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Outcome after unilateral lung volume reduction surgery in patients with severe emphysema

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Abstract

Objective: Bilateral lung volume reduction surgery (LVRS) has emerged as a palliative treatment option in patients with severe pulmonary emphysema. However, it is not known if a sustained functional improvement can be obtained using an unilateral approach. **Methods**: We hypothesized that a palliative effect can also be obtained by unilateral LVRS and prospectively assessed lung function, walking distance, and dyspnea before and 3, 6, 12, 18, 24 and 36 months after unilateral LVRS. **Results**: Twenty-eight patients were operated by the use of video-assisted thoracoscopic surgery (VATS) with a mean follow-up of 16.5 months (range 3–36 months). Forced expiratory volume in 1 s (FEV1) was significantly improved up to 3 months (1007 ± 432 compared to 1184 ± 499 ml, $P < 0.001$), residual volume up to 24 months (4154 ± 1126 compared to 3390 ± 914 ml, $P < 0.01$), dyspnea up to 12 months (modified Borg dyspnea scale 6.6 ± 1.8 compared to 3.9 ± 1.8, $P = 0.01$) and walking distance up to 24 months (343 ± 107 compared to 467 ± 77 m, $P < 0.05$) after unilateral LVRS compared to preoperative values. Overall, 25 of 28 patients reported a subjective benefit after unilateral LVRS. There was no 30-day mortality. Only two patients required surgery on the contralateral side after 4.5 and 6 months, respectively, both suffering from α-1-antitrypsin deficiency. **Conclusions**: Unilateral LVRS by the use of VATS results in a sustained beneficial effect, improving walking distance and dyspnea for up to 24 months in patients with severe emphysema. The preservation of the contralateral side for future intervention if required renders unilateral LVRS an attractive concept in this difficult palliative situation.

Keywords: Pulmonary emphysema; Lung volume reduction surgery; Unilateral; Outcome; Prospective study; Human; Video-assisted surgery

1. Introduction

Lung volume reduction surgery (LVRS) has emerged as a promising option for palliation of selected patients with severe, disabling emphysema. Several studies have shown significant short- and mid-term improvements of dyspnea, lung function, exercise capacity and quality of life after LVRS [1–3]. A bilateral operation is the method of choice in most centers, since the functional short-term results are usually better compared to the unilateral procedure [4–6]. However, the reported results indicate that the pulmonary function declines after LVRS [7,8]. Therefore, patients might require further palliative procedures if lung function and quality of life gradually worsen after the first intervention.

A recent editorial emphasized the question about how much lung tissue has to be removed to get optimal long-term results [9]. We therefore established a protocol with the possibility of a two-step procedure: we hypothesised that the unilateral procedure is adequate to improve dyspnea and exercise capacity, therefore fulfilling two important goals of the palliative intervention. If lung function, dyspnea and exercise capacity deteriorates over time to preoperative levels, LVRS will be repeated on the contralateral side.

Since there are no prospective data on the long-term functional outcome of patients undergoing unilateral LVRS, nor the number of patients who would require a second intervention on the contralateral side, we have prospectively assessed dyspnea, lung function, and walking distance before and after unilateral LVRS. To this end, all patients referred to our institution and qualifying for LVRS were operated unilaterally since 1996.

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2. Material and methods

2.1. Patient selection

Since March 1996, all patients with severe diffuse emphysema qualifying for LVRS according to the published guidelines [10] underwent unilateral LVRS after informed consent. Inclusion criteria consisted of severe dyspnea at rest or at minimal physical activity, forced expiratory volume in 1 s (FEV1) <35% of the predicted value and severe hyperinflation with a residual volume (RV) >200%, without improvement after optimal medical therapy (including systemic corticosteroids), chest physiotherapy and exercise training. Diffuse emphysema was documented in all patients with high-resolution computer tomography and ventilation/perfusion scintigraphy. Patients with bullous disease without emphysema were excluded. Exclusion criteria were age >75 years, a mean pulmonary arterial pressure >35 mmHg determined by right-heart catheterisation, active smoking, a $PaCO_2$ >7.3 kPa, FEV1 <10% of the predicted value, signs for chronic productive bronchitis or evidence of coronary heart disease based on patient history and electrocardiogram. Before LVRS, all patients underwent pulmonary rehabilitation for 3 weeks without satisfying benefit.

