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Lung Function 5 yr after Lung Volume Reduction Surgery for Emphysema

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Current datum more than 2 yr after lung volume reduction surgery (LVRS) for emphysema is limited. This prospective study evaluates pre-LVRS baseline and 5-yr results in 26 symptomatic patients (mean age 67 ± 6 yr) (mean ± SD) who underwent bilateral, targeted upper lobe stapled LVRS using video-assisted thoracoscopy. Baseline forced expiratory volume in 1 s (FEV₁) was 0.7 ± 0.2 L (mean ± SD), 29 ± 10% predicted. Following LVRS, with none lost to follow-up, mortality due to respiratory failure at 0.5, 1, 2, 3, 4, and 5 yr was 4%, 4%, 19%, 31%, 46%, and 58%, respectively. Increase above baseline for FEV₁ > 200 ml and/or FVC > 400 ml at 1, 2, 3, 4, and 5 yr post-LVRS was noted in 73%, 46%, 35%, 27%, and 8% of all patients; decrease in dyspnea grade ≥1 in 88%, 69%, 46%, 27%, and 15%; and elimination of initial oxygen dependence in 18 patients in 78%, 50%, 33%, 22%, and 0%, respectively. Expiratory airflow improved due to the increase in both lung elastic recoil and small airway intraluminal caliber. Five patients decreased FEV₁ 141 ± 60 ml yr and FVC 102 ± 189 ml yr over 3.8 ± 1.2 yr post-LVRS, similar to their pre-LVRS rate of decline. In the 11 patients who survived 5 yr, at 0.5–1.0 yr post-LVRS peak increase in FEV₁ was 438 ± 366 ml, with a decline of 149 ± 157 ml the following year and 78 ± 59 ml yr over 4.0–4.5 yr. Bilateral LVRS provided palliative clinical and physiological improvement in 9 of 26 patients at 3 yr, 7 at 4 yr, and 2 at 5 yr.

Despite best medical therapy, patients with severe chronic airflow limitation due to emphysema suffer from progressive dyspnea, poor exercise tolerance with increased morbidity, and mortality compared to age-matched normal cohorts. When the forced expiratory volume in 1 s (FEV₁) is < 0.75 L or 30% predicted, mortality of 40% to 50% at 3 yr has been noted (1, 2). Furthermore, patients older than 65 yr of age hospitalized in the intensive care unit for an exacerbation of chronic obstructive lung disease, irrespective of the need for invasive or noninvasive ventilation, have an overall 1-yr mortality rate of 30%; whereas in other similar patients older than 65 yr of age, mortality rate is 60% (3).

The surgical modification of lung volume reduction surgery (LVRS) by Meyers and coworkers (4) resulted in marked improvement in dyspnea, exercise tolerance, and lung function. The 2-yr post-LVRS results are in contrast to the progressive deterioration in similar patients accepted for, but denied LVRS by Medicare, and followed for a similar time (4). Prospective long-term studies, beyond 2 yr after LVRS, are very limited (4–6).

We report our prospective 5-yr results following LVRS in 26 patients with non-α₁-antitrypsin deficiency emphysema with none lost to follow-up.

METHODS

Patient Selection

As previously reported (6, 7), the patients with emphysema were markedly symptomatic with grade ≥ 3 dyspnea (able to walk ≤ 100 yd), and had exhausted best medical therapy. This included antibiotics, aerosol and oral bronchodilators, including short-acting and long-acting β₂-agonists, ipratropium bromide, corticosteroids, and repeated attempts at physical conditioning. High-resolution, thin-section computerized tomography (CT) lung demonstrated emphysema severity scores ≥ 60 with heterogeneous distribution, that is, more severe emphysematous destruction predominantly in the upper half lung field, score 84 ± 12 (mean ± SD), compared with 62 ± 15 in the lower half lung field. These ranking scores from 0 to 100 (worst) are a modification of the anatomic emphysema picture-grading technique (6, 7). Nuclear medicine perfusion scans demonstrated similar heterogeneous distribution. Smoking history was 52 ± 13 pack-years (mean ± SD). Patients ceased cigarettes smoking ≥ 6 mo prior to LVRS. Significant peak systolic pulmonary artery hypertension ≥ 45 mm Hg was excluded by clinical and echocardiogram evaluation.

