

LUNG VOLUME REDUCTION SURGERY IN PATIENTS WITH COPD

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INTRODUCTION

Emphysema is a progressive and debilitating disease associated with a high rate of morbidity and mortality as a result of respiratory failure. Medical therapy and pulmonary rehabilitation are useful palliative treatment options and can temporarily improve symptoms. However, they do not alter much the natural history of the disease. End-stage emphysema markedly limits the quality of life and survival of patients. Two surgical procedures are well established: lung-volume reduction surgery (LVRS) and lung transplantation (LTX). Different endoscopic procedures using endobronchial valves or airway bypasses (1-3) are novel methods showing promising short-term results, but long-term evaluation and randomized trials are necessary to evaluate these methods.

Lung volume reduction surgery (LVRS) is a successful, palliative surgical therapy for carefully selected patients with advanced emphysema. Although the experience with LVRS has grown over the last few years, the selection of patients suitable for LVRS is still a matter of controversy in some patients and differs widely between centers (4-8). On the basis of the early work from Brantigen(9) and the review by Cooper(10), the procedure was recommended to be performed as a non-anatomical resection of the most severely destroyed, functionless tissue to reduce lung volume by 20-30%. In the nineties we performed the procedure by VATS as the first group worldwide. Particularly, the results of the large prospective, multicenter national emphysema treatment trial (NETT)(11) which evaluated the outcome of 1218 patients randomized to either medi-

cal treatment or LVRS confirmed that properly selected patients may experience better functional improvements, physical performance and quality of life after surgery than with medical treatment. This was especially the case for patients with upper lobe predominant destruction of the lungs and a poor exercise capacity. The patients in the LVRS group had additionally a lower risk of death than the patients in the medical group. Patients in the so called high-risk group, with an $FEV_1 < 20\%$ predicted who had a homogeneous type of emphysema or a $DLCO < 20\%$ had an increased risk of mortality (mortality rate was 16% as compared with a rate of 0% to a matched medically-treated group) following LVRS and were not considered suitable for LVRS. However this high perioperative mortality was not a surprise and expected by experienced groups beforehand since these patients were excluded from surgery in their programs. A controversy in the indications exists in regard to the morphologic type of emphysema suitable for LVRS.

In most centers, patients who showed no heterogeneity in severity of the emphysematous destruction on CT were either excluded from surgery or thought to experience minor benefits only. In these patients, no distinct areas of non-or poorly perfused lung can be identified on perfusion scans as targets for resection, and they were therefore not considered candidates for LVRS. Since the favorable effects of LVRS are mainly the improvement of respiratory mechanics due to a reduction in static lung volumes, in particular of functional residual capacity (FRC) and residual volume (RV), we postulated that well selected patients with severe hyperinflation and airflow obstruc-

tion should benefit from LVRS even if their emphysema was non-heterogeneously distributed. Our group was the first reporting, that LVRS also improves lung function in patients with non-heterogeneously emphysema, although to a lesser degree (12-13).

The concerns that in patients with a non-heterogeneous emphysema who undergo LVRS, parenchyma contributing to gas exchange will be resected, has to be compensated by a beneficiary effect of downsizing the hyperinflated lung to a more physiologic size. In these patients the selection criteria should be applied very strictly. Only patients with severe hyperinflation in absence of pulmonary hypertension, no signs of recurrent infections or purulent bronchitis and, especially important, with a diffusing capacity higher than 20% predicted are valuable candidates for LVRS.

In a special subgroup of patients, who have emphysema due to an alpha-1 antitrypsin deficiency LVRS can be considered as a therapy to postpone transplantation(14). In these patients, with typically involvement of the lower parts of the lung airway inflammation is often accompanied, selection criteria should be applied even more cautiously and only patients without inflammatory signs of airway disease on the CT-scan should be included.

