Long-term results of lung volume reduction surgery

T. Fujimotoa, H. Teschler b, L. Hillejana, G. Zaboura a, G. Stamatis a, *

a Department of Thoracic Surgery and Endoscopy, Ruhrlandklinik, Tüschener Weg 40, 45239 Essen, Germany.
b Department of Pneumology and Sleep medicine, Ruhrlandklinik, Tüschener Weg 40, 45239 Essen, Germany.

Received 21 August 2001; received in revised form 10 December 2001; accepted 18 December 2001

Abstract

Objective: Lung volume reduction surgery (LVRS) is effective in the short and intermediate term for the improvement of pulmonary function and subjective symptoms in selected patients with advanced emphysema. The purpose of this study was to examine the long-term functional results of LVRS and to investigate which subgroups would benefit in terms of long-term survival.

Methods: All records of the patients who underwent LVRS between 1994 and 1998 at our hospital were reviewed.

Results: Eighty-eight consecutive patients underwent LVRS during the period. There were 62 men and 26 women with an average age of 56.1 years (range 34–72 years). Eleven patients with α1-antitrypsin deficiency were included. The perioperative mortality rate (90 days) was 2.3% (n = 2). Total lung capacity (7.5 ± 0.3 l) and residual volume (4.8 ± 0.3 l) at 3 years remained lower than baseline (9.2 ± 0.2 l, 6.5 ± 0.2 l, each) (P < 0.001). The mean forced expiratory volume in 1 s (FEV1) at 3 years (0.86 ± 0.08 l) was higher than baseline (0.78 ± 0.02 l), but the difference did not reach statistical significance. The FEV1 of the patients with α1-antitrypsin deficiency and of those with respiratory bronchiolitis returned to baseline at one year after LVRS and showed further deterioration. Overall survival rate at 5 years was 71.0% with the mean length of follow-up of 54.2 months. The survival difference was statistically significant between patients with preoperative FEV1 < 28% and those with FEV1 ≥ 28% (P = 0.0152).

Conclusions: The improvement of total lung capacity and residual volume persisted long after the operation. Patients with higher preoperative FEV1 had a survival benefit. The favorable long-term survival might justify LVRS for the treatment of selected patients with severe emphysema.

Keywords: Chronic obstructive pulmonary disease; Emphysema; Forced expiratory volume in 1 s; Long-term survival; Lung volume reduction surgery

1. Introduction

The introduction of lung volume reduction surgery (LVRS) had a great impact, indicating that surgery can play a distinct role in the management of pulmonary emphysema. Numerous reports have shown that LVRS improves the pulmonary function and alleviates subjective symptoms in the short and intermediate term for selected patients with advanced emphysema [1–5]. It is still unknown, however, whether LVRS can offer survival benefits for patients with otherwise poor natural history, as few current reports showed long-term functional results and survivals [6–11].

Since 1994, we have performed LVRS for a heterogeneous group of patients with advanced emphysema. The purpose of this study was to examine the perioperative and long-term functional results of LVRS and to investigate which subgroups would benefit long-term survival.

2. Patients and methods

We prospectively enrolled all patients who underwent LVRS for severe pulmonary emphysema between June 1994 and June 1998 at our institution. Patient selection criteria and the clinical evaluation program have been described previously [12–14], and consist of: (1) marked hyperinflation evident by inspiratory and expiratory chest radiographs; (2) radiographic evidence of heterogeneous emphysema with clear target zones for resection; (3) severe functional impairment (forced expiratory volume in 1 s (FEV1) < 1.2 l or predicted FEV1 20–35%, total lung capacity (TLC) > 120%, residual volume (RV) > 250%); (4) Medical Research Council (MRC) dyspnea score ≥ 2; (5) poor quality of life determined by the short form (SF) 36 questionnaire; (6) dyspnea despite optimized medical therapy; (7) abstinence from smoking, acceptable nutritional...
status; and (8) rehabilitation potential. Contraindication to surgery included age older than 75 years, current cigarette smoking, symptomatic cardiac disease, pulmonary hypertension (pulmonary artery pressure > 35 mmHg), and hypercapnia.