Operative Technique

As previously reported (6), from January to June 1995, after obtaining informed consent, 82 patients underwent immediate sequential, bilateral stapled lung volume reduction for emphysema, using video-assisted thoracoscopic surgery (VATS). Surgical technique and selection have been previously reported (6, 7). It was estimated that approximately 20% to 30% of each lung was excised, and resected lung weighed 30–90 g. Twenty-six of the 82 patients agreed to undergo additional studies, including lung elastic recoil, both pre- and postoperatively, and form the basis of this prospective study.

Lung Function Studies

As previously reported (6, 7), we obtained informed consent and measured lung function and exercise studies after three inhalations (670 µg) of aerosolized albuterol.

Follow-up

All patients were followed for up to 5 yr post-LVRS unless death intervened. No patient was lost to follow-up.

RESULTS

The results of preoperative lung function studies in the 26 patients (18 men), aged 67 ± 6 yr (mean ± SD) are reported in Table 1. Preoperative spirometry, lung volumes, and diffusing capacity in the 26 patients were not significantly (p > 0.05) different from the other 56 patients (data not shown) who underwent LVRS during the same study period, but were not studied in greater physiological detail. Baseline results for 21 of the 26 patients (data not shown) were not significantly different from five patients who had serial annual spirometry prior to LVRS. Although overall smoking history was similar, the
subgroup of five patients quit 3.3 ± 3.0 yr prior to LVRS, and 
two quit 6 mo prior to LVRS.

Actual survival at 0.5, 1, 2, 3, 4, and 5 yr post-LVRS was 
96%, 96%, 81%, 69%, 54%, and 42%, respectively (see Figure 1). All deaths were related to 
respiratory failure, although concomitant lung malignancy was noted in two of four 
patients autopsied. Improvement in FEV\textsubscript{1} > 0.2 L, FVC > 0.4 L, 
or both was 88%, 73%, 46%, 35%, 27%, and 8% of all 
patients, respectively, and they are considered responders (see Figure 1). Six of nine 
patients at 3 yr, five of seven patients at 4 yr, and the two patients at 5 yr who 
performed this physiological improvement post-LVRS had both FEV\textsubscript{1} > 0.2 L as 
well as FVC > 0.4 L when compared with baseline values.

There was a decrease in dyspnea grade ≥ 1 in 88%, 88%, 
69%, 46%, 27%, and 15% of the 26 patients at 0.5, 1, 2, 3, 4, 
and 5 yr post-LVRS. Oxygen dependence (part or full time) 
present initially in 18 patients was eliminated in 78%, 78%, 
50%, 33%, 22%, and 0% of surviving patients at 0.5, 1, 2, 3, 4, 
and 5 yr post-LVRS.

**Maximum Expiratory Airflow**

At 5 yr post-LVRS, we analyzed the mechanism(s) of 
 improvement in expiratory airflow in the two long-term 
responders who increased both FEV\textsubscript{1} > 0.2 L and FVC > 0.4 L. Compared with preoperative baseline, the maximum 
expiratory flow volume curve demonstrated a reduction in both 
total lung capacity (TLC) and residual volume (RV), but more 
so in the latter, such that FVC increased (see Figure 2). Fur-
thermore, maximum expiratory airflow at any lung volume 
was increased when compared with the same lung volume 
post-LVRS, but still far below normal values. In these two 
patients, FEV\textsubscript{1} increased 210 ml and 460 ml, and FVC 
increased 710 ml and 470 ml, respectively, compared with baseline.

