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# Rate of $FEV_1$ Change Following Lung Volume Reduction Surgery*

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***Introduction:*** **Lung volume reduction surgery (LVRS) improves pulmonary function and dyspnea symptoms acutely in selected patients with heterogeneous emphysema. Limited data are available regarding long-term function following LVRS. We analyzed short-term (<6 months) and long-term rate of change of pulmonary function in 376 patients who underwent unilateral or bilateral LVRS using thoracoscopic or median sternotomy, staple, laser, or combined techniques. We hypothesized that the long-term rate of deterioration in lung function would be dependent on the surgical procedure used and would be greatest in those with the largest short-term postoperative improvement.**

***Methods:*** **Pulmonary function was assessed preoperatively and at repeated intervals following LVRS. The change in pulmonary function over time was assessed for each patient by determining the individual change in $FEV_1$ using linear regression analysis short and long term. Overall rate of change in pulmonary function was calculated for the composite group of patients and subgrouped by operative procedure.**

***Results:*** **Lung function appears to improve in the first few months following LVRS in most patients, maximizing at approximately 3 to 6 months and declining thereafter. The short-term incremental improvement following staple procedures is superior to improvements following laser procedures or unilateral surgery: $FEV_1$ increase (mean±SD) of 0.39±0.03 L for bilateral staple, 0.25±0.03 L for unilateral staple, 0.10±0.03 L for unilateral laser, and 0.22±0.1 L for mixed unilateral staple/laser procedures. However, the long-term rate of decline in $FEV_1$ was greatest for bilateral staple LVRS procedures as well: 0.255±0.057 L/yr for bilateral staple, 0.107±0.068 L/yr for unilateral staple, 0.074±0.034 L/yr for unilateral laser, and 0.209±0.12 L/yr for mixed staple laser procedures. There was a general correlation between the magnitude of short-term incremental improvement and the rate of deterioration in $FEV_1$ ($r=0.292$, $p=0.003$).**

***Conclusions:*** **While bilateral staple LVRS procedures lead to greater short-term improvement in $FEV_1$, the more rapid rate of $FEV_1$ decline in these patients and the general association between greater short-term incremental improvement and higher rates of deterioration raise questions regarding optimal long-term procedures. Further studies will be needed to answer these important questions.** ***(CHEST 1998; 113:652-59)***

**Key words:** duration; $FEV_1$; lung volume reduction surgery

**Abbreviation:** LVRS=lung volume reduction surgery

Lung volume reduction surgery (LVRS) has been demonstrated to provide short-term palliative benefits in terms of pulmonary function and dyspnea symptoms in selected patients with heterogeneous emphysema. Limited data are available regarding long-term benefits following LVRS. Understanding of long-term response to lung volume reduction is essential for assessing the overall value of LVRS procedures and their eventual role in management of emphysema.

A number of LVRS approaches have been described, including the following: unilateral, bilateral, thoracoscopic, median sternotomy, staple, and laser LVRS procedures. Acutely, bilateral staple LVRS appears to provide superior incremental benefit and equivalent or improved morbidity in comparison to other LVRS procedures and has gained favor as the

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predominant LVRS procedure at most institutions.[1-11] However, questions arise regarding possible discrepancies between short-term and long-term response. Is the rate of deterioration equivalent among the various surgical procedures? Is the rate of deterioration related to the initial incremental response? Is it possible that sequential unilateral procedures could, in the long run, provide superior palliation in certain subgroups compared with bilateral procedures? In addition to describing long-term postoperative outcomes, examination of these questions will aid in further understanding the optimal approaches to LVRS.

Our research group had the unique opportunity to compare response to these various approaches in a large series of patients treated by a single group of surgeons at Chapman Medical Center over a 3-year period.[2,5] In this study, we analyze the short-term (<6 months) and long-term pulmonary function response as well as the rate of change of pulmonary function in 376 patients who underwent unilateral or bilateral LVRS thoracoscopic or median sternotomy, staple, laser, or combined LVRS techniques based on the initial type of procedure and the initial incremental response to treatment. We hypothesized that the long-term rate of deterioration in lung function would be dependent on the surgical procedure and would be greatest in those with the largest short-term postoperative improvement.