Operative procedures have been described previously as well. Under general anesthesia using a left-sided double-lumen tube, patients underwent either median sternotomy or video-assisted anterolateral mini-thoracotomy. Bilateral procedures were performed as a rule, except for patients with unilateral problems such as prior thoracic surgery and pleurodesis. The side with better-preserved perfusion was operated on first. In the early period of this study, we used median sternotomy as a rule. Recently the latter method has been preferred because of technical difficulties encountered at median sternotomy when the pleural adhesion existed and significant target zone were located in the lower lobes. The target zones for resections were assessed preoperatively by high resolution computed tomography and perfusion-ventilation scintigraphy. Identified target zones correlated well with the portion that still remained inflated after 3–5 min of non-ventilation. The staple line was buttressed with bovine pericardium. When the volume of resection was extensive, pleural tents were created to avoid postoperative residual space of thorax.

All patients underwent baseline pulmonary function testing during 3–4 weeks of inpatient cardiopulmonary rehabilitation. Pulmonary function tests were repeated at our institution whenever possible at 3 months postoperatively, at 6 months, and thereafter at 6-month intervals.

2.1. Statistical analysis

Data are shown as mean and standard error of the mean (SEM). Differences between baseline values and postoperative values were analyzed using the paired t-test. Sequential changes in TLC, RV and FEV\(_1\) from the baseline were compared using repeated-measures of analysis of variance (ANOVA). The overall survival was estimated from the time of LVRS with a Kaplan–Meier model. The comparisons of survivals between subgroups were made with the log rank test. The cause of deaths of patients at the time of surveillance (n = 19) were assessed either by asking their home doctors or by asking a municipal office. All tests were two-tailed and performed by Statview version 5.0 statistical software (SAS Institute Inc., SAS Cary, NC). Differences were considered significant with \(P < 0.05\).

3. Results

A total of 88 patients underwent LVRS during the analysis interval. There were 62 men and 26 women with an average age of 56.1 ± 9.1 years (range 34–72 years). Eleven patients (12.5%) with α1-antitrypsin deficiency were included. The baseline lung function is summarized in Table 1.

3.1. Pathological findings

Other than severe emphysematous change, several coexisting features were discovered at pathological examination. These features included respiratory bronchiolitis in 39, organizing pneumonia in nine, tumorlet in five, pleural fibrosis in four, granuloma in three, interstitial pneumonia and silicosis in one patient. Incidental tumor was discovered in six patients (6.8%); adenocarcinoma in four, squamous cell carcinoma in one, carcinoid tumor in one and hamartoma in one patient.

3.2. Perioperative mortality and morbidity

There were two deaths within 90 days of surgery; mortality rate was 2.3%. The cause of death was adult respiratory distress syndrome in one, and respiratory insufficiency due to postoperative empyema in one patient. Complications occurred in 31 patients (35.2%); prolonged air leak over 2 weeks in 17 (19.3%), pneumonia in eight (9.1%), empyema

