Diaphragm Length and Neural Drive after Lung Volume Reduction Surgery

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Rationale: **Patients with chronic obstructive pulmonary disease have shorter inspiratory muscles and higher motor unit firing rates during quiet breathing than do age-matched healthy subjects. Lung volume reduction surgery (LVRS) in patients with chronic obstructive pulmonary disease improves lung function, exercise capacity, and quality of life.**

Objectives: **We studied the effect of LVRS on length and motor unit firing rates of diaphragm and scalene muscles.**

Methods: **Diaphragm length was estimated by ultrasound and magnetometers, and firing rates were recorded with needle electrodes in patients (five females and seven males) with severe chronic obstructive pulmonary disease, before and after surgery.**

Measurements and Main Results: **Pre-LVRS total lung capacity was 135 ± 10% predicted (mean ± SD), and FEV$_1$ was 30 ± 12% predicted. After surgery, median firing frequency of diaphragmatic motor units fell from 17.3 ± 4.2 to 14.5 ± 3.4 Hz ($p < 0.001$), and scalene motor unit firing rates were reduced from 15.3 ± 6.9 to 13.4 ± 3.8 Hz ($p < 0.001$). Tidal volume and diaphragm length change during quiet breathing did not change, but at end expiration, the zone of apposition length of diaphragm against the rib cage (L_{Zapp}) increased (30 ± 28%, $p = 0.004$). Improvements in quality-of-life measures and exercise performance after surgery were related to increased forced vital capacity and L_{Zapp}.**

Conclusions: **Increased diaphragm length resulted in lower motor unit firing rates and reduced breathing effort, and this is likely to contribute to improved quality of life and exercise performance after LVRS.**

Keywords: chronic obstructive pulmonary disease; electromyography; emphysema; pneumonectomy; ultrasound

Inspiratory muscles of patients with chronic obstructive pulmonary disease (COPD) operate under an increased load and at shorter length than in healthy subjects (1–3), and neural drive to the inspiratory muscles is also increased (4–6). This increased neural drive allows the diaphragm in COPD to shorten and descend normally during quiet breathing (7, 8), although there is a greatly reduced reserve capacity to increase tidal volume (V_T).

Lung volume reduction surgery (LVRS) is used to treat patients with severe emphysema to reduce hyperinflation by removing up to 30% of the worst affected pulmonary areas (9, 10). After LVRS, lung function, exercise performance, and measures of quality of life improve (11–13). These improvements have been attributed to increased vital capacity (VC) (14, 15) and increased lung elastic recoil (16).

Improvements in diaphragm function may also contribute to the functional improvement after LVRS (17). Diaphragm length is increased after LVRS (18–20), resulting in increased maximal transdiaphragmatic pressures (20, 21). The transdiaphragmatic pressure required to generate a given V_T is decreased after LVRS (21). During inspiratory threshold loading to task failure, the relative increase in neural drive to the diaphragm, assessed by esophageal EMG, is decreased after LVRS (22).

To assess the mechanisms by which LVRS improves exercise performance and quality of life in patients with COPD, we measured changes in diaphragm length and inspiratory neural drive in patients before and after LVRS. Diaphragm length was estimated by ultrasound at fixed lung volumes and during breathing (8). Neural drive was determined from single motor unit firing rates during quiet breathing (4, 5, 23). Some data from this study have been previously presented as abstracts (24, 25).

METHODS

Patients and Protocol

Twelve patients (five females and seven males) with severe COPD were studied before and after LVRS. Patient anthropometric and lung function data are listed in Table 1. Most patients (10 of 12) had completed preoperative pulmonary rehabilitation. All patients received bilateral video-assisted thoracoscopic LVRS. Patients provided written, informed consent to the procedures, which were approved by the institutional ethics committee.

Ultrasound and EMG studies were performed on the same day except for one subject with 4 wk between studies. Subjects were seated and given no instructions on breathing strategies or feedback on performance. In separate sessions the patients received standard lung function tests, a cardiopulmonary exercise test, and a 6-min walk test, including 10-point Borg scales for dyspnea and exertion, and they completed a quality-of-life (QOL) questionnaire focused on chronic respiratory diseases (26). The QOL scores quantified feelings of dyspnea, fatigue, emotional function, and mastery. We report the dyspnea score and the average, with a maximum score of 35 for best function. After LVRS (14 ± 6 mo), the ultrasound and EMG studies were repeated. The lung function tests, exercise test, 6-min walk test, and QOL questionnaire were repeated after 10 ± 4 mo.