Selection of patients

The selection of patients is based on physiologic concepts and clinical experience and the goal is to select patients with severely symptomatic disease who may benefit from surgery with a low postoperative mortality. LVRS should be considered in severely impaired patients with dyspnea, poor physical function marked airflow obstruction and hyperinflation without medical contraindications which are known to increase the perioperative complication rate and mortality (table 1). The goal of the NETT study was to assess the safety of LVRS in comparison with medi-

cal therapy in patients with emphysema and to identify subgroups of patients that might benefit or have a higher risk from the LVRS. The only prognostic factors associated with differences in mortality between the treatment groups were the craniocaudal distribution of emphysema and the base-line exercise capacity. To distinguish between the low and high exercise capacity a maximal workload at or below the sex-specific 40th percentile (25 W for women and 40 W for men) was used. In a post hoc analysis they found that the mortality in patients in the LVRS-group with predominantly upper-lobe emphysema and low exercise capacity mortality was lower than in the medical group. A further subgroup analysis revealed that patients with upper-lobe predominant emphysema and high baseline exercise capacity showed no survival benefit from LVRS but an improved exercise capacity, whereas patients with non-upper-lobe emphysema and high exercise capacity had no statistically significant difference in survival or exercise capacity after LVRS as compared with the medical treatment(15). Naunheim and colleagues(16) found that patients with advanced age, non-upper-lobe predominant emphysema and steroid use had a higher risk for cardiovascular complications, therefore it is important to carefully select patients and optimize the preoperative status as far as possible.

Emphysema is defined anatomically. In its severe form it can be easily detected on a plain posteroanterior and lateral chest radiograph. However, the most reliable method of obtaining information on the degree and distribution of emphysema is chest CT scanning. This imaging method plays a major role in the selection process, and in particular lung densitometry measurements are very good for detecting the extent of emphysematous destruction (figure 1). Different morphological grading systems have been developed to quantify the type, severity and distribution of emphysema as a help in identifying candidates for LVRS although no internationally accepted standardised radiological classification exists(17). A specifically LVRS

Table 1. Indications and contraindications

Indications	
Age <75 years	
Marked dyspnea	MRC >3
	Hyperinflation: TLC >%125 pred.
Severe emphysema	RV/TLC >0.65
	FEV ₁ <%35 pred
Contraindications	
Vanishing lung with DLCO <20% pred	
Lung function with FEV1 <20% pred	
Pulmonary hypertension PAP mean >35 mmHg	
Coronary artery disease	

