

Changes in ventilatory mechanics and diaphragmatic function after lung volume reduction surgery in patients with COPD

Edda M Tschernko, Wilfried Wisser, Theodor Wanke, Maria A Rajek, Meinhard Kritzingner, Heinz Lahrman, Manfred Kontrus, Heike Benditte, Walter Klepetko

Department of
Clinical Pharmacology
and Department of
Cardiothoracic
Anaesthesia and
Intensive Care
E M Tschernko
M A Rajek
M Kritzingner

Department of
Cardiac and Thoracic
Surgery
W Wisser
H Benditte
W Klepetko

Department of
Radiodiagnosics
M Kontrus

General Hospital,
University of Vienna,
Austria

Department of
Pulmonology, Lainz
Hospital, Vienna
T Wanke
H Lahrman

Correspondence to:
Dr E M Tschernko,
Department of Clinical
Pharmacology, General
Hospital, University of
Vienna, Wachringergasse
18-20, A-1090 Vienna,
Austria.

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Abstract

Background – Lung volume reduction (LVR) has recently been used to treat severe emphysema. About 25% of the volume of each lung is removed with this method. Little is known about the mechanism of functional improvement so a study was undertaken to investigate the changes in ventilatory mechanics and diaphragmatic function in eight patients after LVR.

Methods – Measurements of work of breathing (WOB), intrinsic positive end expiratory pressure (PEEPi), dynamic compliance (Cdyn), and arterial carbon dioxide tension (PaCO₂) were performed on the day before surgery and daily for seven days after surgery, as well as one, three, and six months after surgery. All measurements were performed on spontaneously breathing patients, simultaneously assessing oesophageal pressure via an oesophageal balloon catheter and air flow via a tightly adjusted mask. Diaphragmatic function was evaluated by measuring oesophageal and trans-diaphragmatic pressure (Pdi) pre-operatively and at one, three, and six months postoperatively.

Results – Mean forced expiratory volume in one second (FEV₁) was 23 (3.6)% predicted, and all patients were oxygen dependent before the operation. One day after LVR the mean decrease in WOB was 0.93 (95% confidence interval (CI) 0.46 to 1.40) joule/l, the mean decrease in PEEPi was 0.61 (95% CI 0.35 to 0.87) kPa, and the mean increase in Cdyn was 182.5 (95% CI 80.0 to 284.2) ml/kPa. Similar changes were found seven days and six months after surgery. PaCO₂ was higher on the day

after the operation but was significantly reduced six months later. Pdi was increased three and six months after surgery. **Conclusions** – Ventilatory mechanics improved immediately after LVR, probably by decompression of lung tissue and relief of thoracic distension. An improvement in diaphragmatic function three and six months postoperatively also contributes to improved respiratory function after LVR.

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Keywords: emphysema, lung volume reduction, ventilatory mechanics.

There has recently been a resurgence in interest in lung volume reduction (LVR) surgery – that is, resection of peripheral segments of the lung tissue – for severe emphysema.¹ It is based on an old concept, originally proposed by Brantigan in 1957,^{2,3} the principle being to reduce the overall volume of emphysematous lungs in order to restore the mechanical properties of a normal thorax and thereby to improve lung function. The Brantigan procedure never gained widespread acceptance, however, because data were only subjective.

Improvement in forced expiratory volume in one second (FEV₁) of 100% has been observed in patients with favourable anatomical conditions after LVR.¹ Concomitantly, residual volume (RV) and total lung capacity (TLC) are reduced from three times the normal value to only twice the normal value. Little is known, however, about the changes in work of breathing (WOB), intrinsic PEEP (PEEPi), dynamic compliance (Cdyn), and respiratory muscle function so we have investigated these factors in a prospective study in eight patients undergoing LVR.