Measurement of Neural Drive

Single motor unit activity in the diaphragm and scalenes was recorded with monopolar electrodes, using methods reported previously (4, 5, 23). The diaphragm electrode was inserted at the ventral end of the seventh or eighth intercostal space. The scalene electrode was inserted 1–2 cm above the clavicle in the posterior triangle of the neck. At each of 10 sites in each muscle, about five quiet breaths were recorded and motor units were subsequently sorted on the basis of spike shape (Figure 1). The instantaneous firing frequency of each unit was smoothed with a 200-ms moving average and the peak was measured for each breath. Rib cage and abdominal movement were measured with inductance bands, and V_T was measured with a pneumotachograph.

Measurement of Zone of Apposition and Chest Diameters

We measured the length of the zone of apposition of the diaphragm against the chest wall (L_{Zapp}), using our previously described method (8). In brief, diaphragm movement was visualized by ultrasound (120-mm linear probe) just anterior to the right midaxillary line. The costal origin of the diaphragm was identified when the patient breathed

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TABLE 1. ANTHROPOMETRIC AND LUNG FUNCTION DATA

					TLC		FEV_1	
Subject	Sex	Age (*yr*)	Height (*cm*)	Weight (*kg*)	L	%pred	L	%pred
1	M	71	180	83	9.6	131	1.2	37
2	F	66	157	38	5.6	123	0.6	33
3	F	71	166	66	7.2	140	0.7	33
4	M	75	167	77	8.5	135	0.8	33
5	M	50	172	62	9.6	144	0.5	15
6	M	69	178	101	8.6	121	1.1	34
7	F	55	166	65	7.1	137	0.8	31
8	M	66	174	83	9.5	139	0.5	18
9	F	64	165	69	7.0	137	0.5	22
10	M	56	162	60	9.4	159	0.6	20
11	F	58	160	64	6.3	131	1.4	61
12	M	57	171	66	8.4	128	0.8	25
Mean		63	168	70	8.1	135	0.8	30
SD		8	7	15	1.4	10	0.3	12

Definition of abbreviations: %pred = percentage of predicted value; F = female; M = male; TLC = total lung capacity.

to total lung capacity (TLC), where L_{Zapp} approaches zero with active inspiration (8). The distance between the costal origin of the diaphragm and the point where the diaphragm peeled away from the chest wall (costal recess) was measured to give L_{Zapp} at any lung volume or time point (± 1 mm). The change in L_{Zapp} with quiet breathing was measured over 5–10 breaths, L_{Zapp} was measured at FRC and residual volume (RV), and measurements were repeated several times. The thickness of the diaphragm and its depth under the skin at FRC were measured midway between the origin and costal recess (± 0.5 mm; 50-mm linear probe).

The anteroposterior diameter (sagittal plane, D_{Ap}) and lateral diameter (coronal plane, D_{Lat}) of the chest wall were measured with magnetometers taped to the skin at approximately the level of the diaphragm at FRC (8), and the signals were adjusted for diaphragm depth. Length of the diaphragm (L_{Di}) in the midaxillary coronal plane was estimated from measurements of L_{Zapp} and D_{Lat}, using an equation validated for patients with COPD (8, 27, 28).

Statistics

Firing rate of all motor units was compared before and after LVRS by analysis of variance with "subject," "muscle," and "surgery" (pre- or post-LVRS) as main effects. All other measurements were compared before and after LVRS with paired *t* tests. Linear mixed model analysis (SPSS version 11; SPSS Inc., Chicago, IL) with "surgery" as a repeated effect within subjects was used to investigate linear relationships between measurements and changes after surgery. Pearson correlation coefficients and linear regression analyses were used to investigate relationships between changes in measurements after LVRS. Not all patients had a complete dataset, so most comparisons contained data from 10 or 11 patients. Data are presented as means ± SD and significance was set at $p < 0.05$.

