Eur Respir J, 1996, 9, 1779–1784
DOI: 10.1183/09031936.96.09091779
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European Respiratory Journal
ISSN 0903 - 1936

Effect of surgical lung volume reduction on respiratory muscle function in pulmonary emphysema

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ABSTRACT: Lung volume reduction surgery (LVRS) in patients with severe lung emphysema restores the thoracic configuration to a more normal functional capacity. The aim of this study was to investigate whether reduction in intrathoracic volume by LVRS improves the inspiratory muscle force generation of the respiratory pump.

Pulmonary function tests, maximal inspiratory mouth pressure (MIP), sniff nasal inspiratory pressure (SNIP), sniff transdiaphragmatic pressure (P_{di}), and inspiratory mouth occlusion pressure ($P_{0.1}$) were measured in 17 emphysematous patients (mean (±SEM) age 53±2 yrs) before and 1 month after LVRS.

The mean value of forced expiratory volume in one second (FEV_1) increased (0.82±0.07 *vs* 1.12±0.08 L; p<0.0001), whilst there was a decrease (p<0.0001) in residual volume (RV) (337±31 *vs* 250±21 % of predicted), functional residual capacity (FRC) (210±9 *vs* 159±9% pred), and total lung capacity (TLC) (138±6 *vs* 110±5% pred). The mean value of MIP increased by 52% from 4.8±0.4 to 7.3±0.6 kPa (p<0.001), the mean value of SNIP increased by 66% from 3.9±0.4 to 6.5±0.5 kPa (p<0.001), and the mean value of P_{di} increased by 28% from 6.0±0.6 to 7.7±0.8 kPa (p<0.05) after LVRS. $P_{0.1}$ decreased on average by 24% from 0.46±0.03 to 0.35±0.02 kPa after LVRS. No significant correlations were found between inspiratory muscle (MIP, SNIP, P_{di}) and respiratory drive ($P_{0.1}$) indices, lung function data, 6 min walk distance, or dyspnoea score.

In conclusion, the observed clinical improvement of patients with severe emphysema after lung volume reduction surgery results, in part, from an increased ability of the inspiratory muscles to generate force, which is paralleled by a significant decrease in central respiratory drive.

Eur Respir J., 1996, 9, 1779–1784.

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Keywords: Emphysema
lung volume reduction
pulmonary function
respiratory muscle function

Received: February 27 1996
Accepted after revision June 11 1996

Severe emphysema of the lung results in detrimental abnormalities in ventilatory mechanics, such as increased airway resistance, diaphragmatic inefficiency, and dynamic hyperinflation [1–4]. Hyperinflation of the lung impairs the efficiency of the muscles of the chest wall and diaphragm by placing them at mechanical disadvantage [4]. The relationship between mechanical abnormalities of rib cage and diaphragm and respiratory muscle function has been studied in animals [5], and in patients with pulmonary emphysema [6–9]. The adverse effects of hyperinflation on diaphragmatic function include foreshortening of diaphragm precontraction length [1, 3, 6, 10, 11], decreased area of apposition of the costal part with the chest wall [7, 8], increased radius of curvature [1], impaired blood flow and decreased insertional action on the rib cage [12], and increased internal elastic inspiratory load [3, 4].

The most widely-applied method of determining global inspiratory strength is the measurement of mouth pressure during maximal inspiratory efforts (MIP), which has been shown to be decreased in severe emphysema [9]. Some investigators have determined the sniff nasal inspiratory pressure (SNIP) as a measure of inspiratory muscle strength; a manoeuvre which is easier to perform for most subjects [13–16]. SNIP values were lower in patients with emphysema than in normals, but underestimated strength compared to MIP [16, 17]. Others have measured the transdiaphragmatic pressure (P_{di}) either during voluntary static or sniff contraction or phrenic nerve stimulation [18–20], to estimate diaphragmatic strength in patients with emphysema more specifically. The reported studies clearly indicate that the transdiaphragmatic pressure is reduced in emphysema. However, the functioning of the diaphragm at equal lung volumes as in normals was found to be similar, suggesting that muscle strength is preserved in emphysema [2].

Respiratory centre drive has also been noted to be increased in chronic obstructive pulmonary disease (COPD) patients with severe hyperinflation of the lung [21–24]. One of the measures of respiratory centre drive, the mouth occlusion pressure ($P_{0.1}$), is consistently elevated in severe COPD. This increase in respiratory drive may, at least in part, be explained by the increased resistance to airflow and decreased dynamic pulmonary compliance in patients with COPD [22, 23].