## Materials and Methods

All patients who underwent LVRS at Chapman Medical Center from May 1994 to July 1996 were included in this evaluation. Patients underwent baseline complete pulmonary function testing, including the following: spirometry, gas exchange measures (room air arterial blood gas measurement, diffusion of carbon monoxide), plethysmography, and gas dilution lung volumes (Table 1). Maximum inspiratory and expiratory flow volume curves and thoracic gas volume were measured in a plethysmograph (Collins/Cybermedic Classic TCI and Body Plethysmograph; Warren E. Collins Inc; Braintree, Mass), and compared with predicted values as previously described.[2,5] All patients underwent LVRS at Chapman Medical Center by one or both of the two thoracic surgeons in the research group (R.J.M., R.J.F.); no procedures were performed at any other center in this protocol.

Repeated pulmonary function studies were requested from patients 3 months postoperatively, at 6 months, and at approximately 6-month intervals thereafter (Table 2). Whenever possible, repeated spirometry was performed at least once at Chapman Medical Center within 3 months of surgery, but subsequent spirometry data were obtained from the referring site.

Selection criteria and operative procedures for thoracoscopic LVRS have been described previously.[2,5] Informed consent was obtained from all patients. Despite maximal medical management, all patients were markedly symptomatic. Chest radiographs showed hyperexpansion of the thorax with flattening or inversion of the diaphragms.

Contraindications to surgery included current cigarette smoking, age older than 80 years, severe cardiac disease (congestive heart failure, significant coronary or valvular disease), history of cancer within the last 5 years, ventilator dependency, or prior thoracic surgery. Relative contraindications included age older than 75 years, severe anxiety, severe depression, or $CO_2$ retention with resting $PaCO_2$ >55 mm Hg.[2,5]

To be accepted for the procedure, the pattern of emphysema on CT had to be severe and heterogeneous. Radionuclide lung perfusion scans were also used to confirm the heterogeneous pattern of emphysema.[2,5]

### *Thoracoscopic LVRS Operative Methods*

Operative procedures for thoracoscopic laser and staple volume reduction surgery have been described previously as well.[2,5] All patients underwent video-assisted thoracic surgery under paralyzed (pipecuronium) general anesthesia (isoflurane) using a left-sided double-lumen tube (Mallincrodt Anesthesia; St. Louis).

All the procedures were performed with patients in the lateral decubitus position by one surgical group (R.J.M., R.J.F., M.B.). The trocar and thoracoscope were placed through the 10th intercostal space in the posterior axillary line. Three additional 1- to 2-cm incisions were made for standard instruments. Patients were turned to the contralateral decubitus position for separate sterile preparation and draping after completion of surgery on the initial side in patients undergoing bilateral thoracoscopic procedures.

Preoperative lung CT scans and ventilation perfusion scans were used to identify areas of dysfunctional or degenerated lung targeted for resection with the staples.[2,5] Ring forceps manipulated the lung into a 60-mm endoscopic stapler (ELC 60; Ethicon; Cincinnati) with bovine pericardium (Peristrips; Biovascular; Saint Paul, Minn) or bovine collagen matrix (Instat; Johnson and Johnson; New Brunswick, NJ) to buttress the staples. The staples were fired an average of 15 times for bilateral operations. Typically, approximately half of the upper lobe was resected in patients with upper lobe disease.

For unilateral laser lung volume reduction procedures, an Nd-YAG laser was used in a contact mode; photocoagulation of emphysematous areas was achieved using 10 W and resulted in nearly complete visual contraction of the affected site.

### *Combined Staple/Laser LVRS Procedures*

Combined staple/laser LVRS procedures were used in patients with focal areas of bullous disease >2 cm in diameter (though no patients were included in this series if bullae were >8 cm). Methods were identical to those described in the individual laser and staple procedures. Staple volume reduction was performed in the most involved regions. The remaining lung surface was then exposed to the contact tip Nd-YAG laser in the usual manner.[5]

### *Median Sternotomy Procedures*

Bilateral staple LVRS was performed on a limited number of patients early in the program using a standard median sternotomy approach and bilateral bovine pericardium buttressed stapling using standard techniques.[3,6] This approach was replaced by the bilateral thoracoscopic method once the bilateral thoracoscopic surgical techniques were developed.[2]

### *Response Assessment*

To be included in the short-term follow-up evaluation analyses in this study, patients were required to have at least two follow-up