RESULTS

Lung Function

After LVRS, there were significant changes in lung function among patients with COPD (Table 2). TLC, RV, and RV/TLC were reduced in 11 of 11 patients to 88 ± 4% of TLC presurgery and to 75 ± 9% of RV presurgery, and were reduced by 10 ± 6% from RV/TLC presurgery. FVC increased in 8 of 12 patients and the average increase for all patients was 12 ± 16% of FVC presurgery. In 8 of 12 patients FEV_1 increased, but the average increase for all patients was not significant (21 ± 29% of FEV_1 presurgery). There was a significant negative relationship between RV/TLC and FEV_1 (percentage of predicted value) before and after surgery (Figure 2A). A mixed model analysis (*see* METHODS) showed no significant effect of surgery on the slope of this relationship, but showed a significant effect on the intercept ($p = 0.004$). The relationship was shifted to the left after surgery, so that the increase in FEV_1 was not as great as expected given the reduction in RV/TLC.

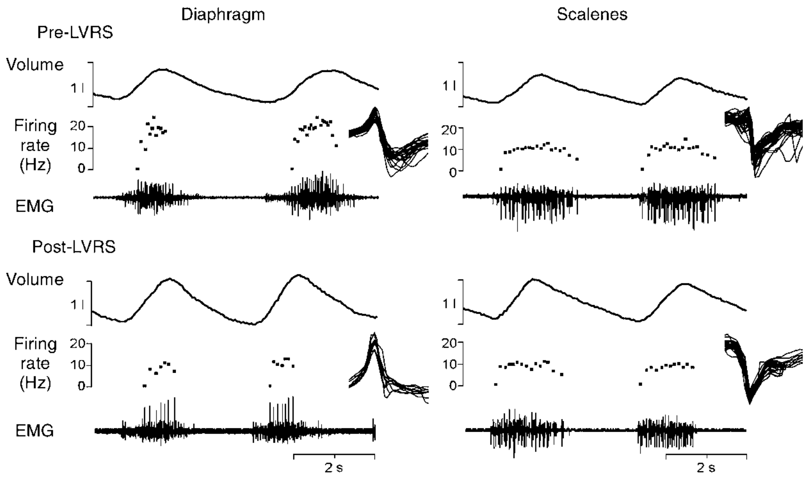

Figure 1. Raw data from one subject, recorded from the diaphragm and scalene muscles before and after surgery. EMG, instantaneous motor unit firing rate, and volume are plotted for two quiet breaths in each *panel*. Each sorted motor unit spike is overlaid to the *right* of each *panel*, showing that the shape is identical throughout the recording. LVRS = lung volume reduction surgery.

TABLE 2. LUNG FUNCTION DATA BEFORE AND AFTER LUNG VOLUME REDUCTION SURGERY

		Presurgery		Postsurgery		
	n	Mean	SD	Mean	SD	p Value
TLC, L	11	8.0	1.4	7.0	1.2	$< 0.001^†$
FVC, L	12	2.9	0.5	3.2	0.4	$0.033^†$
RV, L	11	5.1	1.2	3.8	1.0	$< 0.001^†$
RV/TLC, %	11	64	6	54	6	$< 0.001^†$
FEV_1, L	12	0.8	0.3	0.9	0.2	0.087 (NS)
P_{O_2}, mm Hg	11	76	14	77	12	0.873 (NS)
P_{CO_2}, mm Hg	11	39	5	39	4	0.630 (NS)
PH	11	7.4	0.0	7.4	0.0	0.078 (NS)
L_{Zapp} end inspiration, mm	11	19	9	31	11	$0.001^†$
ΔL_{Zapp} V_T, mm	11	21	5	20	4	0.384 (NS)
L_{Zapp} FRC, mm	11	40	10	51	12	$0.004^†$
L_{Zapp} RV, mm	11	69	17	79	14	0.059 (NS)
L_{Di} TLC, mm	11	296	22	297	19	0.861 (NS)
L_{Di} at end inspiration, mm	11	337	37	358	37	$0.006^†$
ΔL_{Di} V_T, mm	11	42	9	38	8	0.245 (NS)
L_{Di} FRC, mm	11	379	37	396	37	$0.023^†$
L_{Di} RV, mm	11	436	48	453	36	0.091 (NS)
ΔD_{Ap} V_T, mm	11	5.4	3.1	3.8	1.2	0.164 (NS)
D_{Ap} FRC, mm	11	203	41	194	33	0.148 (NS)
ΔD_{Lat} V_T, mm	11	−0.6	2.9	0.5	2.0	$0.038^†$
D_{Lat} FRC, mm	11	250	27	245	22	0.239 (NS)
F_{Di}, Hz	11	17.3	4.2	14.5	3.4	$< 0.001^†$
F_{Scal}, Hz	11	15.3	6.9	13.4	3.8	$< 0.001^†$
Six-min walk distance, m	12	349	86	394	114	0.058 (NS)
Exercise distance, m	10	381	393	551	360	$0.012^†$
QOL dyspnea*	11	18	6	28	5	$< 0.001^†$
QOL average*	11	23	5	31	4	$0.002^†$

