Lung Function 12 Months Following Emphysema Resection*

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Objective: To investigate the mechanism of airflow limitation before and 6 and 12 months after targeted emphysematous resection in 10 male patients aged 67±8 years (mean±SD) with very severe COPD undergoing bilateral thoracoscopic stapling techniques.

Design: Lung function, including static lung elastic recoil, was measured 2 weeks before and 6 and 12 months after surgery.

Results: Twelve months after surgery, there was a significant (p<0.001) reduction in total lung capacity (TLC), 9.5±0.3 L (mean±SEM) to 8.5±0.3 L, functional residual capacity, and residual volume. Airway conductance and FEV1. 0.71±0.1 L (mean±SEM) to 0.95±0.1 L, improved significantly (p<0.01). Lung elastic recoil increased markedly at TLC from 11.7±0.7 cm H2O (mean±SEM) to 15.0±1.0 cm H2O (p<0.01) as did maximum expiratory airflow in every patient. However, when compared with data obtained in each patient at 6 months, lung volumes are significantly increased, and expiratory airflow and lung elastic recoil pressures are significantly reduced (p=0.05). Analysis of maximum expiratory flow-static elastic recoil pressure curve indicates conductance of the S airway segment (Gs) increased from 0.20±0.03 L/s/cm H2O (mean±SEM) to 0.28±0.04 L/s/cm H2O (p<0.02), and critical transmural pressure in the collapsible segment (Ptm') decreased from 3.2±0.2 cm H2O (mean±SEM) to 2.5±0.2 cm H2O (p<0.01).

Conclusion: The improvement in maximal expiratory airflow can be attributed primarily to increased lung elastic recoil and its secondary effect on enlarging airway diameter causing increased airway conductance, increased Gs, and decreased Ptm'. The improvement in lung function and elastic recoil peaks at 6 months.

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

Abbreviations: FRC=functional residual capacity; Gs=conductance of the S airway segment; LVRS=lung volume reduction surgery; MFSR=maximum flow-static recoil; Ptm'=critical transmural pressure in the collapsible segment; SGaw=specific airway conductance; TLC=total lung capacity

Previous reports of surgical intervention to improve lung function in patients with emphysema have noted increased morbidity and/or mortality, and physiologic improvement has been variable and transient ≤1 year.1-6

Recently, there has been renewed interest in thoracic surgical procedures that attempt to provide relief for markedly dyspnic patients suffering from severe generalized emphysema.7-15 Unilateral7-8,11,12 or bilateral7,9,11-15 video-assisted thoracoscopic7,9,12,14,15 or median sternotomy7,10,13 incisions are made and visually the most emphysematous areas are excised using stapling7,10-15 or laser techniques8,9 or both. Results16 indicate variable clinical relief of dyspnea and improvement in lung function in selected patients followed up 6 months,8,12,14,15 1 year,13 and 3 years.7 We and others have reported previously that the increased expiratory airflow and airway conductance following bullectomy in isolated bullous lung disease5,17 and bullous emphysema1,2,4-6 could be accounted for by the measured improvement in lung elastic recoil1,2,4,6,17 Recent short-term (3 to 6 months) studies have noted the mechanism(s) of improvement in lung function following unilateral11 and bilateral14,15 surgical removal of targeted emphysematous tissue lung volume reduction surgery [LVRS] in markedly symptomatic patients with far-advanced COPD could be accounted for by the increase in lung elastic recoil.

The present study evaluates lung function and elas-
tic recoil at 6 and 12 months following LVRS for generalized emphysema.

**Materials and Methods**

**Patient Selection**

We consecutively studied 14 patients (12 men) aged 67±8 years (mean±SD). However, four patients refused to undergo repeated esophageal balloon studies at 12 months. Therefore we report complete data on 10 male patients. As previously described,14,15 all the patients who underwent the procedure were markedly symptomatic with grade ≥3 dyspnea,18 with severe fixed inspiratory obstruction that had not improved despite appropriate therapeutic interventions, including oxygen, antibiotics, aerosol and systemic bronchodilators, corticosteroids, and pulmonary rehabilitation. In addition, high-resolution, thin-section CT of the lung demonstrated emphysema scores19,20 ≥60 with heterogeneous distribution, ie, predominant emphysematous destruction of upper to middle lung fields with relative preservation of normal lung tissue in the lower lung fields. Standard nuclear medicine ventilation and perfusion lung scans demonstrated similar heterogeneous distribution.