Methods

PATIENTS

Eight consecutive patients with non-bullous emphysema showing severe hyperinflation were selected for the study (table 1). The study was approved by the local ethics committee and all patients gave written informed consent. Patients were selected on the basis of significant functional limitation despite maximum medical treatment and the presence of a distended thorax. Five patients were initially referred for lung transplantation, two of whom had already

Table 1 Patient details

Patient no.	Sex	Age (years)	Weight (kg)	Height (cm)	Oxygen dependent* (Y/N)	α_1 -antitrypsin deficient (Y/N)
1	F	51	61	163	Y	Y
2	F	49	43	166	Y	N
3	F	67	50	158	Y	N
4	F	51	39	154	Y	N
5	M	57	44	154	Y	N
6	F	44	67	162	Y	N
7	F	48	37	162	Y	N
8	M	56	47	167	Y	N
Mean (SE)		53 (2.5)	49 (3.7)	161 (1.8)	ALL	(2/6)

* Patient was using oxygen regularly; four patients also needed oxygen at rest.

Table 2 Baseline spirometric values

Patient no.	FVC (l (%))	FEV ₁ (l (%))	TLC (l (%))	RV (l (%))	PaO ₂ (kPa)	Paco ₂ (kPa)
1	1.46 (41)	0.56 (19)	6.67 (132)	5.11 (340)	7.32	5.99
2	1.90 (51)	0.53 (17)	7.48 (142)	5.64 (366)	7.98	6.25
3	2.30 (82)	0.88 (40)	7.24 (174)	4.95 (368)	8.91	5.99
4	1.85 (58)	0.96 (37)	6.14 (135)	4.20 (312)	8.65	5.05
5	2.00 (59)	0.56 (20)	6.61 (131)	4.33 (295)	8.91	5.85
6	1.37 (35)	0.52 (16)	6.13 (114)	4.96 (322)	6.78	5.72
7	1.66 (46)	0.45 (15)	7.74 (152)	6.08 (292)	6.25	6.52
8	2.93 (74)	0.58 (16)	7.95 (169)	6.32 (331)	8.11	6.12
Mean (SE)	1.93 (55) (0.18 (5.7))	0.63 (23) (0.07 (3.6))	7.00 (144) (0.25 (7.2))	5.20 (328) (0.27 (10))	7.86 (0.35)	5.99 (0.15)

PaO₂=arterial oxygen tension determined at rest breathing 2–4 litres oxygen; Paco₂=arterial carbon dioxide tension at rest.

been listed for transplantation, and were thought to be suitable candidates for LVR on the basis of severity of disease, extent of hyperinflation, and anatomical suitability. LVR was offered to these patients as an alternative and all of them decided to undergo the procedure.

PATIENT ASSESSMENT

Preoperative assessment included standard pulmonary function testing (table 2), arterial blood gas measurement (table 2), quantitative nuclear lung perfusion and ventilation scan, and catheterisation of the right side of the heart. Catheterisation of the left side of the heart and coronary angiography were performed if significant coronary artery disease was suspected. Anatomical assessment included posteroanterior and lateral chest radiographs taken in inspiration and expiration and a spiral computed tomographic (CT) scan. Patients were selected according to the following criteria: 10%<FEV₁<40% of predicted value, mean pulmonary artery pressure at rest <5.32 kPa (40 mmHg); Paco₂ at rest <6.65 kPa, CT scan showing structural inhomogeneity despite absence of lesions of more than 5 cm in diameter. Patients with ventilation/perfusion mismatch, those with a severe disease of another organ such as coronary artery disease or signs of cerebral ischaemia, and patients showing a lack of co-operation were excluded.

OPERATIVE TECHNIQUE

A standard median sternotomy incision was made and the side with the worse preoperative lung function was done first. The lung was deflated and one lung ventilation directed to the contralateral side. The goal was to remove 20–30% of the volume of each lung, concentrating on the most destroyed parts of the lung. In patients with homogeneous distribution of the emphysematous process (according to HRCT scan findings), portions of all lobes were excised. In order to avoid air leaks bovine pericardial staple lines were used to buttress the staple line as described previously.⁴

ASSESSMENT OF VENTILATORY MECHANICS

Ventilatory mechanics were assessed with a Bicore CP-100 monitor^{5,6} on the day before surgery, daily for seven days after surgery, and

at one, three, and six months after surgery. All measurements were performed while patients were spontaneously breathing room air and sitting in an upright position.