Definition of abbreviations: D_{Ap} = anteroposterior diameter (sagittal plane); D_{Lat} = lateral diameter (coronal plane); F = female; F_{Di} = firing frequency of diaphragmatic motor units; F_{Scal} = firing frequency of scalene motor units; L_{Di} = Length of diaphragm; L_{Zapp} = zone of apposition length of diaphragm against the rib cage; M = male; NS = not significant; QOL = quality of life; RV = residual volume; TLC = total lung capacity.

* Maximum score of 35 for best function.

† Significant difference between pre- and postsurgery values.

Diaphragm and Rib Cage Dimensions

At FRC, the L_{Zapp} increased by 30 ± 28% after LVRS ($p = 0.004$; Table 2), and total L_{Di} increased slightly (5 ± 6%; $p = 0.023$). At RV, there were nonsignificant increases in L_{Zapp} (20 ± 27%; $p = 0.059$) and L_{Di} (4 ± 7%; $p = 0.091$). L_{Di} at TLC did not change significantly. The small increase in L_{Di} at FRC reflected the substantial increase in L_{Zapp} (11 mm), countered by a slight reduction in the lateral diameter of the rib cage (D_{Lat}) at FRC (5 ± 13 mm, $p = 0.238$). At TLC, FRC, and RV both the anteroposterior diameter of the rib cage (D_{Ap}) and D_{Lat} decreased slightly after LVRS, but these changes were not significant. The calculated cross-sectional area of the rib cage (8) was slightly decreased (96, 94, and 94% of presurgery values for TLC, FRC, and RV, respectively; p = 0.19, 0.08, and 0.08). There was a significant relationship between L_{Zapp} at FRC and RV/TLC (Figure 2B), but no difference in the relationship before and after LVRS. The negative relationship between L_{Di} and lung volume relative to predicted TLC (Figure 3) did not change slope, but was shifted to the left after LVRS ($p < 0.001$), so that for a given lung volume L_{Di} was reduced (8).

V_T during quiet breathing did not change significantly after LVRS. Similarly, there was no significant change in ΔL_{Zapp} during quiet breathing. However, during quiet breathing there was increased inspiratory reserve for diaphragm shortening because L_{Zapp} at end inspiration increased by 12 ± 9 mm ($p = 0.001$) and L_{Di} increased by 6 ± 6% ($p = 0.006$; Table 2). Before LVRS, seven patients showed paradoxical inward motion of the lateral rib cage during quiet breathing ($\Delta D_{Lat} < 0$; Hoover's sign) (29), but after LVRS, only four patients exhibited Hoover's sign. After LVRS, expansion of the lateral rib cage during quiet breathing was significantly increased (ΔD_{Lat} increased by 1.2 ± 1.6 mm; $p = 0.038$). The small decrease in ΔD_{Ap} during tidal breathing after LVRS (1.6 ± 3.5 mm; $p = 0.164$) was not significant.