Recently, COOPER and co-workers [25] demonstrated that the newly resurrected technique of lung volume reduction surgery (LVRS) can be of significant clinical value

for selected patients with severe emphysema. A series of 100 patients [26] showed significant improvement of lung function, gas exchange, 6 min walking distance, dyspnoea, and quality of life 3 months after bilateral surgical lung reduction. Since the mechanical efficiency of the rib cage and diaphragm is sensitive to changes in lung volume [1, 3, 9, 10, 19], LVRS may improve the performance of the respiratory muscles and, thus, reduce dyspnoea.

Our hypothesis was that LVRS beneficially affects the respiratory pump. This hypothesis was tested by measuring indices of global inspiratory muscle force generation, diaphragmatic muscle strength, and respiratory drive in patients with severe emphysema before and 1 month after LVRS.

Methods

Patients

Seventeen patients (2 females and 15 males; mean±SEM age 53±2 yrs; age range 38–63 yrs) with severe emphysema and dyspnoea on minimal exertion participated in this study. The diagnosis was based on physical examination, chest radiograph, computed tomography (CT) scan, lung perfusion scan, and pulmonary function data. None of the patients had a history of asthma and their airflow obstruction was irreversible. Patients with an arterial carbon dioxide tension (P_{a,CO_2}) >6 kPa (45 mmHg) or evidence of left ventricular failure were excluded. One patient had a history of treated pulmonary tuberculosis. Six patients had severe $alpha_1$-antitrypsin deficiency. Three of the $alpha_1$-antitrypsin deficient patients were lifelong nonsmokers, and the other 11 patients had stopped smoking at least 3 months before surgery. Six patients had not been chronically treated with corticosteroids and 12 patients were taking less than 20 mg prednisolone orally per day. Three patients underwent a bilateral LVRS *via* median sternotomy (n=2) or bilateral thoracotomy, nine a LVRS of their right lung and five of their left lung *via* thoracotomies. All patients gave their written informed consent.

Physiological assessment included: dyspnoea score, 6 min walk test, pulmonary function tests, and arterial blood gas analysis. All measurements were performed during the week before surgery and approximately 1 month after surgery. At the same time intervals, measurements of respiratory muscle strength and respiratory drive were performed as described below.

Quantification of dyspnoea

A modified Medical Research Council (MRC) Dyspnoea Scale was used to quantify the degree of dyspnoea [25, 27].

Six minute walk test

A 6 min walk test was performed according to standard procedures [25, 28]. All tests were conducted in a straight 18 m corridor, with the same trained supervisor giving encouragement to the subject to cover as much ground as possible in 6 min. The distance walked was measured.

Lung function testing

Lung volumes were measured by body plethysmography (Bodybox; Fenyves and Gut, Bodelshausen, Germany) and included inspiratory vital capacity (IVC), forced expiratory volume in one second (FEV_1), FEV_1/FVC, functional residual capacity (FRC), residual volume (RV), total lung capacity (TLC), and airway resistance (R_{aw}). The data were expressed as percentage of predicted in each patient. Arterial blood was sampled from the radial artery while patients were breathing room air at rest, and blood gas values were measured using an automatic blood gas analyser (AVL, Bad Homburg, Germany).

Maximum inspiratory pressure

MIP was measured during forceful efforts against a closed mouth valve starting at RV, as described by BLACK and HYATT [29]. The tests were performed in the sitting position with a noseclip in place. The reported values represent the best effort of six trials.

Sniff nasal pressure

The SNIP was measured with a pressure transducer connected to a plug in one nostril during a sniff performed through the contralateral nostril, as described by HERITIER *et al*. [13], using a commercially available system kindly provided by Zan (Zan 400 Sniff; Waldfenster, Germany). Criteria for a suitable sniff were a regular upstroke and sharp peak and a total sniff duration of less than 0.5 s. The tests were performed in the sitting position. The reported values represent the best effort of six trials.

Transdiaphragmatic pressure

The P_{di} was measured with two commercially available 10 cm balloon catheters (PK Morgan, Rainham, UK) each coupled to a pressure transducer. The tip of the gastric balloon to measure gastric pressure (P_{ga}), containing 2–3 mL of air, was positioned 55–60 cm from the nares. The oesophageal balloon to measure oesophageal pressure (P_{oes}) was positioned in the middle third of the oesophagus and contained 0.5 mL of air. P_{di} was derived electronically (Zan 400 P_{di}; Waldfenster, Germany) according to the equation: $P_{di}=P_{ga}-P_{oes}$, and P_{di} at resting end-expiration was used as the zero reference point. All subjects were studied in the sitting position and were asked to perform at least six short sharp sniffs as hard as possible with more than two quiet breaths between each sniff [15]. P_{di} recordings were displayed in front of the patient for visual feedback to encourage maximal efforts. The highest value recorded was used for further analysis.