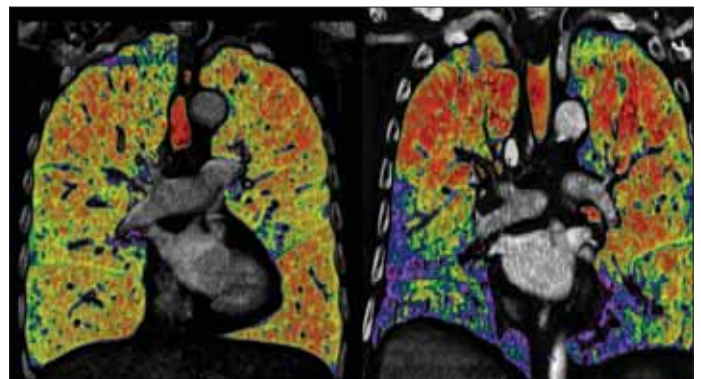


Figure 1. Lung densitometry measurements

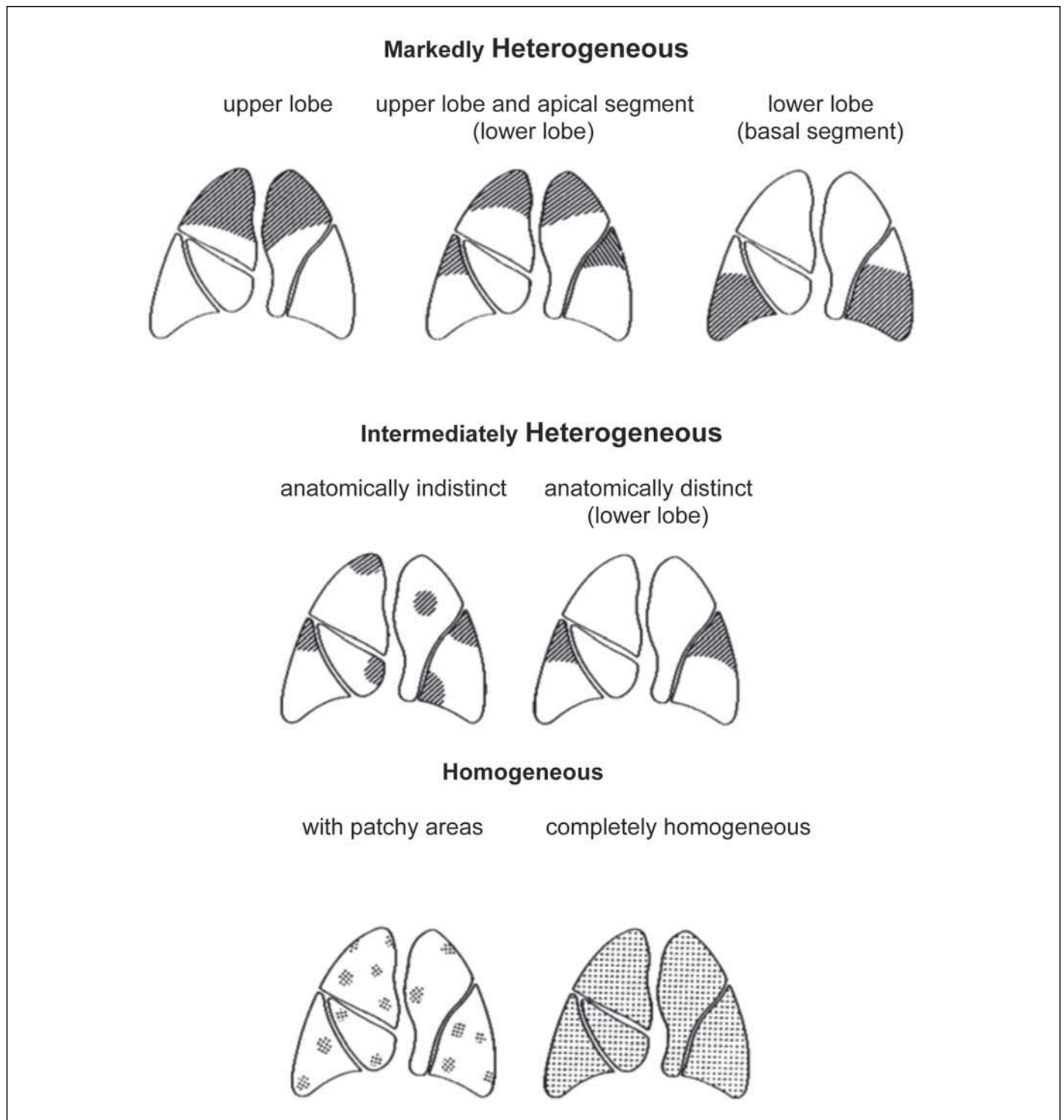


Figure 2. (according to Weder et al. (18)):

Classification system of Emphysema:

Three major types of emphysema distribution were defined

Markedly heterogeneous (upper panel), intermediately heterogeneous (middle panel), and homogeneous (lower panel). For heterogeneous emphysema types, the most affected areas were recorded as disease predominance in either upper lobe, upper lobe and apical segment of the lower lobe, or lower lobe

Among homogeneous types of emphysema (lower panel) some showed multiple small zones of destruction throughout all lobes (patchy). In other emphysematous changes were evenly distributed throughout the entire lungs (homogeneous)

oriented classification system based on CT findings was proposed by our group distinguishing between homogeneous, moderately heterogeneous and markedly heterogeneous emphysema distribution, and the predominance of the involved lobes was considered (18).

The following definitions were applied (figure 2): markedly heterogeneous Emphysema: a distinct regional difference in the severity of emphysema (ie. Decreased density, loss of vascular lung structure) is present in at least two adjacent lung segments of either lung. Intermediately heterogeneous Emphysema: a distinct regional difference in severity of emphysema may be present maximally in the area of one or more than one but not in adjacent lung segments of either lung. Markedly heterogeneous- a distinct regional difference in the severity of emphysema is present in at least the area of two adjacent lung segments of either lung. This classification system is easy to apply, helps to select patients for LVRS and allows comparison of outcome.