**Operative Technique**

As previously described,14,15 after obtaining informed consent, and approval of the Institutional Human Investigation Committee at Chapman Medical Center, patients underwent sequential bilateral video-assisted thoracoscopic surgery at the same operative sitting under vecuronium paralysis and isoflurane general anesthesia with fraction of inspired oxygen of 0.4, sitting under vecuronium paralysis and isoflurane general anesthesia with fraction of inspired oxygen of 0.4, using a left-sided 39F double-lumen endotracheal tube (Mallinckrodt Anesthesia; St. Louis). After single dependent lung ventilation had been achieved, the contralateral upside deflated lung was examined. Visually, the most distended, destroyed, emphysematous areas previously targeted by the preoperative CT lung scan in the upper and middle lung fields were excised and linear staple lines were reinforced with bovine pericardium21 (Pert-Strips; Bio-Vascular Inc; St. Paul, Minn) or bovine collagen (Instastamp; Johnson and Johnson; New Brunswick, NJ) to minimize air leaks. It was estimated that the excised lung volume was approximately 15 to 20% of each lung. Actual weight of each resected lung was 30 to 90 g. Following lung excision, apical pleural tents and/or talc pleurodesis were not required. Operative time ranged from 1 to 2 h.

**Lung Function Studies**

As previously described,14,15 outpatient lung function studies were performed after obtaining informed consent. These included functional residual capacity (FRC) measured by plethysmographic techniques,22 timed spirometry, and single-breath diffusing capacity in accordance with American Thoracic Society recommendations23,24 and values were compared with predictions.25-27 All patients were considered to have fixed airflow limitation since the FEV1 following three inhalations of aerosolized albuterol (670 μg) improved <12% and/or <200 mL.25 Maximum inspiratory and expiratory flow volume curves, thoracic gas volume,25 and airway resistance25 were all measured in a pressure-corrected lung plethysmograph (model 6200; Sensormedics Inc; Yorba Buena, Calif) and compared with predicted values.25,28,29 The reciprocal of airway resistance28 is conductance and it was divided by the thoracic gas volume at which it was measured and specific conductance (SGaw) calculated. Normal values are 0.12 L/sec cm H2O/L.30 Residual volume was calculated by subtracting vital capacity from total lung capacity (TLC). Studies were obtained within 2 weeks prior to and repeated within 5 to 6 months and again 12 months after surgery. RESULTS

Results of lung function studies appear in Table 1 and Figures 1-4. The average hospital stay was 10.9±1.1 days (mean±SD). Dyspnea was improved in every patient by ≥1 grade.18 Oxygen dependence was eliminated in seven of the 10 patients.

Preoperative and 6-month postoperative lung function studies of the four patients who refused to undergo additional esophageal balloon studies at 12 months postoperation have been previously reported15 and were not significantly different (p>0.05) from the patients described herein at comparable time periods. Additionally, their clinical course and spirometry (data not shown) at 12 months post surgery is similar to the patients in the present report. Spirometric studies were available in six patients up to 1 year prior to sur-
Table 1—Results of Lung Function Studies in 10 Patients Preoperatively and, 6 and 12 Months After LVRS*