Flow (\dot{V}) was measured by a flow sensor (Varflex) connected to a tightly adjusted face mask. The fit of the face mask was evaluated by comparing inspiratory and expiratory volumes, a difference of less than 5% being regarded as evidence that the mask was sufficiently tight fitting. Tidal volume was obtained by numerical integration of the flow signal. Airway pressure (Paw) was measured through a catheter attached to the flow sensor and oesophageal pressure (Poes) by a nasogastric tube incorporating an oesophageal balloon. The correct position of the balloon was detected using the occlusion test.⁷ The oesophageal balloon and the flow sensor were connected to a portable monitor (CP-100 Cardiopulmonary Monitor, Bicore Monitoring System Inc, Irvine, California, USA), providing a real-time display of \dot{V} , volume, Paw, and Poes tracings, and loops of Poes/ \dot{V} and Paw/ \dot{V} , and the monitor was connected to a printer. The accuracy of the measurements provided by this monitoring system is satisfactory.⁸

Minute ventilation (V_E) and breathing pattern (tidal volume, respiratory frequency, duration of inspiration and expiration, and the duty cycle) were analysed from the flow signal, and patient work of breathing (WOB) values were provided directly by the Bicore system.⁹ The WOB was defined as the amount of force required to cause a volume change across the opposing forces of the airways (frictional), lung (elastic), and chest wall. Simultaneous measurement of airflow and transpulmonary pressure using the oesophageal balloon and volume measured via the flow transducer during spontaneous respiration defines parameters required to determine the WOB. The changes in pressure and volume can be analysed graphically with the Bicore CP-100 monitor, and the area enclosed within a volume-pressure loop has the units of mechanical work.¹⁰

PEEPi was estimated using the Bicore monitor. In a spontaneously breathing patient an oesophageal balloon catheter system was used to measure PEEPi during unoccluded breathing. This was achieved by calculating the negative deflection in Poes from the start of inspiratory effort to the onset of inspiratory \dot{V} .^{11,12}

Arterial blood gas tensions were measured on the same days as the mechanical measurements.

TRANSDIAPHRAGMATIC PRESSURE MEASUREMENTS

Oesophageal and gastric pressures (Pga) were measured with a water perfused system as described previously.¹³ Transdiaphragmatic pressure (Pdi) was calculated by subtracting Poes from Pga preoperatively and at one, three, and six months postoperatively.

SPIROMETRY AND PLETHYSMOGRAPHY

Spirometric and plethysmographic measurements were made in all patients before sur-

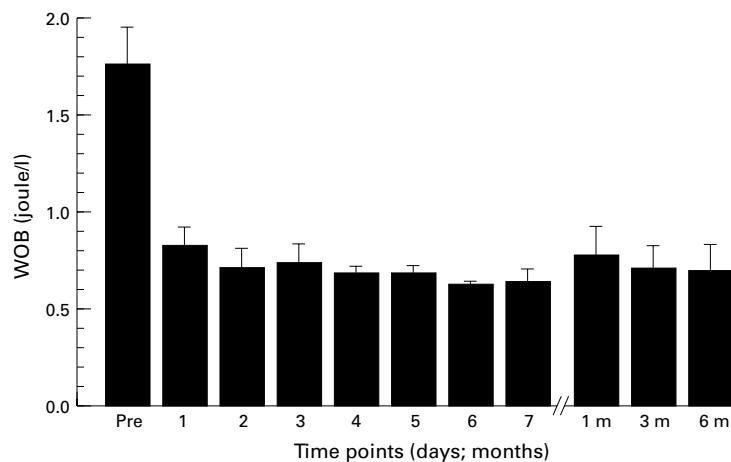


Figure 1 Changes in work of breathing (WOB) at various time points after lung volume reduction (LVR) surgery.