**Figure 1.** Results of survival, part- or full-time oxygen depen-
dence, dyspnea, and lung function studies 0.5 to 5 yr post-LVRS. 
FEV\textsubscript{1}, forced expiratory volume in 1 s; FVC, forced vital capacity.
Lung Elastic Recoil

Prior to LVRS, these two patients had a marked reduction in static lung elastic recoil pressure at TLC: 9 and 12 cm H2O (Figure 3). At 5 yr post-LVRS, elastic recoil pressures remained increased at TLC: 11 and 15 cm H2O, respectively, and at all lung volumes compared with preoperative baseline, but still below normal values. Improvement in lung elastic recoil pressure held steady in the two patients between 1 and 4 yr after LVRS with deterioration at 5 yr post-LVRS.

Mechanism of Expiratory Airflow Limitation

Preoperatively, the slope (conductance small airway S segment, Gs) of the maximum expiratory airflow–static lung elastic recoil pressure (MFSR) curve was reduced compared with normal (6, 7) (Figure 4). This indicates that maximum expiratory airflow was reduced, not only because of loss of lung elastic recoil, but also due to suspected intrinsic small airways abnormalities and/or extrinsic collapse/obstruction of small airways. In the two long-term responders 5 yr after LVRS, maximum expiratory airflow increased, both due to greater lung elastic recoil as well as increased conductance of the S segment slope, reflecting better airway stability with less collapse/obstruction of flow-limiting segments. The increase in the S segment slope remained similar from 1 to 4 yr post-LVRS before deteriorating by 5 yr post-LVRS, but still greater than baseline.

Baseline Physiologic Tests

We previously reported (6) significant differences (p < 0.01) only for VC and FVC of all preoperative baseline parameters between long-term responders when compared with short-term responders. In the present study, sensitivity and specificity for baseline FVC ≥ 65% predicted to detect patients who achieved FEV1 > 0.2 L and/or FVC > 0.4 L at 3 yr post-LVRS is 56% and 71%, respectively, at 4 yr 71% and 74%, and at 5 yr post-LVRS 50% and 63%, respectively.

Follow-up of FEV1 and FVC

In five patients with serial spirometry prior to LVRS, the decline in FEV1 and FVC for 3.8 ± 0.4 yr prior to LVRS was 116 ± 110 ml/yr and 188 ± 154 ml/yr, respectively. After LVRS, following peak improvement and smoking cessation ≥ 6 mo, the subsequent deterioration in spirometry in each patient was similar (p > 0.20) to their pre-LVRS values. The FEV1 decreased 141 ± 60 ml/yr and FVC 102 ± 189 ml/yr over 3.8 ± 1.2 yr post-LVRS with a fastest rate of decline within 1–2 yr after LVRS. In the 11 patients who survived 5 yr, at 0.5–1.0 yr post-LVRS the peak increase in FEV1 was 438 ± 366 ml, with a decline of 149 ± 157 ml the following year and 78 ± 59 ml/yr over 4.0–4.5 yr (Figure 5).

Follow-up Exercise Study

Results of yearly exercise studies in three of 4–5 yr patient responders are reported in Table 2. Following LVRS, there was a modest increase in work performance with increase in oxygen saturation at rest and after exercise, such that all three patients became oxygen independent. Following LVRS, patients who initially improved, but subsequently returned to baseline spirometry and dyspnea values, showed no improvement in exercise performance compared with baseline (data not shown).

DISCUSSION

This prospective study, with no patients lost to follow-up, demonstrates that following bilateral LVRS for emphysema, using VATS technique, durable clinical and significant physiologic improvement was achieved in 9 of 26 patients at 3 yr, 7 patients at 4 yr, and 2 patients at 5 yr. All patients had failed best medical therapy, including numerous rehabilitation efforts prior to LVRS.
These observations, using very strict objective outcome criteria, were noted in elderly patients with end-stage emphysema with an anticipated high morbidity and mortality rate from respiratory failure based on historical cohort data (1–3).

Clinical Outcome

The mortality rate due to respiratory failure of 4%, 4%, 19%, 31%, 46%, and 58% following LVRS in the present study at 0.5, 1, 2, 3, 4, and 5 yr is consistent with previous surgical studies reporting up to 3 yr follow-up.