**Table 1—*Baseline Characteristics****

| | All Patients (n=376) | | Patients With Multiple F/U (n=180) | | Patients Without F/U (n=45) | | Patients With Single F/U (n=151) | |
|---|---|---|---|---|---|---|---|---|
| | Mean | SEM | Mean | SEM | Mean | SEM | Mean | SEM |
| Age, yr | 67.30 | 0.48 | 67.29 | 0.49 | 68.90 | 0.73 | 67.80 | 0.63 |
| Height, in | 67.70 | 0.25 | 67.67 | 0.25 | 67.70 | 0.52 | 67.80 | 0.30 |
| Weight, lbs | 149.90 | 2.20 | 149.86 | 2.20 | 146.36 | 0.40 | 147.90 | 2.57 |
| Dyspnea score† | 2.92 | 0.06 | 2.91 | 0.06 | 3.11 | 0.12 | 3.10 | 0.06 |
| FVC, L | 2.05 | 0.05 | 2.05 | 0.05 | 1.86 | 0.10 | 2.04 | 0.06 |
| $FEV_1$, L | 0.67 | 0.02 | 0.67 | 0.02 | 0.6‡ | 0.03 | 0.67 | 0.02 |
| Dco, mL/mm Hg/min | 5.50 | 0.22 | 5.51 | 0.22 | 3.90 | 0.29 | 4.86 | 0.26 |
| TLC, L | 7.36 | 0.12 | 7.36 | 0.12 | 6.95 | 0.28 | 7.47 | 0.13 |
| RV, L | 4.65 | 0.09 | 4.62 | 0.10 | 4.50 | 0.23 | 4.73 | 0.12 |
| RV/TLC | 0.69 | 0.02 | 0.68 | 0.02 | 6.85 | 0.01 | 0.70 | 0.04 |
| $Pco_2$, mm Hg | 43.00 | 0.55 | 41.00 | 0.55 | 44.90 | 1.20 | 43.10 | 0.73 |
| $Po_2$, mm Hg | 64.80 | 0.88 | 64.00 | 0.89 | 57.49‡ | 1.57 | 62.48 | 1.04 |
| Hospital stay, d | 9.18 | 0.52 | 9.81 | 0.52 | 11.96 | 1.24 | 9.72 | 0.74 |
| Change in $FEV_1$, L | 0.24 | 0.02 | 0.24 | 0.02 | | | | |
| % Change in $FEV_1$ | 61.10 | 3.80 | 61.16 | 3.75 | | | | |

*F/U=follow-up; Dco=diffuse of carbon monoxide; RV=residual volume; TLC=total lung capacity.
†Dyspnea score by Modified Medical Research Council (MMRC) Dyspnea Scale.
‡$p<0.05$ compared with patients with multiple follow-up visits.

pulmonary function tests (at least 30 days apart) within the first 6 months postoperatively. To be included in the long-term follow-up evaluation analyses, patients were required to have at least two follow-up pulmonary function analyses (at least 120 days apart) ≥6 months postoperatively.

The change in $FEV_1$ at the time of initial follow-up was determined for all patients whose initial follow-up visit was within 6 months of surgery (Table 3 and Figure 1). The maximal short-term postoperative improvement was defined as the highest $FEV_1$ measured within the 6 months postsurgery.

Long-term follow-up rate of change in $FEV_1$ was determined from the slope of linear regression of follow-up data in each patient with multiple measurements >6 months postsurgery. The mean of the individual regression slope and SEM are reported as the average decline in lung function long term (using only the data obtained ≥6 months postoperatively) reported on an annualized basis as liters per year.

### *Statistical Analysis*

Differences between baseline characteristic among treatment groups were investigated using *t* tests (for comparisons between two groups) and analysis of variance (comparison of more than two groups). The measure of clinical outcome used in the analyses was change in $FEV_1$. Descriptive statistics mean, SD, SE, median and ranges were performed for all quantitative variables. Linear regression was used to calculate change in lung function over the specified time intervals. Analyses were conducted using a statistical software package (Systat 6.0 for Windows; SPSS Inc; Chicago).