---

**Table 1.** Effect of lung volume reduction surgery: 3-year results

<table>
<thead>
<tr>
<th></th>
<th>Preoperation</th>
<th>6 months</th>
<th>1 year</th>
<th>2 years</th>
<th>3 years</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. of patients (%)</td>
<td>88 (100%)</td>
<td>57 (65%)</td>
<td>57 (65%)</td>
<td>46 (52%)</td>
<td>26 (30%)</td>
</tr>
<tr>
<td>No. of deaths (%)</td>
<td>0</td>
<td>2 (2.5%)</td>
<td>7 (8.0%)</td>
<td>11 (12.5%)</td>
<td>13 (14.8%)</td>
</tr>
<tr>
<td>FVC (l)</td>
<td>2.7 ± 0.1</td>
<td>3.1 ± 0.1*</td>
<td>2.8 ± 0.1**</td>
<td>2.8 ± 0.1</td>
<td>2.8 ± 0.2</td>
</tr>
<tr>
<td>FEV(_1) (l)</td>
<td>0.78 ± 0.02</td>
<td>1.03 ± 0.05*</td>
<td>0.87 ± 0.04*</td>
<td>0.84 ± 0.05</td>
<td>0.86 ± 0.08</td>
</tr>
<tr>
<td>FEV(_1), predictive (%)</td>
<td>27.5 ± 0.8</td>
<td>36.4 ± 1.3*</td>
<td>31.1 ± 1.4*</td>
<td>30.3 ± 1.5</td>
<td>30.1 ± 2.4</td>
</tr>
<tr>
<td>TLC (l)</td>
<td>9.2 ± 0.2</td>
<td>7.8 ± 0.2*</td>
<td>8.0 ± 0.2*</td>
<td>7.8 ± 0.3*</td>
<td>7.5 ± 0.3*</td>
</tr>
<tr>
<td>RV (l)</td>
<td>6.5 ± 0.2</td>
<td>4.8 ± 0.2*</td>
<td>5.2 ± 0.2*</td>
<td>4.9 ± 0.3*</td>
<td>4.8 ± 0.3*</td>
</tr>
<tr>
<td>PaO(_2) (mmHg)</td>
<td>68.7 ± 0.9</td>
<td>71.9 ± 1.1</td>
<td>72.3 ± 1.1</td>
<td>71.8 ± 1.2</td>
<td>69.9 ± 1.9</td>
</tr>
<tr>
<td>PaCO(_2) (mmHg)</td>
<td>39.1 ± 0.50</td>
<td>38.5 ± 0.65*</td>
<td>39.1 ± 0.76</td>
<td>39.6 ± 0.89</td>
<td>39.7 ± 1.0</td>
</tr>
<tr>
<td>MRC dyspnea score</td>
<td>2.8 ± 0.1</td>
<td>1.5 ± 0.1*</td>
<td>2.0 ± 0.1*</td>
<td>2.1 ± 0.2*</td>
<td>2.5 ± 0.2*</td>
</tr>
<tr>
<td>6-min walk (m)</td>
<td>285 ± 14</td>
<td>405 ± 13*</td>
<td>390 ± 19*</td>
<td>349 ± 23</td>
<td>334 ± 45</td>
</tr>
</tbody>
</table>

*FVC, forced vital capacity; TLC, total lung capacity, RV, residual volume; MRC, Medical Research Council. **P < 0.01, *P < 0.05 compared with preoperative value.*
in two, postoperative bleeding which required re-thoracotomy in two, pneumothorax in two, bowel disease in two, and respiratory insufficiency which required mechanical ventilation in two patients (2.3%).

3.3. Long-term results of volume reduction surgery

Overall 3-year results of pulmonary function testing are shown in Table 1. At 1 year after LVRS, all functional parameters except the blood gas at rest showed statistically significant improvement. However, the only persistent benefits at 3 years with statistical significance were the reduction in the TLC and RV. Sequential changes in TLC and RV at the 3-year interval are depicted in Fig. 1 using repeated-measures ANOVA. Only the patients who completed follow-up lung function tests of 3 years (n = 26) were selected for this analysis. LVRS improved both TLC and RV with statistical significance (P < 0.001) and the improvement persisted at 3 years.

The postoperative changes in FEV₁ of the patients with smoker’s emphysema and of those with α₁-antitrypsin deficiency are shown in Fig. 2a. Both groups showed similar improvements of FEV₁ after LVRS (P < 0.001). However, the mean FEV₁ in the group of α₁-antitrypsin deficiency returned to baseline at 1 year, and showed further deterioration at 2 and 3 years of follow-up. In the group of smoker’s emphysema the difference from baseline was significant until 2 years after LVRS (paired t-test, P = 0.0414).

The postoperative changes in FEV₁ of the patients with respiratory bronchiolitis (n = 9) that was recognized in the operative specimen and of those without it (n = 13) were analyzed separately (Fig. 2b). Only the patients without α₁-antitrypsin deficiency who completed follow-up lung function tests of 3 years (n = 22) were selected for this analysis.