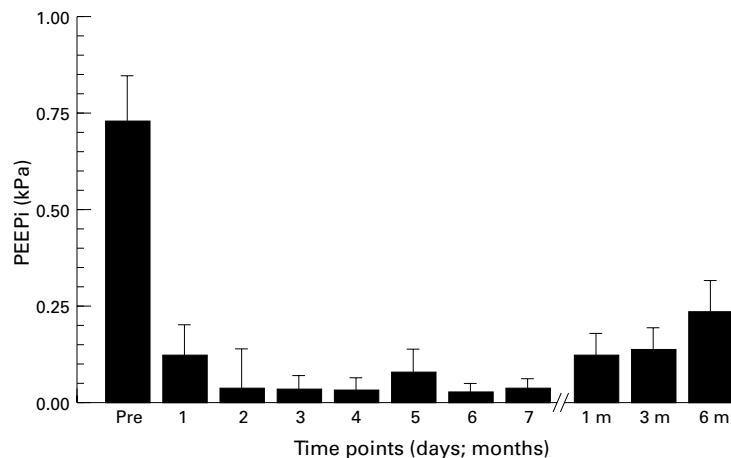


Figure 2 Changes in intrinsic positive end expiratory pressure (PEEPi) at various time points after lung volume reduction (LVR) surgery.

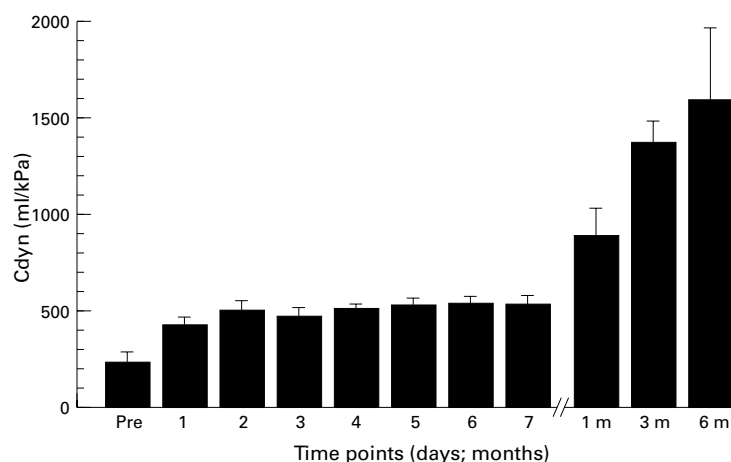


Figure 3 Changes in dynamic compliance (Cdyn) in ml/kPa at various time points after lung volume reduction (LVR) surgery.

ger and at one, three, and six months postoperatively. Spirometric tests were performed using an open system with integration of the flow system, and whole body plethysmography was carried out by the constant

volume method (Jaeger, Wuerzburg, Germany). The lung function parameters were compared with the reference values given by the European Community for Steel and Coal.¹⁴

STATISTICAL ANALYSIS

The paired Student's *t* test was used to test for differences in WOB, PEEPi, Cdyn, and Paco_2 before and after surgery by comparing the pre-operative values with those one day after the operation. Thereafter, we tested whether the differences were sustained at seven days and at six months after surgery. The results from this analysis are presented as mean differences from baseline with 95% confidence intervals and *p* values. In addition, changes from baseline which occurred on the first postoperative day were given as a percentage decrease from baseline. For this purpose baseline was regarded as 100%. The paired Student's *t* test was used to test for significant differences in spirometric values, Poes, and Pdi at one, three, and six months after surgery compared with the pre-operative value. Values are expressed as mean (SE) and a *p* value of <0.05 was considered significant.

Results

Work of breathing improved significantly ($p < 0.001$) after surgery from a preoperative value of 1.76 (0.19) joule/l to 0.93 (95% CI 0.46 to 1.40) joule/l 24 hours after surgery ($p < 0.001$), which represents a decrease of 52.8 (10.8)%. Seven days after surgery WOB decreased 1.1 (95% CI 0.7 to 1.5) joule/l ($p < 0.001$) and at six months it had decreased 1.1 (95% CI 0.7 to 1.5) joule/l ($p < 0.001$; fig 1).

PEEPi, a typical sign of air trapping, was present in all patients preoperatively with a mean value of 0.73 (0.12) kPa (fig 2), and decreased 0.61 (95% CI 0.35 to 0.87) kPa ($p < 0.001$), a decrease of 83.6 (16.2)%, on day 1 after surgery. On day 7 after surgery the mean difference in PEEPi was 0.69 (95% CI 0.38 to 0.99) kPa ($p < 0.001$) and six months after surgery it was still 0.49 (95% CI 0.16 to 0.82) kPa ($p < 0.005$), which represents a decrease in PEEPi of 67.1 (19.2)% ($p < 0.005$).