### *Rehabilitation*

Patients did not receive preoperative rehabilitation at the Medical Center prior to LVRS. All patients underwent a similar regimen of pulmonary rehabilitation at Chapman Medical Center beginning immediately following hospital discharge surgery. The rehabilitation consists of a 10-day outpatient regimen involving a multidisciplinary approach with nursing, respiratory, dietary, nutritional, psychosocial, occupational, and physical therapy. Patient education, physical exercise (walking, flexibility, and strengthening), self-monitoring, breathing retraining, and bronchial hygiene instruction are included.

**Table 2—*Number of Patients with Follow-up Pulmonary Function Tests***

| | Patients Undergoing LVRS | LVRS Patients Without Follow-up | LVRS Patients With Single Follow-up | LVRS Patients With Multiple Follow-up Visits | | |
|---|---|---|---|---|---|---|
| | | | | Total | Short Term | Long Term |
| All patients | 376 | 45 | 151 | 180 | 145 | 110 |
| Unilateral thoracoscopic laser | 46 | 7 | 5 | 34 | 24 | 18 |
| Unilateral thoracoscopic staple | 111 | 16 | 49 | 46 | 22 | 35 |
| Bilateral thoracoscopic staple | 184 | 15 | 79 | 90 | 90 | 49 |
| Bilateral median sternotomy staple | 14 | 4 | 7 | 3 | 3 | 3 |
| Combined unilateral thoracoscopic staple and laser | 21 | 3 | 11 | 7 | 6 | 5 |

**Table 3—*Change in FEV₁ Following LVRS****

| | n | Preop $FEV_1$, L Mean | Preop $FEV_1$, L SEM | Postop $FEV_1$, L Mean | Postop $FEV_1$, L SEM | 6-mo Postop $FEV_1$, L Mean | 6-mo Postop $FEV_1$, L SEM | Maximal Change in $FEV_1$ at 6 mo, L Mean | Maximal Change in $FEV_1$ at 6 mo, L SEM | Slope of $FEV_1$ Long Term (>6 mo L/yr) Mean | Slope of $FEV_1$ Long Term (>6 mo L/yr) SEM | Median Follow-up, d Median | Median Follow-up, d Range |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| All patients | 180 | 0.66 | 0.013 | 0.87 | 0.02 | 0.94 | 0.02 | 0.28 | 0.01 | −0.163 | 0.035 | 356 | 34-891 |
| Unilateral thoracoscopic laser | 34 | 0.64 | 0.04 | 0.7 | 0.04 | 0.74 | 0.04 | 0.1 | 0.03 | −0.074 | 0.034 | 371 | 328-793 |
| Unilateral thoracoscopic staple | 46 | 0.71 | 0.03 | 0.86 | 0.03 | 0.86 | 0.01 | 0.25 | 0.03 | −0.107 | 0.068 | 426 | 48-891 |
| Bilateral thoracoscopic staple | 90 | 0.69 | 0.02 | 1.08 | 0.03 | 1.13 | 0.05 | 0.39 | 0.03 | −0.255 | 0.057 | 230 | 35-742 |
| Bilateral median sternotomy staple | 3 | 0.73 | 0.087 | 1.03 | 0.09 | 0.97 | 0.7 | 0.3 | 0.09 | −0.081 | 0.187 | 297 | 34-538 |
| Combined unilateral thoracoscopic staple and laser | 7 | 0.64 | 0.07 | 0.78 | 0.06 | 0.86 | 0.15 | 0.22 | 0.1 | −0.209 | 0.12 | 428 | 69-826 |

*Preop=preoperative; postop=postoperative.

## Results

### *Composite Results in All Patients*

A total of 376 patients underwent LVRS in this program during the analysis interval: 46 patients underwent unilateral laser LVRS; 111 had unilateral thoracoscopic staple LVRS; 184 had bilateral thoracoscopic staple LVRS; 21 had mixed thoracoscopic laser and staple procedures; and 14 had bilateral staple LVRS via median sternotomy. There were 15 perioperative deaths (mortality rate, 3.98%). In the overall group; follow-up pulmonary function results are available on 331 of the 361 surviving patients (92%) at some time following surgery (Tables 4 and 5).