2.2. Preoperative assessment

Preoperative evaluation included a patient history and clinical examination. Patients were asked to classify their degree of dyspnea according to the ATS shortness of breath dyspnea scale (ranging from 0 to 4, meaning 0 without any dyspnea and 4 with severe dyspnea at rest) and the modified Borg dyspnea scale (ranging from 0 to 10, 10 with severe dyspnea at rest). In addition, standard pulmonary function test, body plethysmography, measurements of CO diffusion capacity, 6-min walking test, chest X-ray, high-resolution computed tomography, ventilation/perfusion scintigraphy and right heart catheterisation were performed in each patient. Left heart catheterisation was done if coronary artery disease was suspected based on the patients history and the ECG.

2.3. Operative approach and technique

All patients were operated unilaterally. The side with the more heterogeneous pattern of emphysema was chosen based on ventilation-perfusion scintigraphy and high-resolution computed tomography. Patients underwent video-assisted thoracoscopic surgery (VATS) using double-lumen intubation and continuous thoracic peridural analgesia. Typically, 20–30% of the lung were resected by use of an Endo-GIA stapler without buttressing the stapled resection line.

2.4. Follow-up and re-evaluation for LVRS on the contralateral side

Follow-up examinations included dyspnea grading, pulmonary function tests and 6-min walking test at 3, 6, 12, 18, 24 and 36 months after LVRS. LVRS on the contralateral side was considered in patients with dyspnea and exercise intolerance comparable to preoperative levels in absence of exclusion criteria as mentioned above.

2.5. Statistics

Data are expressed as mean ± standard deviation (SD). Data of lung function testing, blood gas analysis and walking test were analysed using a linear mixed model with the SAS procedure 'mixed' (SAS Institute Inc., NC USA; Version 6.12). *P*-values were adjusted by the Dunnett–Hsu-correction for multiple comparisons with one control. Data regarding degree of dyspnea according to the ATS shortness of breath scale and the modified Borg dyspnea scale were analysed by use of the Wilcoxon signed-rank test and Bonferroni-adjustment. Pre- and postoperative steroid dependency was compared by use of the paired Wilcoxon signed-rank test. A two-sided hypothesis was used and a *P*-value of less than 0.05 was considered statistically significant. All data were analysed by D. Dietrich, Institute of Mathematical Statistics, University of Bern, Switzerland.

3. Results

Twenty-eight patients (three women and 25 men) underwent unilateral LVRS between March 1996 and October 1999. The mean age was 62.5 years, ranging from 51 to 75 years. Twenty-six patients had emphysema due to smoking. Two patients were included with α-1-antitrypsin deficiency, one with a homozygote and one with a heterozygote phenotype. According to the emphysema morphology classification [11], all patients had moderate to marked heterogeneous emphysema. Twelve patients were operated on the right upper lobe, eight on the left upper lobe, one on the right lower lobe and five patients on the left lower lobe. One patient underwent resection on the left upper and the left lower lobe, one on the right upper and lower lobe.

All patients were extubated immediately after surgery. No re-intubation, ICU stay for more than 2 days or tracheotomy were necessary. The mean duration of hospital stay was 29.9 days, ranging from 14 to 71 days.

There was no 30-day postoperative mortality. Morbidity consisted of persistent air leaks >7 days in six patients (21%), pneumonia in five (18%), and iliofemoral venous thrombosis in one patient. One patient developed a bronchopleural fistula 3 months after the operation.

Follow-up ranged from 3 to 36 months (mean follow-up 16.5 months). One year follow-up data were available in 17 patients, 2 years data in nine, and 3 years data in seven.