| Preoperative vs | 6 mo | Preoperative vs | 12 mo | 6 mo vs | Preoperative vs |
|-----------------|------|-----------------|-------|---------|-----------------|
| VC, 2.8±0.2 (x±SEM) (L) (64±5) | 3.2±0.7 | 0.01 | 2.9±0.2 | 0.17 | p=0.3 |
| (74±6) | | | (69±6) | | |
| FVC, 2.3±0.2 (L) (55±5) | 3.1±0.2 | 0.003 | 2.6±0.2 | 0.02 | 0.06 |
| (72±6) | | | (62±6) | | |
| FEV₁, 1.71±0.06 (L) (24±2) | 1.19±0.1 | 0.001 | 0.95±0.1 | 0.001 | 0.01 |
| (41±5) | | | (33±5) | | |
| FEV₁/FVC (%) | 38±3 | 0.03 | 35±2 | 0.2 | 0.04 |
| | | | | | |
| FRC, 7.5±0.3 (L) (195±9.0) | 5.7±0.2 | <0.001 | 6.2±0.3 | 0.05 | <0.001 |
| (147±6) | | | (163±8) | | |
| RV, 6.8±0.3 (L) (275±11) | 4.9±0.3 | <0.001 | 5.5±0.3 | 0.004 | <0.001 |
| (198±10) | | | (225±13) | | |
| TLC, 9.5±0.3 (L) (148±5) | 8.0±0.3 | <0.001 | 8.5±0.3 | 0.03 | <0.001 |
| (126±6) | | | (133±4) | | |
| RV/TLC (%) | 71±2.0 (180±6) | 60±2 | <0.001 | 65±3 | 0.03 | 0.01 |
| (153±7) | | | (161±9) | | |
| Dco, 5.0±1.0 (18±4.0) | 8.6±0.7 | <0.01 | 10±1 | 0.71 | 0.01 |
| (43±3) | | | (48±3) | | |
| Dco/VA, 0.9±0.3 (17±10) | 1.7±0.1 | 0.06 | 2.2±0.2 | 0.17 | 0.05 |
| (46±3) | | | (58±5) | | |
| FSTAT, 1.3±0.2 FRC | 2.8±0.2 | 0.001 | 3.0±0.2 | 0.4 | 0.002 |
| (25±3.0) | | | (32±5) | | |
| Gaw, 0.19±0.02 (22±3) | 0.23±0.02 | 0.18 | 0.28±0.03 | 0.09 | 0.01 |
| (16±2) | | | (19±3) | | |
| SGaw, 0.03±0.00 (12±2) | 0.06±0.02 | 0.21 | 0.04±0.01 | 0.5 | 0.01 |
| (16±2) | | | (19±3) | | |
| FSTAT, 1±0.7 TLC | 17±0.9 | 0.003 | 15±1.0 | 0.03 | 0.01 |
| Gs, 0.20±0.03 | 0.28±0.04 | 0.03 | 0.28±0.04 | 0.5 | 0.02 |
| Ptm, 3.2±0.2 | 2.5±0.2 | <0.01 | 2.5±0.2 | 0.5 | <0.01 |

*VC=vital capacity; RV=residual volume; Dco=diffusing capacity (mL/min/mm Hg); VA=alveolar lung volume (L); Fstat=static lung elastic recoil pressure (cm H2O); Gaw=airway conductance (L/cm H2O); Gs=conductance s airway segment.

surgery, and results were similar for FVC and FEV₁ when compared with preoperative baseline values despite aggressive therapeutic intervention, including physical rehabilitation. Six-month postoperative data for cases 1, 2, 4, and 6 through 10 have been reported previously.15

There was improvement in both static and dynamic lung function studies. Twelve months following surgery, TLC, residual volume, and the FRC decreased significantly (p<0.001) (Table 1). Total lung capacity decreased from 9.5±0.3 L (mean±SEM) (148±5.0% predicted) to 8.5±0.3 L (133±4.0% predicted) (p<0.001). However, the values at 12 months are significantly (p<0.001) greater than the values at 6 months (Table 1), indicating increasing hyperinflation.

There was significant (p=0.01) improvement at 12 months postsurgery in SGaw, airway conductance, and FEV₁. FEV₁ increased from 0.71±0.06 L (mean±SEM) (24±2.0% predicted) to 0.95±0.1 L (33±5.0% predicted) (p<0.01). SGaw increased from 0.03±0.00 to 0.04±0.01 L/cm H2O/L (p=0.01). Compared with baseline preoperative studies, the entire maximum inspiratory and expiratory flow volume loop shifted downward on the lung volume axis (Fig 1). While values for FEV₁ 12 months postsurgery are significantly lower (p<0.001) when compared with 6-month values, the 6-month and 12-month values for airway conductance and SGaw are similar (p=0.09).

Preoperatively, diffusing capacity was markedly abnormal in every patient, 5.0±1.0 mL/min/mm Hg (mean±SEM) (18±4% predicted), and increased 12 months postoperatively to 10.0±1.0 (48±3% of predicted) (p<0.01). The values at 6 and 12 months were similar.