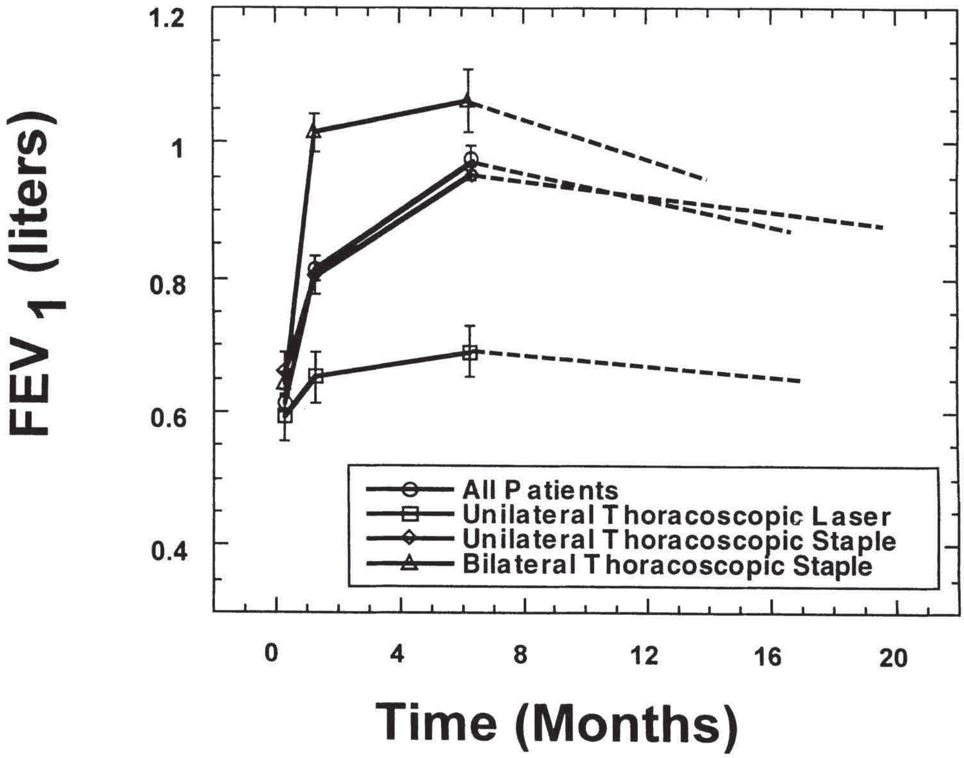


FIGURE 1. Lung function ($FEV_1$) following LVRS procedures. Time in months is shown on the x-axis. Dotted lines show slopes of deterioration in $FEV_1$ from the 6-month average $FEV_1$ based on procedure. Error bars denote SEM.

Table 4—*Mortality Following LVRS*

| | Total No. of Patients | Average Follow-up Days, Mean±SEM | Total No. Died | Expiration Days Postoperative |
|---|---|---|---|---|
| All patients | 376 | 505±16 | 76 | |
| Unilateral laser | 46 | 507±46 | 8 | 30,60,190,210,270,640,840,870 |
| Unilateral staple | 111 | 591±32 | 31 | 5,6,10,11,30,30,42,44,50,51,51,60,63,135,139,156,194,210, 210,220,240,309,365,395,485,503,540,690,750,760,970 |
| Bilateral median sternotomy | 184 | 430±15 | 5 | 10,70,183,600,660 |
| Bilateral staple | 14 | 479±55 | 26 | 3,3,5,10,14,20,25,30,30,37,38,49,51,66,90,165,182,270, 284,365,380,405,510,580,640,745 |
| Combined laser and staple | 21 | 560±21 | 6 | 6,80,128,250,360,780 |

Baseline $FEV_1$ for all patients in this study was 0.66 L±0.013 L (SEM). Mean improvement in $FEV_1$ for all patients was 0.28 L±0.02 L SEM (42%±3% SEM change from baseline) at the time of 6-month follow-up.

One hundred eighty of the patients had multiple follow-up visits (short and long term) following surgery enabling them to be analyzed for the rate of postoperative $FEV_1$ over time following surgery. Those with multiple follow-up had similar preoperative presentations and similar postoperative results as those with single follow-up visit data, with a mean baseline $FEV_1$ of 0.67 L±0.014 L (SEM), and improvement in $FEV_1$ of 0.28 L±0.016 L (SEM) (42%±3% change from baseline at the time of 6-month follow-up.