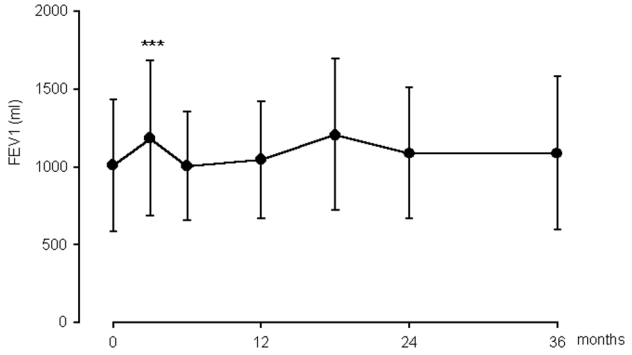

Fig. 1. FEV1 in patients before and after unilateral LVRS (mean ± SD); ***$P < 0.001$.

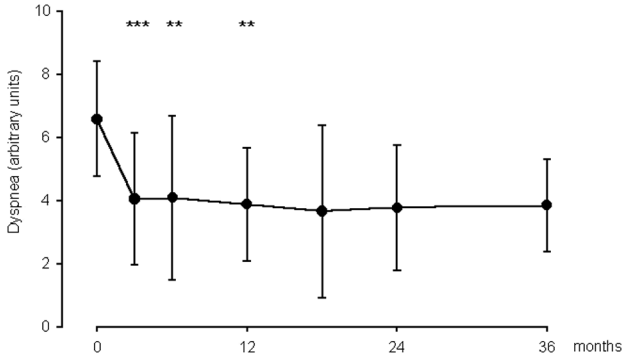

Fig. 3. Assessment of dyspnea according to the modified BORG dyspnea scale before and after unilateral LVRS (mean ± SD); **$P < 0.01$; ***$P < 0.001$.

Three patients were lost during follow-up due to moving ($n = 1$, 6 months) or unwillingness to further participate ($n = 2$, 12 months). Four patients (14%) died during the observation period, one from chronic pulmonary infection at 3 months, one from perforated sigma diverticulitis at 6 months, one from right heart failure at 12 months and one from a bronchopleural fistula of the ipsilateral lung 16 months after LVRS.

Pulmonary function testing and subjective assessment revealed a significant increase of FEV1 up to 3 months (1007 ± 432 compared to 1184 ± 499 ml, $P < 0.001$), a significant decrease of the RV up to 24 months (4154 ± 1126 compared to 3390 ± 914 ml, $P < 0.01$), and a significant decrease of dyspnea up to 12 months (modified Borg dyspnea scale 6.6 ± 1.8 compared to 3.9 ± 1.8, $P = 0.01$) after unilateral LVRS, as compared to preoperative values (Figs. 1–3). No significant differences were found between preoperative and postoperative values regarding DLCO, PaO_2 and $PaCO_2$.

The 6-min walking distance increased significantly up to 24 months after unilateral LVRS (343 ± 107 compared to 467 ± 77 m, $P < 0.05$) (Fig. 4). Twenty-two patients required daily steroid medication before compared to nine patients after LVRS. The mean dose of steroid was 11.8 ± 6.4 mg prednisone equivalent per day before and 2.9 ± 5.1 mg after LVRS at discharge ($P = 0.01$). Five of 28 patients (18%) had continuous oxygen therapy before LVRS, which was unchanged after LVRS. Overall, 25 of 28 patients (89%) reported a benefit after LVRS in terms of relief of dyspnea and improvement of walking distance. Three patients did not improve after LVRS; one of those patients developed an ilio-femoral venous thrombosis after the right heart catheterisation, one a bronchopleural fistula and aspergillus infection within the operated chest cavity, and one had chronic productive bronchitis with Serratia marcescens infection.