Mouth occlusion pressure

Mouth occlusion pressure 0.1 s after the beginning of inspiration ($P_{0.1}$) was measured in the sitting position

Table 1. – Pulmonary function data of the 17 study patients with severe emphysema 1 week before and 1 month after lung volume reduction (LVRS) surgery

	Before LVRS	After LVRS	p-value
Dyspnoea score n	3.4±0.2	1.6±0.2	<0.0001
6 min walk m	229±18	405±23	<0.0001
IVC % pred	54±3	57±3	NS
RV % pred	337±31	250±21	<0.0001
FRC % pred	210±9	159±9	<0.0001
TLC % pred	138±6	110±5	<0.0001
FEV_1 % pred	31±2	41±2	<0.0001
FEV_1 L	0.8±0.07	1.1±0.08	<0.0001
FEV_1/IVC	43±3	57±3	<0.0001
R_{aw} kPa·L^{-1}·s	0.57±0.07	0.44±0.05	<0.001
P_{a,O_2} mmHg	64±2	70±3	<0.001
P_{a,CO_2} mmHg	40±2	37±1	NS

IVC: inspiratory vital capacity; RV: residual volume; FRC: functional residual capacity; TLC: total lung capacity; FEV_1: forced expiratory volume in one second; R_{aw}: airway resistance; % pred: percentage of predicted value; P_{a,O_2}: arterial oxygen tension; P_{a,CO_2}: arterial carbon dioxide tension; NS: non-significant. 1 mmHg=0.133 kPa.

with a commercially available recorder (Andos, Hamburg, Germany) as described previously [22, 23]. Occlusion pressure was determined from the mean of six measurements.

Statistical analysis

All data are given as mean±SEM. Statistical significance was determined by the paired t-test. Correlation was calculated using the Spearman correlation coefficient. A p-value of less than 0.05 was considered significant.

Results

The results of the dyspnoea score, 6 min walk test, lung function data, and blood gas analysis before and after LVRS are summarized in table 1.

The results for MIP, SNIP, and P_{di} are shown in figure 1. The MIP measurements were reproducible, with a mean coefficient of variation for values within the same subject of less than 12%. The amplitude of MIP increased in 16 of the 17 patients and on average by 52% from 4.8±0.4 before to 7.3±0.6 kPa after LVRS (p<0.0001) (fig. 1a). There was a positive correlation (r=0.86) between MIP before and after surgery. The difference of MIP before and after surgery did not correlate with the improvement of dyspnoea score, 6 min walking distance, lung function and blood gas data.

The coefficient of variation for SNIP values within the same subject was less than 17%. SNIP values measured before and after lung volume reduction increased in all study patients, on average by 66% from 3.9±0.4 before to 6.5±0.5 kPa after LVRS (p<0.0001) (fig. 1b). There was a positive correlation (r=0.78) between SNIP values before and after surgery, but no correlation was found between the difference of SNIP values and the improvement of dyspnoea score, 6 min walking distance, lung function or blood gas data.

The coefficient of variation for P_{di} values within the same subject was less satisfactory (28%). P_{di} values before and after LVRS were available in only 12 of the 17 patients. There was a clinically important improvement of P_{di} in 10 of 12 patients. The average pressure increased by 28% from 6.0±0.6 before to 7.7±0.8 kPa after LVRS (p<0.01) (fig. 1c). There was a positive correlation (r=0.81) between P_{di} values before and after surgery. The difference in P_{di} before and after surgery did not correlate with improvement in 6 min walking distance and dyspnoea score, nor with lung function or blood gas data.

Figure 2 shows the effect of LVRS on $P_{0.1}$. There was a clinically important decrease of $P_{0.1}$ in 15 of the 17 patients after LVRS. $P_{0.1}$ decreased on average by 24% from 0.46±0.03 before to 0.35±0.02 kPa after surgery (p<0.0001). Although significantly reduced after surgery, $P_{0.1}$ remained above the upper limit of normal (0.25 kPa) in 13 of the 17 subjects. There was a significant correlation (r=0.69) between the $P_{0.1}$ values before and after LVRS. No correlation was found between the change of $P_{0.1}$ and the improvement in 6 min walking distance and dyspnoea score, nor between lung function or blood gas data.