Surgical approach and definition of the target area for resection

LVRS is typically performed under general anaesthesia, during one lung ventilation via median sternotomy, thoracotomy or VATS (video-assisted thoracoscopic surgery), buttressed or not buttressed with bovine pericardium or synthetic reinforcement material. It can be performed uni- or bilaterally. The target areas and the extent of resection differs between various types of emphysema. The lung is resected in areas that show the most severe emphysematous destruction on imaging studies (CT scan) corresponding to a loss of perfusion on quantitative perfusion scan (heterogeneous type)(19) This is either in the upper lobes or the basal segments of the lower lobes. Some patients have a combination of upper lobe (apical) and lower lobe (apical segment) destruction. In those patients approximately 20% to 30% of the upper lobe is resected, in combination with the apical segment of the lower lobe. In patients with homogenous emphysema it is more difficult to define the amount and site of resection since clearly defined target areas are absent. In these cases we preferentially choose the upper lobes for resection and the amount of resection is the volume which is needed to reduce the total lung capacity its predicted volume, usually approximately 40% to 50% of both upper lobes. Since the resected volume cannot be quantified during surgery the ideal volume of resection cannot be assessed scientifically. In patients with complete destroyed lobe and simultaneously detected lung malignancy the surgical procedure is performed according to the degree of the lung destruction and the size and localization of the tumor.

RESULTS OF SURGERY

Operative morbidity

The major postoperative complications are air leaks. The NETT study (20) didn't find any association using buttressed material and fewer or less prolonged air leaks. In contrast, our group found that buttressing the staple line significantly shortens the duration of air leaks and the drainage time(21). To reduce the incidence of air leaks we recommend a controlled and cautious reinflation of the lung and applying low suction (<5 H₂O). Most leaks will seal spontaneously within a few days after surgery, when larger leaks persist a reoperations should be considered.

Pulmonary function

LVRS significantly improves lung function and quality of life, with the best results 3-6 months postoperatively. The NETT group found greater functional benefits in the surgical cohort when compared with the medical group, this was especially the case in patients with predominantly upper-lobe emphysema and high base-line exercise capacity and in patients with non-upper lobe emphysema and low base-line exercise capacity.

The improvement may last for up to 5 years postoperatively depending on the morphological emphysema type. (6) Ciccone et al showed that six months after operation FEV₁ increased in 94% of patients with a mean change of 54%. 5 years postoperatively 53% of the patients still had an increase compared to preoperatively. Six months and 1 year after operation, RV decreased by 30%, and 90% of the patients showed improvement. At 5 years postoperatively, 79% of the patients still showed an improvement. The DLCO showed a 25% increase from preoperative values on follow up at 6 months and 1 year. Gelb et al.(22) found an improvement in FEV₁ > 200ml in 88% of the patients after 6 months, respectively in 8% after 5 years.

Three months after LVRS, we found relevant symptomatic and functional improvements in heterogeneous as well as in homogenous emphysema (figure 3). Maximal values were observed 3 to 6 months after operation with a subsequent decline towards preoperative levels over the following years.(23). FEV₁ increased from 27 to 45% predicted in the heterogeneous group and from 27% to 35% in the non-heterogeneously group and remained significantly improved for up to three, respectively two years postoperatively (figure 3). TLC decreased from 7.77 (±1.5) L to 7.14 (±1.4) L and RV decreased from 5.31 (±1.3) L to 4.15 (±1.07) L at 3 months after LVRS (p<0.001) resulting in a reduction of the RV/TLC ratio from 0.68 (±0.07) to 0.58 (±0.08) (p<0.001) in the non-heterogeneously group,