Motor Unit Firing Rates

Measurements were made from 110 motor units in the diaphragm before LVRS and from 227 after LVRS (Figure 4). The firing frequency of diaphragmatic motor units (F_{Di}) during quiet breathing was reduced after LVRS in 9 of 11 patients with COPD, with an average for all patients of 87 ± 23% of F_{Di} before surgery ($p < 0.001$; Table 2 and Figure 4). In the scalenes 203 motor units were measured before surgery and 223 were measured after surgery (Figure 4). The firing frequency of scalene motor units (F_{Scal}) was slightly decreased after LVRS (98 ± 35% of pre-LVRS, $p < 0.001$; Table 2), but only 6 of 11 patients had a decrease in firing rate. F_{Di} was significantly greater than F_{Scal} both before and after surgery ($p < 0.001$). The analysis of variance revealed significant effects due to "subject," "muscle," and "surgery," as well as significant interactions between these effects. The effect of LVRS on motor unit firing rate depended on the muscle and the subject. Figure 5 shows that for both muscles the change in motor unit firing rate after LVRS was linearly related to firing rate before surgery, so that the change was greater for those subjects with high firing rates pre-LVRS (diaphragm: $R^2 = 0.44$, $p = 0.025$; scalenes: $R^2 = 0.71$, $p = 0.001$). The proportion of volume change measured at the rib cage increased from 56 ± 9% of tidal volume before surgery to 69 ± 9% afterward ($p = 0.006$).

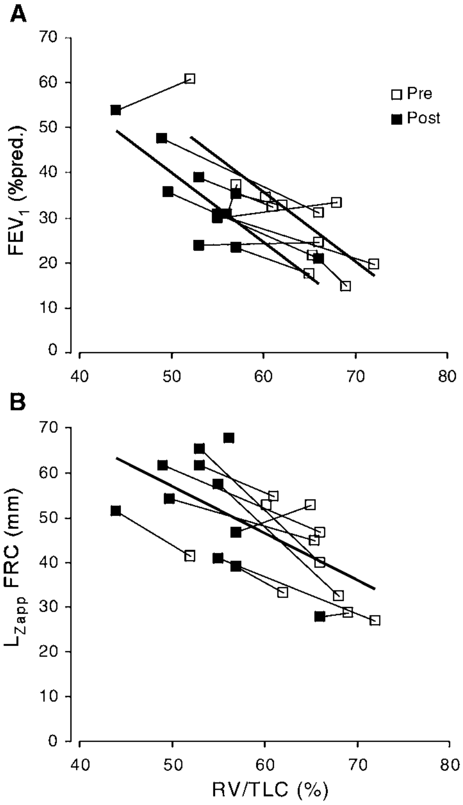

Figure 2. FEV$_1$ as a percentage of predicted FEV$_1$ (*A*) and L$_{Zapp}$ at FRC (*B*) are plotted against RV/TLC. Values pre- and post-LVRS for each patient are joined by a *line*, and the *thick lines* represent the linear models of the data. (*A*) For the FEV$_1$ relationship ($R^2 = 0.70$, $p < 0.001$), pre- and postsurgery showed no difference in slope, but a significant shift in the intercept occurred ($p = 0.004$). The reduction in FEV$_1$ was not as great as expected for the reduction in RV/TLC. (*B*) For L$_{Zapp}$ at FRC, there was no difference between the pre- and postsurgery relationships, so the relationship for all data is plotted ($R^2 = 0.43$, $p = 0.001$). Data from two patients with incomplete datasets are plotted (one without L$_{Zapp}$ pre-LVRS and one without RV/TLC post-LVRS).

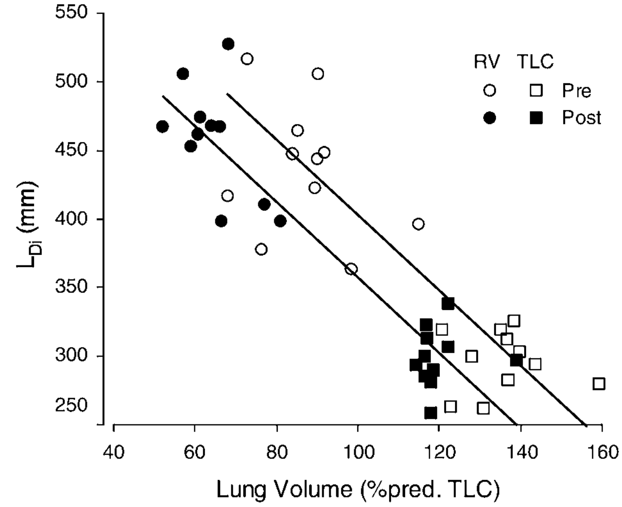

Figure 3. Length of the diaphragm (L$_{Di}$) is plotted against lung volume at RV and TLC expressed as a percentage of predicted TLC. *Thick lines* represent the linear model of the data ($R^2 = 0.80$, $p < 0.001$). The relationship did not change slope after surgery, but was shifted to the left so that, for a given lung volume, L$_{Di}$ was reduced. Points from two patients with incomplete datasets are plotted (one without L$_{Di}$ pre-LVRS and one without RV and TLC post-LVRS).

