We presented oxygen cost of breathing as a ratio \( (V_{O_2}/Ve) \) that represents energy output \( (V_{O_2}) \) and respiratory work \( (Ve) \), respectively.

In our study, patients had a significant increase in \( V_{O_2}/Ve \) ratio during the performance of lower extremity exercise, reflecting an improvement in the efficiency of energy expenditure following LVRS. We show that patients experiencing the smallest change in \( V_{O_2}/Ve \) ratio from low to maximum workload (ie, more energy-efficient WOB) had significantly decreased SIP scores and, thus, the most significant improvement in QOL after LVRS.

In our investigation, changes in QOL scores did not correlate with changes in routine spirometry or exercise measurements. Several previous studies also have failed to show a significant correlation between changes in the severity of airflow obstruction and QOL assessment.39,30,36

Because the SIP QOL assessment, like any other QOL tool, measures behaviorally related parameters, it would be expected to correlate best with improvements in behavioral and psychological indicators. The strongest correlations in our study were observed between improvements in SIP scores and decreased requirements for systemic steroids. Long-term steroid treatment is known to have a profound effect on mood, sleep, food intake, and general appearance.37 Patients might tend to characterize their QOL as being best when they did not experience the adverse side effects associated with steroid use. The behavioral nature of this relationship is further supported by the significant correlation between psychological subscore and the above-mentioned parameters. Moreover, there was a trend toward a correlation between improved SIP score and a reduced need for daily oxygen requirement post-LVRS, which may also reflect an improvement in the functional daily activity of patients after undergoing LVRS, another finding that most likely is based on psychological factors.

We realize that there are limitations for this study, which include the relatively small number of studied subjects and the subjective character of QOL assessment. However, SIP scores remain a commonly applied, validated tool in the clinical assessment of the QOL that have been shown to improve after a variety of therapies, both surgical and nonsurgical, for patients with a variety of chronic lung diseases.

In this study, we demonstrated an association between an improvement in QOL and more efficient ventilation, as evidenced by changes in oxygen cost of breathing and an increased range of daily activity. The more efficient WOB during exercise after LVRS is likely to be due to reduced hyperinflation. We did not find strong correlations between changes in QOL, as assessed by the SIP questionnaire, and changes in lung function, exercise, and gas exchange.

Finally, the most significant correlation we found was between the changes in the SIP scores and the changes in steroid requirements, which most likely reflects a behavioral response to an improved QOL.

**REFERENCES**