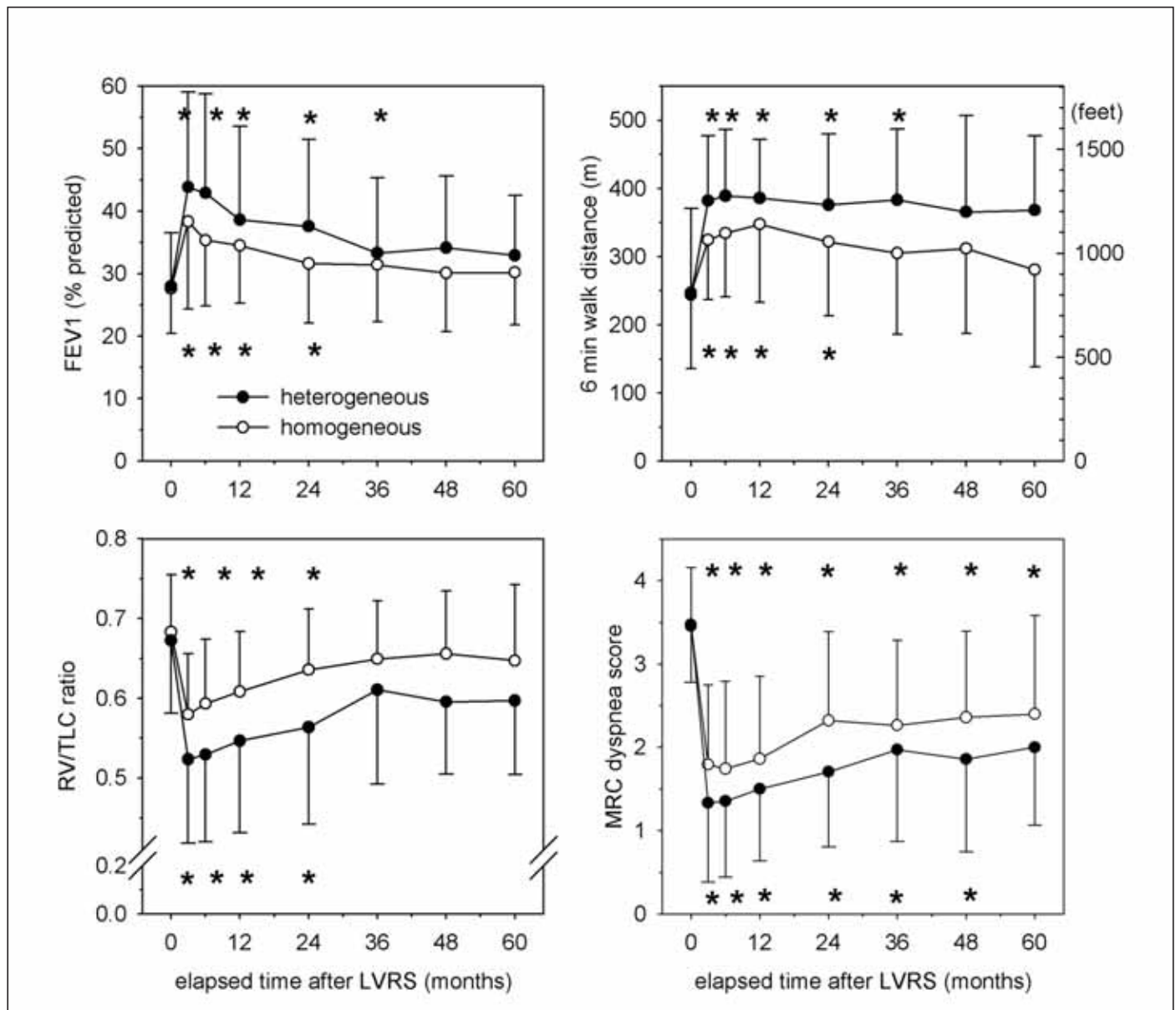


Figure 3. (according to Weder et al. (12)): Time course of FEV₁, RV/TLC, MRC dyspnea score, and 6 minute walk distance

whereas the RV/TLC ratio decreased from 0.67 (± 0.09) to 0.52 (± 0.11) ($p < 0.001$) in the heterogeneous group (12). The beneficial effect on hyperinflation remained statistically significant for up to two years in both groups (figure 3). figure 5 a-b illustrates the effect of LVRS on the x-ray in a patient with Emphysema. The preoperative severe hyperinflation of the lung with the depressed and flattened diaphragm is postoperatively clearly diminished; it is visible in the regain of the clear dome shape of the diaphragm. Independent of the emphysema morphology, the values of FEV₁ and the 6 min walking distance return to values near baseline after a median period of 36 months (figure 3) although patients perceive persistent improvements in dyspnea for a much longer time, i.e. for 4 to 5 years.