Analysis of the Static Lung Elastic Recoil Pressure Curves

Twelve months postoperatively, there was an increase in lung elastic recoil pressure at the same lung volume when compared with preoperative values with a shift in the curve to the right (Fig 2). There was no significant (p=0.2) change in lung compliance at FRC plus 0.4 L; preoperative value was 0.32±0.03 L/cm H2O (mean±SEM) and postoperative value was 0.28±0.03 L/cm H2O. At 12 months postsurgery, there was a significant (p<0.01) increase in static lung elastic recoil pressure at TLC; preoperative value was 11.0±0.7 cm H2O (mean±SEM) and postoperative value was 15.0±1.0 cm H2O. However, this is significantly reduced (p=0.03) when compared with values obtained 5 to 6 months after surgery, 17.0±0.9 cm H2O. There was also a significant increase in static lung...
FIGURE 1. Adapted from Gelb et al. Results of maximum expiratory and inspiratory flow volume loops 2 weeks before and 6 and 12 months after LVRS for emphysema. In each of 10 patients, the loops initially shifted to a lower lung volume following surgery. After 12 months, the loops in eight patients have shifted to a higher lung volume. Preoperative and postoperative values for FEV1 (liter) and (percent predicted) are included. For comparison with normal data, maximum expiratory flow at 80% TLC (4.6 L) is 5.8 ± 1.5 L/s (range). The preoperative loop in each patient is at the highest lung volume.
Figure 2. Adapted from Gelb et al.\textsuperscript{15} Results of static lung elastic recoil pressure curves in each of 10 patients obtained 2 weeks before and 6 and 12 months after LVRS for emphysema. Actual lung volume is plotted. Separate curves were obtained in each patient at least five times and data pooled and line of best visual fit are described. Normal data (mean±2 SDs) were obtained in seven healthy subjects aged 61 to 74 years.\textsuperscript{29} Initially following surgery, the curves are shifted to the right in each patient, and after 12 months, the curves in every patient demonstrate subsequent loss of lung elastic recoil.
elastic recoil pressure at FRC at 12 months postsurgery, 3.0±0.2 cm H2O compared with baseline, 1.3 ±0.2 cm H2O (p=0.002). The values at 6 and 12 months postsurgery are similar.

Analysis of the MFSR Curve

Preoperatively, the intercept (Ptm') was shifted toward higher pressures in all patients, 3.2±0.2 cm H2O (mean±SEM) and the Gs was markedly reduced, 0.20±0.03 L/sec/cm H2O (mean±SEM), when compared with normal values (Fig 3). This suggests maximum expiratory airflow was severely reduced not only due to loss of lung elastic recoil, but also due to intrinsic narrowing and/or collapse of the airways.

Twelve months following surgery, with increased lung elastic recoil, airflow increased and the intercept on the pressure axis at zero maximum flow (Ptm') of the MFSR slope shifted toward lower pressures, 2.5±0.2 cm H2O (mean±SEM), and the Gs (MFSR slope) improved in every patient to 0.28±0.04 L/sec/cm H2O (mean±SEM). The decrease in Ptm' and increase in Gs was significant (p<0.01) and suggests that airway collapse was partially relieved due to increased elastic recoil with better airway traction and support and enlarged airway caliber. The values for Ptm' and Gs are similar at 6 and 12 months postsurgery.

Following surgery, persistent airflow limitation in four patients (cases 1, 4, 7, and 10) could be accounted for almost completely by loss of lung elastic recoil. In the remaining patients, persistent airflow limitation in the S segment could be accounted for in part by loss of lung elastic recoil and reduced caliber of the airway lumen due to intrinsic disease and/or airway collapse due to reduced airway traction and/or compression.

Analysis of the Airway Conductance Lung Elastic Recoil Pressure Curve

Twelve months following surgery, despite the reduction in lung volume at FRC, there was an increase in airway conductance that could be accounted for by the mean increase in lung elastic recoil (1.7 cm) at FRC (Fig 4). However, airway conductance remains borderline normal in relation to elastic recoil due to marked decrease in traction support and/or intrinsic narrowing of the airway lumen and/or bronchial compression.

Analysis of Predictors of Postoperative Increase in FEV1

After 12 months, the postoperative increase in FEV1 was poorly correlated with baseline preoperative static lung elastic recoil at TLC (r=0.3, p=0.3), static elastic recoil at TLC/TLC (coefficient of retraction38) (r=0.28, p=0.3), and Gs (r=0.4, p=0.2). Multiple linear regression analysis revealed moderately good correlation between postoperative increase in FEV1 with postoperative increase in coefficient of retraction and Gs at 6 months (r=0.70, p=0.05)15 and (r=0.70, p=0.10) at 12 months.