Blood Gases, Exercise, and Quality of Life

There were no significant changes in blood gas concentrations after LVRS (Table 2). The 6-min walk distance was greater in 10 of 12 patients, but this change was not significant (114 ± 22% of presurgery values; $p = 0.058$). However, the Borg scores for exertion and dyspnea during the 6-minute walk test declined after LVRS (by 1.3 ± 1.1, $p = 0.002$ and 1.2 ± 1.6, $p = 0.032$, respectively). There was an increase in distance walked during the cardiopulmonary exercise test in 8 of 12 patients (mean increase for all patients, 220 ± 226%; $p = 0.012$). After LVRS, there was also a significant increase of 10 ± 7 ($p < 0.001$) in QOL scores related to dyspnea and of 8 ± 6 ($p = 0.002$) for the average QOL scores (Table 2).

Correlations

There was a significant negative relationship between F$_{Di}$ and L$_{Zapp}$ at end inspiration before and after LVRS (Figure 6). After surgery, the increase in L$_{Zapp}$ was associated with a decrease in F$_{Di}$, such that the relationship did not change. The 6-min walk distance was positively correlated with ΔD$_{Lat}$ during quiet breathing ($p < 0.001$; Figure 7), with Hoover's sign (negative ΔD$_{Lat}$) more prominent in patients with a shorter 6-min walk distance. After surgery, the relationship did not change and the increase in ΔD$_{Lat}$ was associated with increased 6-min walk distance.

The variable outcomes of the surgery are illustrated in Figure 8. Although the increase in 6-min walk distance after LVRS was not significant ($p = 0.058$), it was positively correlated with the increase in QOL score for dyspnea ($p = 0.012$; Figure 8A). Increased 6-min walk distance after surgery also correlated with increased FVC ($p = 0.005$; Figure 8B). In addition, the increase in L$_{Zapp}$ at FRC was linearly related to increased FVC after LVRS ($p = 0.023$; Figure 8C). In summary, the increase in FVC after surgery was the best predictor for the increase in L$_{Zapp}$ at FRC and the 6-min walk distance. In turn, patients with greater increases in 6-min walk distance reported greater increases in their QOL score for dyspnea.

The patients with the greatest hyperinflation had the largest decrease in TLC after surgery ($p = 0.015$; Figure 9A). Similarly, those patients with lowest QOL scores for dyspnea had the greatest increase in QOL score after surgery ($p = 0.014$; Figure 9B).

DISCUSSION

In the present study, diaphragm dimensions and neural drive were examined in 12 patients with severe emphysema and COPD before and after LVRS, which reduced TLC by an average of 12%. After LVRS, there was a significant increase in the L$_{Di}$ and the L$_{Zapp}$ at FRC and RV. Tidal changes in L$_{Di}$ and L$_{Zapp}$ during quiet breathing were not different after LVRS, so that L$_{Zapp}$ at end inspiration was increased, providing a greater reserve capacity for diaphragm shortening (8).

After LVRS, the firing rate of motor units in the costal diaphragm (F$_{Di}$) during quiet breathing decreased, despite no change in V$_T$ or tidal movement of the diaphragm, consistent with a net reduction in neural drive. F$_{Scal}$ during quiet breathing was also decreased after LVRS. However, in both the diaphragm and scalenes, the reduction in firing rate was most apparent in patients with high firing rates before surgery. The firing rate of motor units in the diaphragm was greater than that in the scalenes, which is consistent with our previous findings in healthy