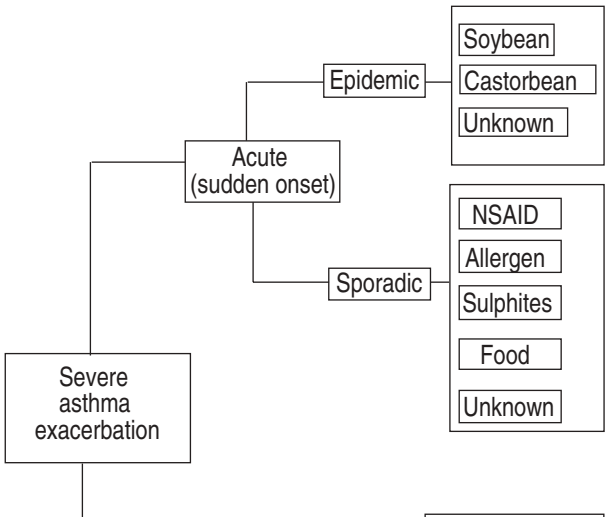

Fig. 1. – Various parameters of respiratory muscle performance 1 week before and 1 month after lung volume reduction surgery (LVRS). a) Changes in maximal inspiratory mouth pressure (MIP); b) changes in sniff nasal inspiratory pressure (SNIP); c) changes in transdiaphragmatic pressure (P_{di}). Mean values±SEM are shown.

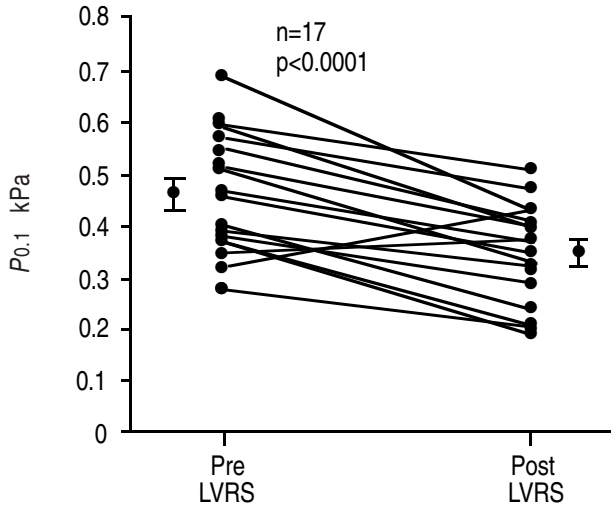

Fig. 2. – Mouth occlusion pressure ($P_{0.1}$) 1 week before and 1 month after lung volume reduction surgery (LVRS). Mean values±SEM are shown.

Discussion

This study demonstrates that in patients with severe emphysema the impaired respiratory muscle performance can be improved by LVRS. Moreover, the improved respiratory muscle performance is associated with a significant reduction in the ventilatory drive as measured by the $P_{0.1}$.

The loss of pulmonary parenchyma in emphysema decreases the elastic recoil of the lung [2, 3, 10, 19, 30, 31]. This results in an abnormally low expiratory flow rate, increased expiratory airway resistance, and a greater lung volume at any given transpulmonary pressure [19, 30, 31]. This leads to increased TLC, FRC and RV. Dynamic air-trapping further increases FRC. The hyperinflation impairs the function of the inspiratory muscles due to shorter operative fibre length and flattening of the diaphragm [9, 19, 20, 29, 30].

LVRS has been shown to increase elastic recoil, perhaps by selectively removing highly compliant regions or by tethering regional and more remote lung parenchyma [25, 31]. The observed improvement in MIP after LVRS is reliable, because measurements were satisfactorily reproducible and patients were carefully coached to perform their best efforts. The most likely explanation for the observed improvement in MIP is an increase in elastic recoil, leading in turn to improved resting muscle length and diaphragm geometry. This is consistent with published data from SCIURBA *et al*. [31], demonstrating an increase of maximal transpulmonary pressure as indicator of elastic recoil from 9.5 to 12.1 cmH_2O after LVRS.

