# Outcome After Lung Volume Reduction Surgery in Patients With Severely Impaired Diffusion Capacity

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*Background.* **Lung volume reduction surgery (LVRS) has been proven to be a successful procedure and can be performed with low mortality when defined selection criteria are met. We hypothesized good outcome and low mortality after LVRS for selected patients with severe hyperinflation and nonhomogeneous morphology even when diffusion capacity of the lung for carbon monoxide (DLCO) is less than 20%.**

*Methods.* **The study included all patients scheduled for LVRS between March 2005 and May 2014 with a preoperative DLCO of less than 20%. Postoperative 90-day mortality was the primary end point. Secondary end points were postoperative lung function and surgical morbidity at 3, 6, and 12 months.**

*Results.* **Included were 33 patients with a median forced expiratory volume in 1 second of 23% (interquartile range, 19% to 28%), a median diffusion capacity of 15% (interquartile range, 13% to 18%), and a median hyperinflation of 76% (residual volume–to–total lung capacity ratio of 70% to 76%). Mean follow-up was 44.8 months (range, 10 to 141 months). Heterogeneous emphysema was present in 26 patients, and 7 showed intermediately heterogeneous morphology. Sixteen procedures were bilateral, and 31 were performed by video-assisted thoracoscopic surgery. The 90-day mortality was 0%. Median forced expiratory volume in 1 second percentage predicted at 3 months increased from 23% to 29% ($p < 0.001$). Median DLCO increased from 15% to 24% ($p < 0.001$), and median hyperinflation decreased from 76% to 63% ($p < 0.001$). A prolonged air leak exceeding 7 days occurred in 16 patients (48.5%), and 6 required reoperation for fistula closure. The 7 patients with intermediately heterogeneous emphysema showed a median increase in forced expiratory volume in 1 second from 20% preoperatively to 28% postoperatively ($p = 0.028$).**

*Conclusions.* **Selected patients with severely impaired DLCO of less than 20% can cautiously be considered as potential candidates if hyperinflation is severe and the lungs show areas with advanced destruction as targets for resection.**

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Lung volume reduction surgery (LVRS) has been proven successful when certain selection criteria are met. The National Emphysema Treatment Trial (NETT) showed improved lung function, dyspnea, exercise capacity, and even a survival advantage for patients with upper lobe–predominant emphysema and low baseline exercise capacity [1]. However, selected symptomatic patients with less favorable morphologies or less favorable selection criteria may profit from LVRS, as shown in the NETT and other large single-center studies. Nevertheless, a low diffusion capacity of the lung for carbon monoxide (DLCO) in patients planned for LVRS might be a risk factor. Patients during the NETT had to complete a DLCO test but were not excluded based on a cutoff (ie, 20% predicted) [2]. The 30-day mortality rate was 16% for 69 patients with the combination of forced expiratory volume in 1 second ($FEV_1$) of no more than 20% predicted and homogeneous emphysema or low DLCO of no more than 20% predicted. This combination of selection criteria fulfilled the stopping guidelines as found by the NETT data and safety monitoring board [2].

Previous concerns that patients with such a low DLCO cannot sustain resection of lung parenchyma because of the limited remaining tissue contributing to gas exchange have been confirmed [3, 4]. Because the favorable effects of LVRS are mainly caused by improvement of respiratory mechanics, even patients with a low DLCO and areas of major destruction beside better preserved lung tissue (heterogeneous emphysema) may profit from the operation without elevated risk of the procedure [5, 6]. The correction of preoperative hyperinflation plays a key role in a favorable outcome after LVRS [7], and therefore, downsizing the emphysematous lung to a physiologic size compensates the disadvantage of resection of some tissue that may contribute to gas exchange.

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We postulate a favorable and safe outcome after LVRS for selected patients with severely impaired DLCO in combination with heterogeneous and intermediately heterogeneous morphology as long as severe preoperative hyperinflation is present.

## Patients and Methods

This study was approved by the Swiss local ethics committee (KEK #2016-00716). The institution's database was searched for patients with a preoperative DLCO of less than 20% predicted who underwent LVRS between 2003 and 2014.