Dynamic compliance (Cdyn) averaged 234.7 (40.8) ml/kPa before surgery (fig 3) and during the postoperative course it increased significantly ($p < 0.001$). On the first postoperative day Cdyn increased 182.5 (95% CI 80.8 to 284.2) ml/kPa ($p < 0.01$), which represents an increase of 75.5 (18.8)% ($p < 0.01$). The mean difference in Cdyn on day 7 after surgery was 293.7 (95% CI 193.2 to 394.2) ml/kPa ($p < 0.001$) and six months after surgery it was 1364.5 (95% CI 553.8 to 2037.8) ml/kPa ($p < 0.0001$).

In addition, we found a significant reduction in airway resistance; the mean difference from the baseline value of 18.0 (2.0) cm H_2O /l/s was 8.9 (95% CI 4.9 to 12.9) cm H_2O /l/s seven days after the operation ($p < 0.01$) and 8.6 (95% 5.1 to 12.1) cm H_2O /l/s ($p < 0.01$) six months after LVR.

Table 3 Mean (SE) transdiaphragmatic (Pdi) and oesophageal (Poes) pressure

	Pdi (kPa)	Poes (kPa)
Preoperatively	6.44 (0.45)	5.32 (0.36)
1 month postoperative	7.66 (0.76)	5.53 (0.6)
3 months postoperative	9.02 (1.32)*	6.81 (0.54)*
6 months postoperative	8.70 (0.76)*	7.08 (0.38)*

*p<0.05.

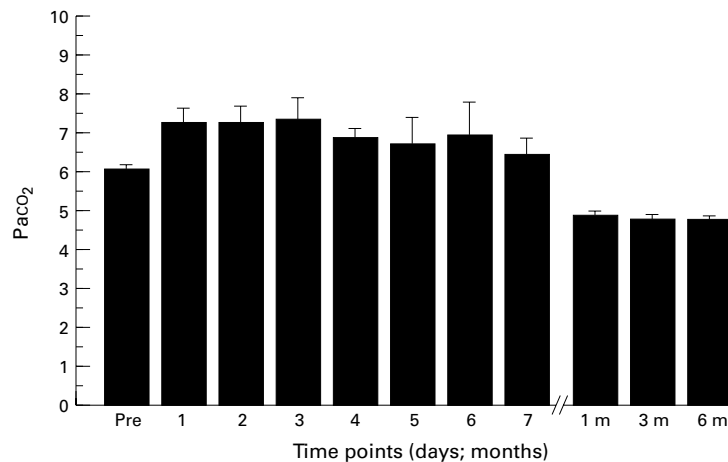


Figure 4 Changes in arterial carbon dioxide tension (PaCO₂) in kPa at various time points after lung volume reduction (LVR) surgery.

Table 4 Mean (SE) preoperative and postoperative spirometric values

	Preoperative	One month after surgery	Three months after surgery	Six months after surgery
FEV ₁ (l)	0.63 (0.1)	1.05 (0.19)*	1.23 (0.32)*	1.10 (0.24)*
FEV ₁ (%)	23 (3.6)	38.2 (7.1)*	45.1 (11.9)*	40.0 (8.6)*
RV (l)	5.20 (0.3)	3.48 (0.21)*	3.69 (0.18)*	3.48 (0.33)*
RV (%)	328 (10)	220.0 (13)*	232.9 (11.4)*	219.8 (21.1)*
FVC (l)	1.93 (0.18)	2.10 (0.07)*	2.88 (0.37)*	2.86 (0.30)*
FVC (%)	55.0 (5.7)	60.0 (2.1)*	82.0 (10.7)*	81.4 (8.5)*
TLC (l)	7.00 (0.25)	5.39 (0.27)*	6.09 (0.20)*	5.95 (0.39)*
TLC (%)	144 (7.2)	110.9 (5.7)*	125.3 (4.1)*	122.4 (8.0)*

FEV₁=forced expiratory volume in one second; FVC=forced vital capacity; RV=residual volume; TLC=total lung capacity.