Naunheim and coworkers (5) reported 1–3 yr mortality rate of 14%, 25%, and 31%, respectively, in 330 patients undergoing unilateral LVRS using VATS technique, and 10%, 19%, and 26% after bilateral LVRS in 343 patients. Patient selection, including baseline lung function and lung CT heterogeneity, was similar to the present study with 99% clinical follow-up. Lung function was reported only at 6 to 12 mo post-LVRS (8). However, patients’ perceptions regarding improved quality of life and dyspnea relief at 2 yr after LVRS were between 71% and 88%, with bilateral LVRS yielding superior improvement (8).

Hamacher and coworkers (9) noted a mean increase of 36% from baseline FEV₁ in 16 patients studied with marked heterogeneity on lung CT 2 yr after bilateral LVRS using VATS technique, with 3% mortality. Alternatively, they noted only a 13% increase from baseline FEV₁ in 12 patients with lung CT homogeneity 2 yr after LVRS, with 23% mortality (6 of 26 patients). Relief from dyspnea was significantly improved (p < 0.01) in surviving patients at 2 yr following LVRS.

Flaherty and coworkers (10) noted improved clinical and exercise tolerance without corroborative increase in mean FEV₁ in seven patients followed for 3 yr after bilateral LVRS using a mediansternotomy technique, with a 3 yr mortality rate of 16% (14 of 89 patients). Although baseline lung function was similar to the present study, lung CT emphysema heterogeneity was not a surgical prerequisite.

Yusen and coworkers (11) noted a 1 to 5 yr actuarial mortality of 6%, 12%, 18%, 28%, and 38%, respectively, in 192 of 200 patients with lung CT heterogeneity who underwent bilateral LVRS using a mediansternotomy technique. Baseline lung function was similar to the present study. Approximately

### Table 2. Work Performance Before and 5 yr After LVRS in Three Patients (A–C)

| Time (yr) | $V_{O_2,max}$ (ml/kg/min) | $\dot{V}_E$ (L/min) | Dyspnea Grade | $O_{2sat}$ (%) | FEV₁ (L) (% pred) | TLC (L) (% pred) | PSTL at TLC (cm H₂O) |
|-----------|---------------------------|---------------------|---------------|---------------|------------------|----------------|----------------------|
| Baseline A | 5.4                        | 11                  | 3             | 87            | 0.47 (30)        | 6.2 (162)       | 12                   |
| 1 yr post  | 6.9                        | 14                  | 2             | 92            | 0.77 (51)        | 5.4 (141)       | 15                   |
| 2 yr post  | 8.0                        | 19                  | 2             | 94            | 0.77 (51)        | 5.7 (149)       | 15                   |
| 3 yr post  | 6.9                        | 14                  | 2             | 93            | 0.75 (50)        | 5.5 (146)       | 15                   |
| 4 yr post  | 7.6                        | 12                  | 2             | 93            | 0.69 (38)        | 5.8 (153)       | 15                   |
| 5 yr post  | 6.5                        | 12                  | 2             | 93            | 0.68 (37)        | 5.5 (147)       | 15                   |
| Baseline B | 5.6                        | 20                  | 4             | 86            | 0.91 (37)        | 8.7 (148)       | 9                    |
| 1 yr post  | 12.4                       | 43                  | 2             | 94            | 1.76 (71)        | 8.4 (143)       | 18                   |
| 2 yr post  | 10.1                       | 42                  | 2             | 94            | 1.61 (65)        | 8.3 (141)       | 16                   |
| 3 yr post  | 9.5                        | 33                  | 2             | 94            | 1.50 (59)        | 8.0 (136)       | 12                   |
| 4 yr post  | 9.5                        | 31                  | 2             | 94            | 1.40 (55)        | 8.0 (136)       | 11                   |
| 5 yr post  | 9.4                        | 30                  | 2             | 87            | 1.40 (55)        | 8.1 (137)       | 11                   |
| Baseline C | 5.5                        | 33                  | 3             | 85            | 0.78 (27)        | 10.1 (172)      | 10                   |
| 1 yr post  | 8.0                        | 33                  | 2             | 92            | 1.37 (49)        | 8.7 (149)       | 12                   |
| 2 yr post  | 9.5                        | 40                  | 2             | 93            | 1.18 (43)        | 8.7 (149)       | 11                   |
| 3 yr post  | 9.4                        | 38                  | 2             | 91            | 1.24 (45)        | 9.1 (156)       | 11                   |
| 4 yr post  | 7.1                        | 25                  | 2             | 91            | 0.91 (32)        | 9.0 (156)       | 12                   |
| 5 yr post  | 6.5                        | 24                  | 3             | 87            | 0.82 (30)        | 8.5 (146)       | 9                    |