### *Patient Selection*

Inclusion criteria for LVRS are reported in Table 1. DLCO of less than 20% predicted in case of nonhomogeneous emphysema was not considered a contraindication if severe hyperinflation (residual volume–to–total lung capacity ratio of ≥60% predicted) existed. Morphology was assessed on chest computed tomography and graded as shown in Figure 1, as previously described [8]:

- Markedly heterogeneous is defined as a distinct regional difference in the severity of emphysema in at least two adjacent lung segments of either lung.
- Intermediately heterogeneous is a distinct regional difference in the severity of emphysema with a maximum in the area of one or more than one but not in adjacent lung segments of either lung.
- Homogeneous emphysema shows no regional or only minor differences in the severity of emphysema.

Purely homogeneous emphysema has not been considered for LVRS in case of DLCO of less than 20% predicted. Patients with intermediately heterogeneous types have been considered in addition to the typical heterogeneous type.

All patients who were potential candidates for LVRS were discussed at our interdisciplinary emphysema board.

### *Operation*

LVRS was performed bilaterally in bilateral morphology or unilaterally in unilateral predominant disease by video-assisted thoracoscopic surgery or by thoracotomy in case of severe adhesions. The decision for a bilateral or unilateral operation depended on the predominance of disease distribution. In these borderline patients, the decision for unilateral LVRS was made liberally in case of lateral predominance. According to the above-mentioned gradation, the latter is defined as unilateral markedly heterogeneous emphysema accompanied by intermediately heterogeneous emphysema on the contralateral side. The unilateral heterogeneous emphysema was chosen as preferred target area for LVRS (Fig 2).

If severe adhesions were encountered in a scheduled bilateral LVRS, the operation was terminated after performing one side. Patients with LVRS already planned as bridge to transplantation were generally scheduled for a unilateral operation. Areas of greatest destruction on computed tomography scans were resected with standard staplers (Endo GIA Ultra Universal [Covidien, Mansfield, MA] or Echelon ENDOPATH [Ethicon, Somerville, NJ]). The expected volume after resection was planned from chest computed tomography and the expected volume was the predicted total lung capacity.

### *Follow-Up and Outcome Measures*

All pulmonary function tests (PFTs) were performed using a standard body plethysmograph and DLCO. Most patients were only monitored for 3 months after LVRS at our institution. Patients referred from institutions in other districts were sent back for follow-up as soon as possible after LVRS. Referring physicians were asked to perform PFTs 3 months after the operation. Decisions about further lung function tests were left to the treating physicians. Data about subjective parameters are not routinely collected at our institution.

The primary care physicians or the patients themselves were contacted by phone for follow-up (survival). When available, PFTs were searched up to 1 year after LVRS. Complete PFTs were available for 33 patients (100%) at baseline and after the operation for 26 patients (78.8%) at 3 months, 17 patients (51.5%) at 6 months, and 20 patients (60.6%) at 12 months. In 7 patients monitored in other Swiss districts, no PFTs at 3 months after LVRS were available from the referring institution and no postoperative PFTs were available for 2 patients. The PFTs at 6 or 12 months, or both, were available in 5 patients. All available lung function values were included for statistical analysis and comparison of the preoperative and postoperative outcome. Testing for significance was samples related.

### *Statistical Analysis*

Descriptive variables are expressed as medians with interquartile ranges (IQR) or counts with proportions, unless otherwise specified. Comparisons were done using the Wilcoxon matched-pair signed rank test. A $p$ value of less than 0.05 was determined as significant. Kaplan-Meier estimation was used to depict survival. All data and graphs were produced using IBM SPSS Statistics for Windows 22.0 software (IBM Corp, Armonk, NY).

## Results

LVRS was performed in 278 patients within our searched time window, and 33 patients with DLCO of less than 20% predicted were identified. They were a mean age of 65 (range, 51 to 78 years), and 19 patients (57.6%) were men. Bilateral LVRS procedures were performed in 16 patients (48.5%), and 31 (93.9%) were by video-assisted thoracoscopic surgery. The reasons for unilateral LVRS were severe adhesions in 4 patients (2 were converted to an open operation), lateral predominance of emphysema in 12, and LVRS as bridge to transplantation in 1. Emphysema was heterogenous in 26 and intermediately heterogeneous in 7 patients (21.2%).