During the observation period, two patients (7%) underwent LVRS on the contralateral side due to subsequent deterioration after a period of subjective and objective improvement following their first operation. Both suffered from α-1-antitrypsin deficiency. One patient (heterozygote phenotype) showed a decline of pulmonary function 5 months after the first operation and was subsequently operated on the contralateral side. Pulmonary function testing, dyspnea and walking distance were improved 6 months after the second intervention. The other patient (homozygote phenotype) showed a modest improvement of symptoms for only 3 months and underwent contralateral LVRS 18 weeks after the initial operation. Since the second operation was without subjective and objective benefit, lung transplantation had to be performed. All other patients revealed

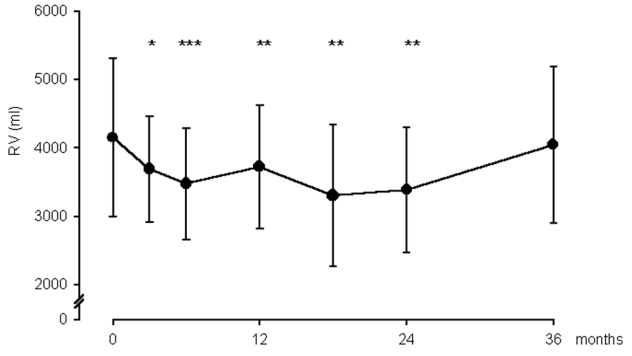

Fig. 2. Residual volume in patients before and after unilateral LVRS (mean ± SD); *$P < 0.05$; **$P < 0.01$; ***$P < 0.001$.

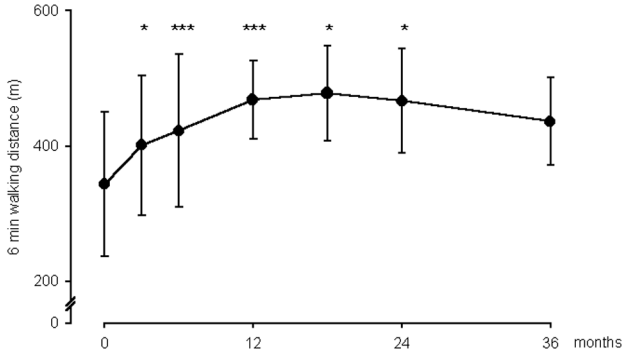

Fig. 4. Six-minute walking test before and after unilateral LVRS (mean ± SD); *$P < 0.05$; ***$P < 0.001$.

subjective and objective improvement after unilateral LVRS and denied the need for a contralateral intervention during the 3 years observation period.

4. Discussion

This prospective study indicates that patients with severe, disabling emphysema show a substantial and clinically relevant benefit after unilateral LVRS. Both dyspnea and exercise capacity improved significantly after unilateral LVRS for at least 2 years. Only two patients had to be operated on the contralateral side during the observation period, because dyspnea and exercise capacity deteriorated to preoperative levels. Both patients undergoing the second intervention had suffered from α-1 antitrypsin deficiency.

To our knowledge, this is the first prospective study with a systematic unilateral LVRS approach for patients with diffuse emphysema, meaning that all patients fulfilling the criteria for LVRS were treated unilaterally, without the intention to treat the contralateral side sequentially after a scheduled period of time [12].

At date, most authors consider the bilateral LVRS as the procedure of choice, since the improvements of pulmonary function are better after bilateral than unilateral LVRS [3,5,6,13–15]. Our results suggest that patients with severe emphysema fulfilling the criteria for LVRS show a significant benefit after unilateral LVRS, in accordance with recently published results from patients with unilateral LVRS [16]. Unilateral LVRS resulted in a significantly reduced RV in our patients up to 24 months postoperatively. In addition, a significant improvement of FEV1 up to 3 months following unilateral LVRS was observed with a mean gain of 177 ml. Kotloff and Brenner reported a similar increase of FEV1 of 160 and 150 ml, respectively, after unilateral LVRS [6,17]. Although the initial increase of FEV1 is greater after the bilateral than the unilateral approach, recent publications demonstrated that the initial gain in FEV1 tends to decrease after time following LVRS, with a correlation between the magnitude of short-term improvement of FEV1 and the rate of annual postoperative decline. Patients with unilateral LVRS showed a lower annual decline as compared to bilateral LVRS (100 vs. 250 ml) [17]. These data indicate that a two stage, unilateral procedure, in which a second, contralateral resection is performed following significant deterioration in symptoms, might be superior to a bilateral procedure in the long-term follow-up. However, randomized, controlled studies need to be performed to further study the two stage, unilateral approach.