One hundred forty-five patients had multiple follow-up pulmonary function analyses within the first 6 months following surgery. $FEV_1$ increased from 0.67±0.01 L (SEM) to 0.87±0.02 L (SEM) at the time of initial follow-up after surgery (mean, 38 days postoperatively). On average, pulmonary function continued to improve during this early postoperative period with a mean additional increase in $FEV_1$ of 0.067±0.027 L (SEM) (*ie*, a further 10%±4% increase from baseline) during an average follow-up interval 99.6±37 days postoperatively. Overall, the mean change in $FEV_1$ from preoperative to the maximal value reached within 6 months postoperatively was 0.28 L (31%±7% change from baseline).

One hundred ten patients had multiple long-term follow-up pulmonary function analyses from 6 months following surgery to as long as 891 days postoperatively (mean follow-up time, 505±16 days [SEM]). After the initial 6-month rise, pulmonary function showed a general decline with a mean slope in $FEV_1$ of −0.163±0.035 (SEM) L/yr.

Table 5—*Causes of Death in LVRS-Treated Patients*

| Cause of Death | No. Patients |
|---|---|
| Amyotrophic lateral sclerosis | 1 |
| Aortic aneurysm | 1 |
| Bacterial colitis | 1 |
| Cancer | 1 |
| Cardiac arrest | 7 |
| Cardiovascular collapse | 1 |
| GI bleed | 1 |
| Ischemic bowel | 1 |
| Myocardial infarction | 1 |
| Pulmonary emboli | 3 |
| Respiratory failure | 49 |
| Stroke | 2 |
| Suicide | 1 |
| Trauma | 1 |
| Unknown | 5 |
| Total | 76 |

### *Unilateral Thoracoscopic Laser LVRS-Treated Patients*

Mean improvement in $FEV_1$ was 0.10 L±0.03 L (15%±9% [SEM] change from baseline $FEV_1$ of 0.64±0.04 L) at the time of initial follow-up in 34 unilateral laser-treated patients, which was significantly lower than the improvement seen in unilateral or bilateral staple-treated patients ($p<0.05$).

In long-term follow-up after 6 months postoperatively, unilateral thoracoscopic laser-treated patients had an average decline in $FEV_1$ of 0.074±0.034 L/yr (average follow-up, 507±46 days).

### *Unilateral Thoracoscopic Staple LVRS-Treated Patients*

Mean improvement in $FEV_1$ was 0.15±0.02 L (SEM) (21%±3% change from baseline $FEV_1$ of 0.71±0.03 L) [SEM] at the time of initial follow-up in 90 unilateral staple-treated patients. The 22 staple-treated patients with multiple short-term follow-up visits showed further improvement in $FEV_1$ in the initial 6 months following surgery, with a rise of 0.10 L to a maximal value reached of 0.96±0.1 L (SEM) (35%±14% [SEM] change from baseline).

In long-term follow-up after 6 months postoperatively, unilateral thoracoscopic staple-treated patients had an average decline in $FEV_1$ of 0.107±0.068 L/yr (mean follow-up, 591±32 days).

*Bilateral Thoracoscopic Staple LVRS-Treated Patients*

Mean improvement in $FEV_1$ was 0.39±0.03 L (SEM) (56%±4% [SEM] change from baseline $FEV_1$ of 0.69±0.02 L [SEM]) at the time of initial follow-up in 170 thoracoscopic staple-treated patients. The 90 bilateral staple-treated patients with multiple follow-up visits showed progressive improvement in $FEV_1$ in the initial 6 months following surgery, with a further rise to the maximal value reached, 1.13±0.05 L (SEM) (60%±6% [SEM] change from baseline).

In long-term follow-up after 6 months postoperatively, bilateral thoracoscopic staple-treated patients had an average decline in $FEV_1$ of 0.255±0.057 L/yr (mean follow-up, 420±15 days).

*Median Sternotomy Bilateral LVRS Patients*

Mean improvement in $FEV_1$ was 0.30±0.09 L (SEM) (41%±13% change from baseline $FEV_1$ of 0.73±0.087 L [SEM]) at the time of initial follow-up in nine median sternotomy bilateral staple LVRS-treated patients. Maximum $FEV_1$ reached within 6 months by the five patients with median sternotomy with multiple follow-up was 0.97±0.7 L.