Dyspnea

LLVRS considerably improved dyspnea in patients with LVRS. Ciccone et al.(6) demonstrated the reduction of the MRC-Dyspnoe score at 6 months postoperatively when 88% of the patients reported an improvement. At 5 years after the operation, only 20% of the patients reported a worse score. Similar improvements were found from Gelb et al.(22) who showed a decrease in the MRC score > in 88% of the patients at 6 months and 15% after 5 years. In our group the MRC score decreased significantly in the heterogeneous group by 2.1 points from 3.47 (± 0.7) to 1.3 (± 0.9) ($p < 0.001$) after LVRS and remained significantly decreased for up to 5 years. In the non-heterogeneously group it decreased by 1.6 points from 3.46 (± 0.7) to 1.8

(± 0.9) ($p < 0.001$) after LVRS and remained below baseline for up to 4 years(12).

Survival

The perioperative mortality in centers, experienced in choosing and operating emphysema patients is low (2-7%), (6, 24) the percentage was similar in the NETT study, after excluding patients from the high-risk subgroup. In this group of patients (1078 patients were analyzed) with either upper-lobe predominant emphysema, or non-upper-lobe predominant emphysema and low baseline exercise, the 30-day mortality rate was 2,2% and the 90-day mortality 5,2%. Naunheim and colleagues(16) demonstrated in there follow-up article the overall survival advantage for the LVRS group compared to the medical group, with a 5-year risk ratio (RR) for death of 0.86 ($p = 0.02$). The total mortality rate was 0.11 deaths per person-year in the surgical group and 0.13 in the medical group (overall RR, 0.85; $p = 0.02$).

We observed similar survival curves in patients with non-heterogeneously and heterogeneous emphysema, in the

perioperative period and up to 1 year (figure 4). The hazard ratio of patients with heterogeneous vs. non-heterogeneously emphysema was 0.81 (95% confidence interval 0.66 to 0.98, $p = 0.03$) when controlling for potential confounders including age, gender, body mass index, alpha1 anti-trypsin deficiency, baseline FEV1, RV/TLC ratio, diffusing capacity, MRC score, and 6 min walk distance.

Summary

An unacceptable high mortality in a subgroup of NETT patients resulted in an early press release of a widely noted article in the New England Journal of Medicine(11). For the 69 patients who had an FEV1 no more than 20 percent of predicted and either a homogeneous distribution of emphysema or a carbon monoxide diffusing capacity less than 20 percent of predicted, the 30-day mortality rate after surgery was 16 percent, as compared with a rate of 0 percent among 70 medically treated patients ($p < 0.001$). Most experienced centers have excluded such patients from surgery from the beginning of their LVRS program since they expected such a dismal outcome when lung reduction