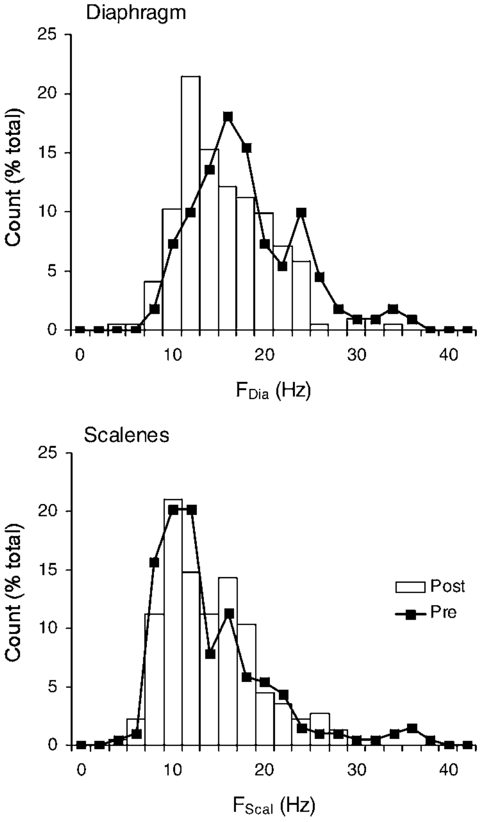

Figure 4. Frequency histograms are shown for the peak firing rate of diaphragm (F_{Di}) and scalene (F_{Scal}) motor units before and after LVRS. The *y axis* is normalized for the number of motor units: 110 diaphragm motor units before and 227 after surgery; and 203 scalene motor units before and 223 after surgery. Median firing rates decreased from 17.3 ± 4.2 to 14.5 ± 3.4 Hz after LVRS for the diaphragm, and from 15.3 ± 6.9 to 13.4 ± 3.8 Hz for the scalene muscles.

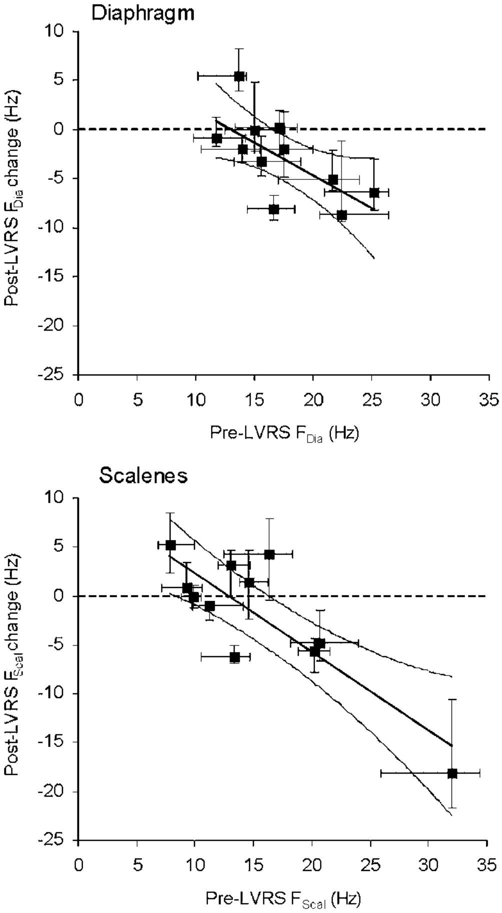

Figure 5. Change in peak motor unit firing rate for each patient after surgery is plotted against the value before surgery for the diaphragm and scalene muscles. *Points* represent the median value with the 25–75% interquartile range indicated by *error bars*. A linear regression line (*thick line*) and 95% confidence intervals of the mean (*thin lines*) are also plotted. No change in firing rate is shown by the *dotted line*. Note that in 9 of 11 patients the median firing rate in the diaphragm was decreased after surgery, whereas the median firing rate in the scalenes decreased for only 6 of 11 patients.

subjects when inspiratory drive is increased (23) and in patients with COPD compared with control subjects (4, 5).

The firing rates for diaphragm motor units in the present study before LVRS are similar to those reported in patients with COPD in previous studies using the same methods (17 vs. 18 Hz, respectively) (4), but the scalene firing rates were greater in the present study (15 vs. 11 Hz, respectively) (5). By comparison, in healthy subjects in whom inspiratory drive is increased threefold, the motor unit firing rates averaged 18 Hz in the diaphragm and 10 Hz in scalenes (23). After LVRS, the firing rates of motor units in the patients with COPD fell to 15 Hz for the diaphragm and 13 Hz for the scalenes, still greater than those of age-matched control subjects in the previous studies (11 and 9 Hz, respectively) (4, 5). Motor unit firing rate is unaffected by changes in recording conditions (30) and is therefore a more reliable measure of neural drive than surface EMG. However, the present results are still consistent with previous findings that during inspiratory threshold loading, diaphragm EMG from esophageal electrodes was reduced after LVRS (22).