Only three patients with median sternotomies had repeated follow-up data available >6 months postoperatively to allow calculation of long-term rate of deterioration in $FEV_1$. In long-term follow-up after 6 months postoperatively, bilateral median sternotomy-treated patients had an average decline in $FEV_1$ of 0.081±0.187 L/yr (mean follow-up, 479±55 days) in these three patients.

*Combined Bilateral Thoracoscopic Staple- and Laser-Treated LVRS Patients*

Mean improvement in $FEV_1$ was 0.14±0.07 L (SEM) (22%±10% [SEM] change from baseline) at the time of initial follow-up in 18 unilateral combined staple- and laser-treated patients. The 10 combined staple- and laser-treated patients with multiple follow-up visits also showed continued improvement in $FEV_1$ in the initial 6 months following surgery, with a rise to the maximal value reached of 0.86±0.15 L (SEM) (28±7% [SEM] change from baseline).

Only seven patients with combined staple and laser thoracoscopic LVRS procedures had repeated follow-up data available. In long-term follow-up after 6 months postoperatively, these seven patients experienced an average decline in $FEV_1$ of 0.209±0.118 L/yr (mean follow-up, 560±72 days).

*Correlation Between Initial Response to LVRS and Long-Term Rate of Decline in $FEV_1$*

A weak correlation was found between the short-term incremental gain in $FEV_1$ postoperatively and the long-term rate in decline in $FEV_1$. Overall, patients with the greatest increase in $FEV_1$ had a greater long-term decline in $FEV_1$ after 6 months, though there was considerable individual variability in the relationship ($r=0.292$, $p=0.003$), and individual response could not be predicted.

When examined by individual procedure, this relationship between magnitude of short-term response and rate of deterioration was less evident, but trends persisted: for unilateral staple-treated patients, $r=0.417$, $p=0.12$; for unilateral laser-treated patients, $r=0.95$, $p=0.05$; for patients undergoing bilateral staple procedure, this relationship was not seen ($r=0.162$, $p=0.29$).

When the subgroup of bilateral staple-treated patients who had a small incremental benefit from LVRS was examined (improvement in $FEV_1$ <0.200 L), the rate of deterioration was 50 mL/yr lower than for patients with larger short-term $FEV_1$ improvement (improvement in $FEV_1$ >0.250 L).

## Discussion

LVRS has been shown to be acutely effective in providing palliative improvement in pulmonary function in patients with heterogeneous emphysema in a number of studies.[1-6,9,12-17] Postoperative pulmonary function appears to maximize at approximately 3 to 6 months following surgery. Limited available data suggest that benefit may be sustained for at least 1 to 2 years following surgery in most patients.[4,17] However, there is widely variable response to surgery as well as duration of improvement. Measurable physiologic deterioration has been seen by 1 year in some patients.[18] It is very difficult to assess the rate of regression of pulmonary function in many series since consistent patient follow-up at regular, repeated intervals is extremely difficult to achieve long term at many centers.

We evaluated the rate of pulmonary function decline long term following LVRS by comparing the slopes of change in $FEV_1$ long term following LVRS using linear regression of lung function vs time. Individual regression lines were determined for $FEV_1$ from 0 to 6 months following surgery. A second regression line was determined for each patient 6 months postoperatively and beyond. In this manner, variability in the time of follow-up visits was taken into account. Using this method, a rate of decline for each individual patient was determined. This reduced errors that occur from having different patient groups followed up at different time points. This also reduced errors in calculated deterioration rates due to samples containing different patients at each follow-up time or by reducing the total number of patients to cohorts with relatively small numbers who were followed up at all time points.

Using this method, we found that, on average, pulmonary function improved in the early postoperative period, and in most patients it appeared to peak between 3 and 6 months following surgery. These findings are consistent with our clinical experience and unpublished reports from other centers (A.F.W., R.Y.). The incremental improvements occurring in the first 6 months were variable and dependent to some degree on the procedure performed in patients in this series. The immediate and 6-month postoperative improvement was greatest for patients who underwent bilateral staple lung volume reduction procedures, and is reasonably comparable to other bilateral staple LVRS published series.[1,3,4,6]