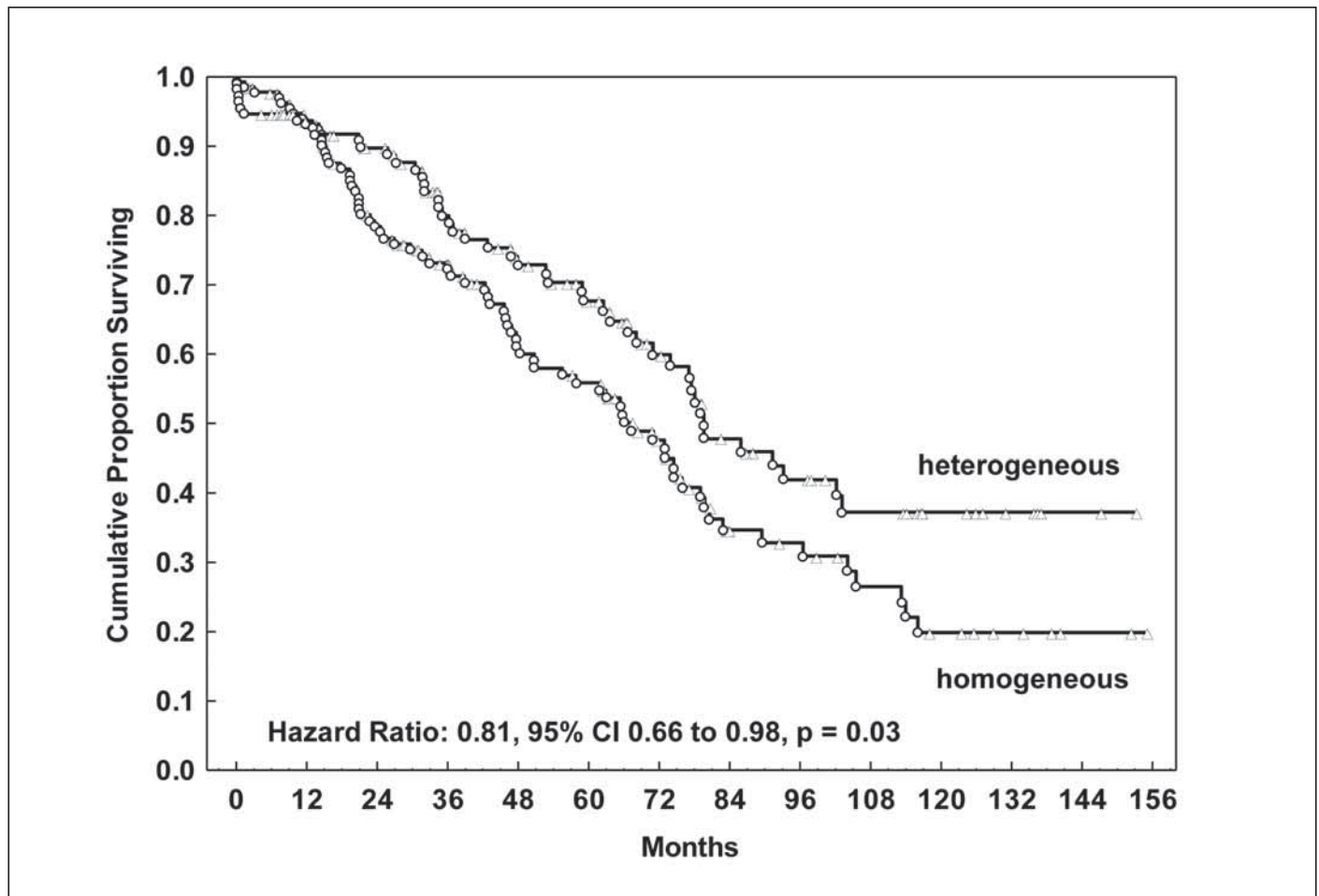


Figure 4. (according to Weder et al. (12)): Survival without lung transplantation according to emphysema morphology