Our and other results suggest that pulmonary function measurements do not necessarily correlate with the relief of symptoms after LVRS. In our series, dyspnea was significantly decreased up to 12 months and walking distance significantly increased up to 2 years after the operation. Similar results were reported from bilateral LVRS [3,13,18]. An important predictor regarding subjective assessment of the results after LVRS seems to be steroid dependency. In our series, daily steroid administration could be avoided in 13 out of 22 patients at discharge following unilateral LVRS.

LVRS is considered by most authors as an entirely palliative approach in patients with diffuse emphysema, with the goal to reduce dyspnea and improve quality of life [4,9,19,20]. This goal should be achieved with the least invasive and aggressive procedure in these fragile and risky patients. Our results suggest that this goal might be achieved by unilateral LVRS for at least 2 years. The follow-up data 3 years after unilateral LVRS indicate that the beneficial effect of LVRS is still present. However, these data do not reach statistical significance, probably due to the low patient number.

No 30-day-mortality was observed in our series, and the perioperative morbidity was rather low, without need for reintubation, prolonged ICU stay or tracheotomy, indicating that unilateral LVRS is safe and well tolerated in patients fulfilling the criteria for LVRS. Previously published trials comparing unilateral and bilateral LVRS have documented a higher incidence of postoperative mortality, re-intubation, pneumonia and air leaks after bilateral than after unilateral LVRS [6,21]. These data might further support the unilateral approach, particularly in patients at high preoperative risk, since the complication rate is lower in patients with unilateral LVRS compared to bilateral LVRS.

During follow up, four out of 28 patients (14%) died at 3, 6, 12 and 16 months after surgery, respectively. Previous reports investigating the mortality during follow-up after unilateral or bilateral LVRS came to controversial conclusions. Serna et al. showed a 2-year survival advantage after bilateral LVRS as compared to unilateral LVRS, whereas Naunheim et al. did not find a better survival after bilateral than after unilateral LVRS [21,22]. However, caution in the interpretation might be indicated since both studies were retrospective.

Two patients were reoperated on the contralateral side after a short-lasting benefit after unilateral LVRS, both of them had α-1-antitryspin deficiency. Recent studies suggest that patients with α-1-antitrypsin deficiency might not benefit from LVRS, neither unilateral nor bilateral [7,13]. This indicates that the necessity to perform LVRS on the contralateral side was primarily related to poor patient selection criteria than to the unilateral approach per se.

Overall, 25 of 28 patients (89%) reported a benefit after unilateral LVRS over an observation period of up to 3 years. The vast majority of the patients were satisfied with the effects of the unilateral LVRS and did not need a second intervention during the observation period. This indicates that the palliative goal of the intervention can be reached by the unilateral approach.

In summary, a substantial and clinically relevant benefit can be achieved in patients with severe emphysema by unilateral LVRS. However, relatively little data exist about the long-term outcome of uni- and bilateral LVRS.

Although bilateral LVRS appears to be superior to the unilateral approach in the short term [14–16], the unilateral approach may represent an effective and safe palliative treatment, offering a substantial long-term benefit. Since the published follow-up studies clearly indicate that lung function is deteriorating over time after LVRS [15], we assume that the unilateral approach might be a valuable alternative to the bilateral procedure, because the unilateral approach with the preservation of the non-operated side offers the possibility of a further palliative intervention if required. Larger prospective long-term follow-up studies are required to define the optimal surgical procedure in patients with severe emphysema.

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