When examined as a composite group, lung function deteriorated long term (>6 months postoperatively). When long-term data were averaged, the rate of decline in $FEV_1$ was 163 mL/yr. Since the average incremental gain from the preoperative values to the 6-month maximum value was 280 mL, one could predict from this rate of decline that the average patient should return toward preoperative baseline levels by about 2 years postoperatively. However, validity of such a prediction is limited by a number of factors. First, the rate of decline appears to be related to the operative procedure and to the short-term incremental benefit following surgery. The conditions of those patients with the greatest incremental gains in lung function following surgery appeared to deteriorate more rapidly than those with smaller postoperative gains. Individual variability was extremely high and predictions cannot be applied to an individual patient. Additionally, some patients had relatively short intervals between follow-up visits. When such patients had significant changes in their lung function between visits, a very large slope was obtained. When these large slopes are averaged with the slopes of patients with much longer follow up, they receive disproportionate weight in calculating the rate of change in lung function. In other words, averaging the slopes does not equitably "weight adjust" for the total follow-up duration for individual patients.

As previously reported,[2,3,6] we found that bilateral stapled LVRS appears to provide the greatest short-term benefits in terms of improvement in $FEV_1$. However, bilateral stapled lung volume reduction procedures also were associated with the greatest rate of decline in lung function long term. While such a finding may be expected, it again raises questions as to whether sequential unilateral procedures could be potentially more beneficial over a very long period of time. Obviously we cannot answer this question from the current study.

In this series, bilateral staple LVRS patients showed deterioration of $FEV_1$ at an average annualized rate of 0.255 L/yr long term. Cooper et al[11] reported a drop in $FEV_1$ of 0.1 L in a cohort of 56 patients from the time of 6-month follow-up until 12-month follow-up. This could represent up to 0.2-L annualized decrease, though longer-term data are needed.[11] If the patient cohort of Cooper et al[11] experienced a slower rate of decline than that found in our patients long term, careful analysis of possible reasons for the differences would be warranted.

Unilateral laser LVRS procedures resulted in very small benefits in patients in our series. However, they had a correspondingly lower rate of deterioration of lung function. There were too few patients in this study who had serial long-term follow-up after median sternotomy LVRS procedures or combined laser and staple LVRS to draw any conclusions regarding their relative rates of decline in lung function long term.

There are a number of important limitations of this study. The long-term rate of deterioration in lung function was calculated using linear regression of the $FEV_1$ over time for each patient. It is possible that the change in $FEV_1$ postoperatively is not linear after 6 months. If the rate of decline in $FEV_1$ is greatest around 6 months, and slows later (as might be expected from stress relaxation), the rate of decline would appear greater for the bilateral procedures, since these patients have been followed up for the shortest average time. This might explain some of the steeper $FEV_1$ deterioration slopes seen in the bilateral staple-treated patients. Nonlinear regression analyses could be considered when more data are available on larger numbers of patients in the future. We examined $FEV_1$ as the only measure of pulmonary function outcome. Clearly, other pulmonary function variables could lead to different conclusions. We selected $FEV_1$ since it is objective, widely reported, reproducible, and obtained spirometrically. However, $FEV_1$ has well-described limitations as an isolated end point for measurement of emphysema and response to surgery. Additionally, we evaluated $FEV_1$ response in absolute numbers (liters) to arrive at a deterioration rate in liters per year. This does not account for differences in age, size, predicted $FEV_1$, or percent change from baseline.

The selection criteria for patients in the various procedures differed to some degree, as did the experience of the surgeons at the time of enrollment for some of the patient groups. This could affect duration of response and rate of deterioration of lung function.

A substantial percentage of patients in each group did not have multiple long-term follow-up visits necessary to include them in rate of change of $FEV_1$ analyses. Bias may have occurred based on resulting follow-up selection. Finally, interpretation of the long-term value of these procedures is complicated since the natural rate of decline in a comparably matched control group of patients is also difficult to determine.

In summary, we have found that lung function appears to improve in the first few months following LVRS and appears to maximize at approximately 3 to 6 months following surgery in most patients. The short-term incremental improvement following bilateral staple procedures is superior to improvements following other procedures or unilateral surgery. However, the more rapid rate of decline in patients with bilateral staple lung volume reduction procedures (and the general association between greater incremental improvement and higher rate of the deterioration) raises questions regarding optimal long-term procedures. Further studies will clearly be needed to answer these important questions.

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