*p<0.05 compared with baseline.

A significant difference ($p<0.05$) was noted in Pdi and Poes three and six months after surgery compared with preoperative values, but no significant improvement was found at one month after surgery (table 3).

Minute ventilation (VE) showed comparable values during the whole observation period: 8.4 (0.7) l/min before surgery, 7.6 (0.6) l/min on the first day after surgery, and 9.0 (0.6) l/min on the seventh postoperative day. Six months after surgery the VE was 9.2 (0.6) l/min. Similarly, we found no significant changes in respiratory frequency (20 (1) breaths/min before surgery, 22 (1.3) breaths/min one day after surgery, 21 (2) seven days after the operation, and 18 (2) breaths/min six months after surgery) or duty cycle (Ti/Ttot) 0.39 (0.01) before surgery compared with 0.36 (0.02) on day 1 after surgery, 0.41 (0.01) seven days after surgery, and 0.42 (0.02) six months after LVR surgery.

Paco₂ was significantly ($p<0.05$) raised on the first postoperative day (fig 4) with a mean (95% CI) increase of 1.19 (0.48 to 1.90) kPa,

but showed no significant difference compared with the preoperative value by day 7 ($p>0.05$) after LVR. Six months after surgery Paco₂ showed a mean decrease of 1.29 (95% CI 1.10 to 1.48) kPa ($p<0.05$) compared with the baseline value of 6.06 (0.13) kPa, which represents a decrease of 21.3 (1.3) %.

Spirometric tests showed significant ($p<0.05$) increases in FEV₁, VC, and significant decreases in RV and TLC one, three, and six months postoperatively (table 4).

Discussion

We found an immediate and sustained reduction in WOB and PEEP_i, as well as an increase in C_{dyn}, Pdi, and Poes after LVR.

In patients suffering from chronic obstructive pulmonary disease (COPD) lung emptying is slowed and expiration is interrupted by the next inspiratory effort before the patient has exhaled to static relaxation volume.¹⁵ This dynamic hyperinflation has a number of adverse effects:¹⁶ (1) the respiratory muscles operate at an unfavourable position on their length-tension curve; (2) elastic recoil of the chest wall is directed inwards, causing an extra elastic load; and (3) breathing takes place at the upper less compliant portion of the pressure-volume curve of the lung. These factors cause a decrease in the efficiency of force generation by the respiratory muscles and an increase in the work of breathing.

Preoperatively, WOB was markedly increased compared with healthy normal subjects,¹⁷ but after LVR it was significantly reduced as early as 24 hours after surgery (fig 1). There are several possible explanations for this reduction. Work per litre closely reflects abnormalities in pulmonary mechanics such as decreased compliance.¹⁸ In healthy subjects, during quiet breathing, expiration is passive and the WOB is usually performed entirely by the inspiratory muscles. About 50% of inspiratory work is dissipated as heat in overcoming resistive forces and the remaining 50% is stored as potential energy in the deformed tissues of the lung and chest wall and is used during expiration.¹⁹ In contrast, in patients with asthma expiratory work constitutes 57% of the total work per breath.^{20,21} One of the reasons for this phenomenon is the high resistance of the airways due to airway collapse caused by hyperinflated surrounding tissue and increased compliance of the airways.²² Hyperinflated lung tissue is removed by LVR and extramural pressure on the airways is diminished. This should lead to a reduction in airways resistance and reduced WOB.

Changes in minute ventilation or respiratory pattern can contribute to changes in WOB and PEEP_i. As no significant change in minute ventilation and respiratory pattern were observed compared with preoperative values, a change in respiratory pattern is not responsible for the reduction in WOB or PEEP_i observed postoperatively.

LVR also reduces thoracic distension which leads to increased inspiratory work performed by the inspiratory muscles against the elastic

recoil of the lungs and the chest wall. The reduction in thoracic distension might therefore be another explanation for the observed reduction in WOB.