*Definition of abbreviations: LVRS = lung volume reduction surgery; PSTL at TLC = lung elastic recoil at total lung capacity; $\dot{V}_E$ = maximum minute ventilation at peak exercise; $V_{O_2,max}$ = maximum oxygen consumption at peak exercise.*
75% of surviving patients noted clinical improvement. Long-term lung function follow-up was not reported.

Pinto and coworkers (12) noted a 3-yr mortality rate of 30% in 18 patients following bilateral LVRS, with significant clinical improvement and mean increase in FEV$_1$ of 26% from baseline at 2 yr after LVRS.

In the present study, the mean age was 67 yr, similar to the studies of Hamacher and coworkers (9) and Nauheim and coworkers (5), whereas the mean age was 61 yr in the studies of Yusen and coworkers (11), 60 yr in Flaherty and coworkers (10), and 63 yr in Pinto and coworkers (12).

Surgical mortality risk for bilateral LVRS of 5% (11, 12), 5% (unilateral) (5), 7% (5), 6% (10), and 9% (9) were previously noted.

Comparing current patient results to historical (1–3) or similar nonrandomized case–controls (4) may be problematic because of clinical, pathological, and smoking history differences. However, using each patient as their own control does not systematically overestimate the magnitude of the effects of treatment as compared with those in randomized, controlled trials on the same topic (13).

An extensive review of LVRS experience has been reported (14). Three recently published randomized, controlled bilateral LVRS studies with crossover and 3–12 mo follow-up confirmed the short-term benefits of LVRS, including improvement in lung function, exercise tolerance, and quality of life (15–17). Unfortunately, for patient selection, other than upper lobe emphysema heterogeneity on lung CT baseline, lung function studies do not offer sufficient sensitivity and/or specificity to predict long-term improvement.

**Decline in FEV$_1$ after LVRS**

The present results are in agreement with our previously reported (18) decline in FEV$_1$ of 255 ± 57 ml/yr in 90 patients post-LVRS with mean follow-up of only 420 ± 15 d. The fastest decline in FEV$_1$ was noted 1–2 yr following LVRS. Furthermore, we previously noted a weak correlation between short-term increase in FEV$_1$ post-LVRS and long-term rate of decline in FEV$_1$ (r = 0.162, p = 0.29) (18). There are obvious limitations to data interpretation including comparison of post-LVRS nonsmokers with pre-LVRS smokers, and comparison of FEV$_1$ decline from varying lung volumes with different mechanical properties.

**Dyspnea and Exercise Tolerance Post-LVRS**

The improvement in dyspnea and exercise tolerance following LVRS best correlates with the reduction in hyperinflation and increase in transdiaphragmatic pressure due to repositioning of the diaphragm with recruitment of inspiratory respiratory muscles (19–23) and increased neuromechanical coupling (23), often irrespective of changes in FEV$_1$. Our limited 5-yr exercise results in three patients confirm the imperfect relationship among dyspnea, lung function, work performance, and oxygen saturation (see Table 2). We believe the persistent reduction in hyperinflation and subsequent increase in transdiaphragmatic pressure are consequent to the maintained increase in lung elastic recoil following LVRS.

In summary, LVRS provided significant clinical and physiological improvement in 9 of 26 selected patients up to 3 yr, 7 at 4 yr, and 2 at 5 yr.

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