Discussion

Results in the present study extend our earlier short-term (6 months) observations. Marked clinical and physiologic improvement persists in lung function at 1 year following bilateral targeted excision of severely emphysematous areas in patients with very severe expiratory airflow limitation. As previously noted, the improvement in lung function can be accounted for primarily by increased elastic recoil properties of the lung with greater driving pressure and to secondary increases in airway diameter.

The magnitude of the 12-month improvement in lung function in the present study appears similar to that reported by Gaissert et al13 after bilateral emphysema resection using a median sternotomy incision.

We believe the decrease in lung volumes and increased expiratory airflow and airway conductance are accounted for by the increase in lung elastic recoil that was measured in each patient. These changes reach their greatest magnitude at 5 to 6 months following excision of the most severely emphysematous lung tissue. After 12 months, the lung elastic recoil pressures in the remaining lung are submaximal. Moreover, the 6- and 12-month changes in lung volume and expiratory airflow reflect the initial increase and then loss of lung elastic recoil (Table 1 and Figs 1 and 2).

Results of MFSR curves 12 months after emphysematous lung resection demonstrate a parallel slope to that observed at 6 months after surgery. The increased slope of the MFSR curves together with the decrease in Ptm' when compared with preoperative values suggests greater airway diameter and stability with less collapse in the S segment and can be attributed to the increase in lung elastic recoil. Atrophy and/or compression of the airway wall and/or increased bronchomotor tone and/or intrinsic small airways disease could also lead to increased airway collapse (increased Ptm') and decreased slope of the MFSR curve. We suspect that the increase in the slope of the MFSR curve and decrease in Ptm' may be attributed to increases in lung elastic recoil with better traction around the airways, thereby increasing airway diameter. Alternatively, the failure to increase the slope of the MFSR curve postsoperatively probably reflects persistent intrinsic airway disease and/or airway compression.

As previously discussed, our studies in asymptomatic patients with mild physiologic abnormalities yet moderately advanced macroscopic anatomic emphy-
FIGURE 3. Adapted from Gelb et al.\textsuperscript{15} Results of maximum expiratory flow-static lung elastic recoil pressure curve in 10 patients obtained 2 weeks before and 6 and 12 months after LVRS for emphysema. Prior to surgery, airflow limitation is accounted for by a decrease in lung elastic recoil pressure as well as decreased airway caliber due to impaired airway traction and/or bronchial compression and/or intrinsic airway obstruction (decreased Gs). Initially after surgery, there was a modest to large (four patients) increase in Gs and lung elastic recoil with a decrease in P_{\text{tm}} suggesting that increased flow was predominantly accounted for by increased lung elastic recoil and secondarily to increased airway caliber and stability probably due to increased traction around the airway. Even after surgery, the Gs is abnormal in six patients suggesting maximal flow is reduced due to decreased intraluminal airway caliber in addition to loss of lung elastic recoil. In four patients (cases 1, 4, 7, and 10), airflow limitation is almost completely accounted for by loss of lung elastic recoil with near normal Gs even at 12 months after surgery. Changes in Gs and P_{\text{tm}} are similar at 6 and 12 months.
emphysema demonstrated that airflow limitation was primarily due to loss of lung elastic recoil and/or increased bronchial obstruction. Patients without α1-antitrypsin deficiency, Black et al.40 found that decreases in lung elastic recoil could account for abnormal flow and pulmonary conductance in only five of 10 patients. In the other five patients, concomitant intrinsic airways disease and/or increased bronchial compression were suspected. They noted that a decreased MFSR slope was characteristic of COPD patients without α1-antitrypsin deficiency. The improvement in lung function attributable to increased lung elastic recoil following LVRS in emphysema in this and our previous studies14,15 is similar to increased lung elastic recoil measured following bullectomy in bullous emphysema1,2,4,6 and in isolated bullous lung disease.17 The study by Sciurba et al.11 has also noted improvement, but of lesser magnitude in lung elastic recoil and lung function 6 months following unilateral excision of targeted emphysema using combined laser and/or stapling techniques.

In summary, we have demonstrated persistent clinical improvement in lung function 12 months after bilateral LVRS for emphysema. There is an increase in lung elastic recoil and improved lung function that peaks at 5 to 6 months. There is a parallel decrease in lung volumes and increased expiratory airflow that peaks at 5 to 6 months. Longer-term follow-up will be needed to assess the impact on lung function over time. Proper selection of patients is crucial to optimize potential benefits.

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