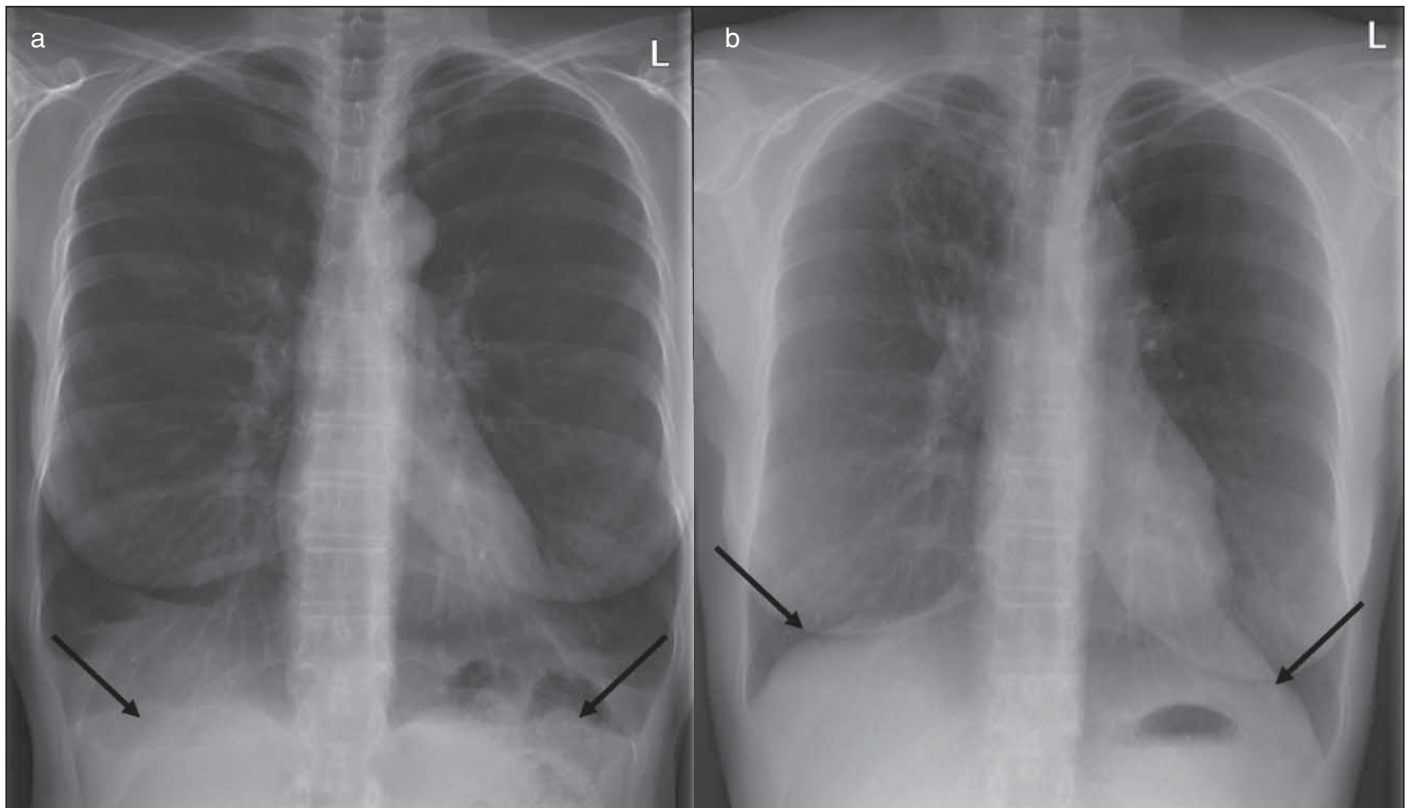


Figure 5. According to Weder et al (25) a) preoperative chest x-ray b) postoperative day

is performed in patients with uniformly destroyed (vanished) lung.

It is obvious that resection of functionless tissue such as in heterogeneous emphysema with or without bullae can be advised to the patient with a relative low risk and a high chance of significant improvement in dyspnea, walking distance, quality of life and lung function. FEV₁ improves in a range of 40-80% from baseline with a peak at 3-6 months and lasts for several years.

The selection of patients with homogeneous emphysema or patients with alpha-1 antitrypsin deficiency has to be done particularly cautious. It is crucial to exclude patients with a very low functional reserve such as with diffusing capacity below 20% predicted or with pulmonary hypertension and with extreme parenchymal loss (vanished lungs) on CT from LVRS. Additionally, co-factors which may potentially interfere with a smooth postoperative course such as previous recurrent infections, extensive scarring of the lungs or previous surgery have to be taken into consideration.

Based on our own experience, we conclude that LVRS can be recommended to selected symptomatic patients with advanced emphysema associated with severe hyperinflation, if the FEV₁ and the diffusing capacity are not below 20% of predicted values, if the CT scan does not show aspects of vanished lungs and the amount of resected lung volume is substantial.

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