PEEPi was present in all our patients before the operation. In spontaneously breathing patients PEEPi might be overestimated because of activity of the abdominal muscles during expiration, which cannot be completely ruled out by our data²³ as gastric pressure was not assessed during the early postoperative period. Nevertheless, a sudden and sustained change in expiratory muscle activity, which we think is very unlikely, would be necessary to explain our results. On the other hand, underestimation of PEEPi can be caused by the measuring technique as PEEPi determined in spontaneously breathing patients represents the minimum PEEPi. It is the minimum PEEPi to be counterbalanced in order to initiate inspiratory flow,¹² whereas PEEPi determined with the occlusion technique represents average PEEPi.¹² The fact that we determined minimum PEEPi does not diminish the value of our results as we would have underestimated PEEPi in all measurements.

PEEPi is present in patients with emphysema and is caused by air trapping, and dynamic pulmonary hyperinflation is caused by collapse of airways during expiration and an increase in airway resistance.²⁴ This airway collapse is said to be caused by collapse of airways and compression of intact lung tissue by surrounding hyperinflated lung tissue.²⁴ Airways resistance is usually increased after thoracic surgery even without resection of lung tissue,²⁵ and resection of lung tissue with normal ventilatory function adds to the post-thoracotomy increase in airways resistance.²⁶ In addition, it is unlikely that raised airways resistance due to bronchospasm is cured by surgery. The only reasonable explanation for the early reduction in airways resistance, PEEPi, and WOB determined during comparable minute ventilation therefore seems to be decompression of airways, which leads to an increase in the total bronchial diameter and thus to a reduction in airways resistance causing a reduction in dynamic pulmonary hyperinflation closely related to PEEPi,²⁷ and overall to a decrease in total WOB.²⁸

As PEEPi was markedly reduced immediately after surgery in our patients we conclude that removal of destroyed and hyperinflated lung tissue is responsible for re-opening of airways and leads to a rapid decrease in PEEPi. With the technique we used to assess air trapping (determination of minimal PEEPi) we assessed the parts of the lung where airflow occurs first. We therefore conclude that lung tissue with better mechanical properties would show a significant reduction in PEEPi after surgery. The fact that we found a reduction in the minimal PEEPi therefore confirms our theory that there must have been a beneficial effect on "good lung", probably due to decompression of lung tissue. This reduction in PEEPi leads to a reduction in WOB. The observation that PEEPi increases again six months after LVR can be explained by the

progressive nature of emphysema. LVR is probably not a cure for end stage emphysema but can lead to a transient reduction in hyperinflation.

Cdyn, which was markedly reduced in our patients compared with healthy subjects,²⁹ was improved significantly on the day after surgery ($p < 0.01$). This finding was surprising as we had expected Cdyn to be reduced immediately after the operation due to surgical trauma of the lung tissue. Decompression of lung tissue seems to be responsible for this rapid and sustained rise in Cdyn postoperatively. During the postoperative observation period Cdyn rose further, probably because of tissue healing. The values determined three and six months postoperatively are still in the normal range.²⁹

Higher values for Pdi and Poes were observed three and six months after surgery whereas no difference was noted in the first postoperative measurement made one month after surgery, probably because the patients were still recovering from the operation and it is well known that diaphragmatic function is impaired after thoracotomy and upper abdominal surgery due to reflex changes and postoperative pain.³⁰ Transdiaphragmatic pressures determined three and six months after LVR are therefore probably more representative of diaphragmatic function. The improvement in diaphragmatic function three and six months after surgery agrees well with the findings of other studies that have examined the relation of lung volume to diaphragmatic force generation in patients with COPD after lung transplantation and healthy volunteers.³¹ Improved respiratory muscle function after LVR seems to be one of the factors contributing to functional improvement after LVR. The improvement in spirometric values (table 4) in our study was similar to that in other studies.¹

We conclude that WOB is dramatically reduced after LVR and the reduction is sustained due to improvement in lung compliance and reduction in PEEPi. This reduction is accomplished by removal of hyperinflated lung tissue and thus decompression of the remaining tissue as well as a reduction in thoracic distension. Respiratory muscle function is also improved after LVR and results in functional improvement. Lung volume reduction seems to be an attractive alternative to transplantation or might be used as an interim measure.³²⁻³⁴

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