The both groups showed the improvement at 6 months but it did not persist more than 1 year in the group with respiratory bronchiolitis.

The mean length of follow-up was 54.2 ± 2.2 months. The overall survival curve is depicted in Fig. 3a. Three and five-year survival rate was 83.5 and 71.0%, respectively. The causes of late death (n = 17) were progressive respiratory failure in nine, pneumonia in six, cardiac failure in one, and adult respiratory distress syndrome in one patient.

Survival differences in the subgroups described in Table 2 were analyzed using a log rank test. Patients with higher preoperative FEV₁ (≥28.5%, n = 53) had improved survival compared with those with lower preoperative FEV₁ (<28.5%, n = 35) (Fig. 3b, P = 0.0152). Five-year survival was 86.4% for those with FEV₁ ≥ 28.5%, and 60.9% for
those with $\text{FEV}_1 < 28.5\%$. No statistical differences were observed in the other subgroups.

4. Discussion

The fundamental concept of LVRS is to improve elastic recoil, reduce airflow limitation and improve the mechanics of respiration by excision of some of the most destroyed portions of the lung for patients with severe emphysema [1]. With regards to an optimal extent of resection, we should strike a balance between the extent that offers the maximal functional improvement and the extent that causes the minimal perioperative morbidity and mortality. On the one hand, the larger the volume of non-functional lung parenchyma is resected, the greater the functional improvement can be achieved [15]. On the other hand, the pulmonary vascular bed, which can be represented by diffusing capacity ($D_{LCO}$), may limit the possible extent of resection [16]. In this study, adult respiratory distress syndrome (ARDS) developed immediately after operation, followed by early postoperative death in one patient. Probably the volume of resection was too much for this patient and we should have examined $D_{LCO}$ preoperatively, as it was not routinely done in our hospital. We should keep it in mind that LVRS is still a challenging procedure with the early operative mortality up to 10% [1–5].

A standard approach of LVRS is either by median sternotomy or video-assisted thoracic procedure. Both approaches were shown to result in a similar improvement [4,5]. Recently we have preferred to choose the latter approach, because the lower lobe can be better visualized and incidental pleural adhesion, especially located dorsally, can be more easily resected. Consequently, we encountered relatively few complications of postoperative air leak ($>1$ week: 30%; $>2$ weeks: 17%), compared with the reported ones (40–50%).

Patients who are selected as candidates for LVRS should be carefully evaluated for possible lung cancer with its rate of discovery 1–4% [17,18]. In our study, coexisting lung cancer was discovered incidentally in five patients (5.7%). Of these, one patient died of respiratory failure, not related with cancer. Cancer recurrence (distant metastasis) occurred in one patient who was still alive at the time of surveillance. Thus, the coexisting lung cancer did not influence on the prognosis in our study. However, if the coexisting cancer is evident or suspected preoperatively, lobectomy that contains a cancer should be planned in addition, if the cancer is located in a target lobe. If the cancer is located in the area of best-preserved lung, one might well consider a wedge or segmental excision of it with LVRS [18].

As the surgery itself cannot stop the natural history of the disease, the gradual deterioration of remaining emphysematous lung will apparently occur. It is generally believed that this deterioration begins after approximately 6 months following LVRS [7]. Our study also supported this view.

![Fig. 3. A Kaplan–Meier model. (a) Overall survival curve following LVRS. The survival rate was 83.5% at 3 years and 71.0% at 5 years. (b) Survival difference between patients with higher preoperative $\text{FEV}_1 (\geq 28.5\%)$ and those with lower $\text{FEV}_1 (<28.5\%)$. The difference was statistically significant with $P = 0.0156$.](image_url)