MIP is the most widely-used noninvasive test of global inspiratory muscle performance in clinical practice [9, 29]. However, MEAD *et al*. [32] have reported that the antagonistic contraction of the abdominal muscles may limit the development of high inspiratory mouth pressures in untrained subjects, and many older patients have particular difficulties with this static technique. LAROCHE *et al*. [14] showed that inspiratory muscle strength is better reflected by the oesophageal pressure changes during a maximal sniff than by the static mouth pressure after a forceful inspiratory effort. According to HERITIER *et al*. [13], the same information can be obtained by measuring SNIP in one occluded nostril whilst sniffing through the contralateral nostril. SNIP has the advantage of being a noninvasive measure involving a more natural manoeuvre for most subjects. Alterations of lung mechanics are known to reduce the transmission of alveolar pressure to the upper airways [16], as would functional obstruction of the upper airways. However, in the present study population, consisting of patients with severe emphysema, the SNIP was satisfactorily reproducible with a coefficient of variation within the same subject of less than 17%. LVRS resulted in a mean increase of SNIP from 3.9 to 6.5 kPa, which was on average higher than the observed increase of MIP. ULDRY and FITTING [17] observed that SNIP underestimates strength compared to MIP, because it is a shorter manoeuvre. In COPD, transmission of the pressure response from oesophagus to mouth and nose takes longer than in individuals with normal airway resistance and conductance. Therefore, the more pronounced increase in SNIP after LVRS may be partially explained by improved pressure transmission, and not only by improved respiratory muscle strength. Nevertheless, the present study demonstrates that SNIP is a potentially useful noninvasive measurement to monitor respiratory muscle strength after LVRS, especially in patients with difficulties in reproducing static manoeuvres.

P_{di} has been shown to decrease with increasing lung volume in control subjects as well as patients with COPD [18, 20]. In the present study population of patients with severe emphysema, the amplitude of the P_{di} varied widely among subjects, but was significantly reduced compared with our laboratory and published reference values [15, 18, 20]. The sniff technique [15] had the advantage of ease of performance for the patients. In spite of the broad range of P_{di} values after LVRS, the increase in P_{di} after LVRS was significant. However, P_{di} values remained in most patients at levels much lower than those in normal subjects. The persistent abnormality in P_{di} is consistent with the incomplete restoration of the curvature of the flattened diaphragm after LVRS. It is important to emphasize that the noninvasive tests, MIP (+52%) and SNIP (+66%), demonstrated a better improvement of respiratory muscle performance than did P_{di} (+28%), probably because MIP and SNIP reflect the combined strength of all respiratory muscles (rib cage, diaphragm, and abdominal wall). From a clinical perspective, the present data indicate that most changes in respiratory muscle function after LVRS can be estimated by the simple measurement of MIP and SNIP. Since the determination of P_{di} does not substantially contribute to the clinical management, the technical difficulties preclude the routine use of this invasive measurement to monitor patients after LVRS.

The $P_{0.1}$ has been found to be useful in assessing respiratory centre and neuromuscular coupling in patients with COPD [22–24]. If $P_{0.1}$ is considered an index of central inspiratory drive, the results from the present study are in agreement with earlier studies, demonstrating that patients with severe emphysema have a high respiratory centre output, despite certain mechanical disadvantages of the inspiratory muscles resulting from the hyperinflated lung [23, 24]. In 15 of the 17 patients a significant decrease of $P_{0.1}$ was observed after LVRS. These

improvements may be partially explained by the observed decrease in airway resistance and residual volume after LVRS, since occlusion pressure response to flow resistive loading is increased in COPD patients [16, 21]. In particular, flow resistive loading is increased in severe emphysema as a result of reduced elastic recoil and increased airway resistance.

There are two other possible explanations for the decrease of $P_{0.1}$ after LVRS. Firstly, $P_{0.1}$ might return towards normal because of a significant reduction in the work of breathing and of intrinsic positive end-expiratory pressure (PEEP), as hypothesized by COOPER and co-workers [26]. Secondly, improvement of oxygenation is associated with a decrease in respiratory centre drive as measured by $P_{0.1}$. This hypothesis has been suggested by the finding that COPD patients reduce their $P_{0.1}$ during oxygen breathing [23]. Nevertheless, the $P_{0.1}$ values 1 month after LVRS remained, in 13 of the 17 patients, at levels higher than those in normal subjects despite an average increase in arterial oxygen tension (P_{a,O_2}) from 8.5 to 9.3 kPa (64 to 70 mmHg) after LVRS. The residual increase in respiratory drive could be due to adaptive processes to chronic hypoxia which are not completely reversed after 1 month or due to the fact that the mechanical load of breathing, albeit reduced after surgery, was still elevated at 1 month. Follow-up studies are required to determine whether mechanical or chemical effects predominate in the persistently increased respiratory drive of patients with severe emphysema after LVRS.

In conclusion, this study demonstrates that the clinical improvement seen in patients with severe emphysema following lung volume reduction surgery is due not only to an improved pulmonary function related to the increased elastic recoil but also to an increased ability of the respiratory muscle to generate force and a decreased respiratory drive presumably because of a reduced work of breathing.

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