Table 2

<table>
<thead>
<tr>
<th>Subgroups</th>
<th>$n$</th>
<th>$P$</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male</td>
<td>62</td>
<td>NS</td>
</tr>
<tr>
<td>Female</td>
<td>26</td>
<td></td>
</tr>
<tr>
<td>Smokers’ emphysema</td>
<td>77</td>
<td>NS</td>
</tr>
<tr>
<td>$\alpha_1$-Antitrypsin deficiency</td>
<td>11</td>
<td></td>
</tr>
<tr>
<td>VATS</td>
<td>60</td>
<td>NS</td>
</tr>
<tr>
<td>Sternotomy</td>
<td>28</td>
<td></td>
</tr>
<tr>
<td>Target zone dominated in the upper lobe</td>
<td>46</td>
<td>NS</td>
</tr>
<tr>
<td>Others</td>
<td>42</td>
<td></td>
</tr>
<tr>
<td>Preoperative $\text{PCO}_2 \leq 45 \text{mmHg}$</td>
<td>79</td>
<td>NS</td>
</tr>
<tr>
<td>Preoperative $\text{PCO}_2 &gt; 45 \text{mmHg}$</td>
<td>9</td>
<td></td>
</tr>
<tr>
<td>Preoperative $\text{FEV}_1 \leq 28.5%$</td>
<td>54</td>
<td>0.015*</td>
</tr>
<tr>
<td>Preoperative $\text{FEV}_1 &gt; 28.5%$</td>
<td>34</td>
<td></td>
</tr>
</tbody>
</table>

* VATS, video-assisted thoracic surgery. *$P < 0.05$; NS, not significant.
In spite of this deterioration of the lung function, some parameters still remain improved after a considerable interval compared with the preoperative value. Cooper and Lefrak reported 3-year cohort study of their experience and showed the persistent benefits in FEV1, RV and TLC [6]. Our data showed almost the same results, although the difference in FEV1 did not reach statistical significance at 3 years. As the persistent reduced thoracic hyperinflation would contribute to the reduction of exertional breathlessness [19], the long-persistent reduction in TLC and RV may improve quality of life of the patients.

During the early period of this study, we included the patients with α1-antitrypsin deficiency in the indication of LVRS. However, the benefits of the operation persisted only short for them. The functional improvements returned to baseline at 1 year and showed further deterioration after then, as we reported previously [14]. Recently, we excluded the patients with this disease from the indication of LVRS, although it might be used as a transitional operation for the lung transplantation, because of the chronic shortage of the donor’s lung [20].

FEV1 has been shown to correlate well with the long-term survival of the patients with emphysema. As LVRS improves FEV1 in the most patients, it is presumed that this operation would offer a survival benefit. Anthonisen reported that the natural prognosis of patients with severe emphysema was poor with 3-year survival of 50%, if the patients were over 60 years and predictive FEV1 was below 30% [21]. Other reports showed similar poor survival of the patients with FEV1 < 30% with 1-year survival of 90% and 5-year survival of 40% [22–24]. However, these reports were relatively old studies without current medical therapy for emphysema (supplementary O2, inspiration of anticholinergic medication, respiratory physiotherapy, etc). Simple comparison of these results with the survivals of patients with LVRS should be avoided. Geddes et al. [11] showed the better functional results in the surgical group compared with the medical therapy group in their randomized study, but the survival benefit was not clear. The ongoing randomized-control study by the National Institutes of Health (NIH) will address this matter strictly in the near future [25]. Nonetheless, our 5-year survival rate of 71.0% seemed better and might justify the risk of LVRS, taking into consideration that the procedure can offer the functional improvements.

Brenner et al. described that the patients with younger age, higher baseline FEV1 and PO2 showed significantly better survival [9]. It is not surprising to suppose that the patients with good preoperative conditions would show better survival. Indeed our results showed survival advantage in the patients with higher preoperative FEV1 (≥28.5%), although the survivals of other subgroups were not significantly different.

In conclusion, the improvement of the lung function after LVRS can persist in a selected group of patients with severe emphysema. Patients with higher preoperative FEV1 had a survival benefit. The favorable long-term survival may justify the procedure for the treatment of patients with poor prognosis.

References


[18] DeMeester SR, Patterson GA, Sundaresan RS, Cooper JD. Lobectomy combined with volume reduction for patients with lung cancer...