Previous studies have measured L_{Di} and L_{Zapp} in patients with COPD (2, 3, 27, 31, 32). The values measured in the present study largely agree with the previous studies, given methodologic differences related to identification of the diaphragm origin, posture, and muscle contraction (*see* also Reference 8). For comparison, L_{Di} and L_{Zapp} at FRC were 456 and 71 mm, respectively, in matched healthy subjects, compared with 381 and 35 mm in patients with COPD (8), and 379 and 40 mm in the present study before surgery. In other studies of diaphragm dimensions after LVRS, similar results were found by Bellemare and colleagues (20), but Lando and colleagues (19) reported a small increase in L_{Di} at TLC, unlike the present study in which L_{Di} increased only at FRC and RV after LVRS. The tidal change in L_{Zapp} during quiet breathing (ΔL_{Zapp}) was similar to that in our previous study (8), with average values unchanged after LVRS (only one patient participated in both studies). After LVRS, L_{Zapp} and L_{Di} at FRC and end inspiration approached, but did not reach, values for control subjects (8).

Some tests were conducted on different days, so there is a potential source of variability in the relationships between measurements. Diaphragm mechanics and neural drive were measured about 4 mo after the other post-LVRS measurements and this may have reduced the ability to find statistically significant correlations between the variables measured. We attempted to reduce measurement errors with multiple motor units measured for each person, and with ultrasound and chest diameter measurements averaged over a number of breaths or maneuvers.

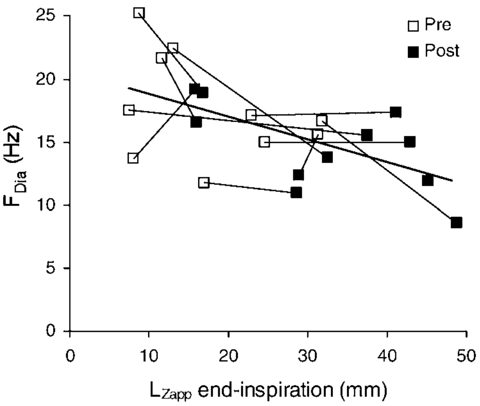

Figure 6. Peak firing rate for diaphragm motor units (F_{Di}) is plotted against L_{Zapp} at end inspiration for each patient with COPD. Values pre- and post-LVRS for each patient are joined by a *line*. The negative relationship (*thick line*) was significant ($R^2 = 0.36$, $p = 0.004$) and there was no difference in the relationship before and after LVRS. One patient with only a post-LVRS L_{Zapp} measurement is included.

The improvement in lung volume, exercise performance, and QOL found in these patients with COPD was related to their presurgical status. In general, patients with more severe disease before surgery improved the most after LVRS. This was consistent with the findings of Fessler and coworkers (33) that the more severely affected patients with the largest RV/TLC ratio exhibited the biggest changes in FVC after surgery. The change in VC has been considered the main determinant of improvement in FEV_1 (15, 34). It is likely that the patients with the greatest hyperinflation had more diseased lung removed and this would also help account for the relationships between pre- and postsurgical measurements (35).

This study was conducted on the earliest patients in the LVRS program in one hospital, so with changes in criteria for LVRS, the outcomes of surgery for these patients may not reflect current outcomes. The improvement in FEV_1 and other measures of lung function and in exercise capacity were less than often reported (40–80% increase in FEV_1) (10, 36), but in agreement with a large randomized trial (~ 21% in FEV_1 at 12 mo postsurgery) (37). The long period between pre- and postsurgical observations (up to 30 mo) also contributed to the lack of significant improvement in FEV_1, which after the initial increase post-LVRS declines at a relatively fast rate in the first 1–2 yr and then declines at a rate similar to presurgical values (35, 38, 39). The lack of significant change in FEV_1 and its variability may have mitigated against finding significant changes in other measures of lung and respiratory function and exercise performance. However, with this sample we have a large range in the changes resulting from LVRS, which may have increased the likelihood of finding relationships between measures of lung function, diaphragm function, exercise capacity, and quality of life.

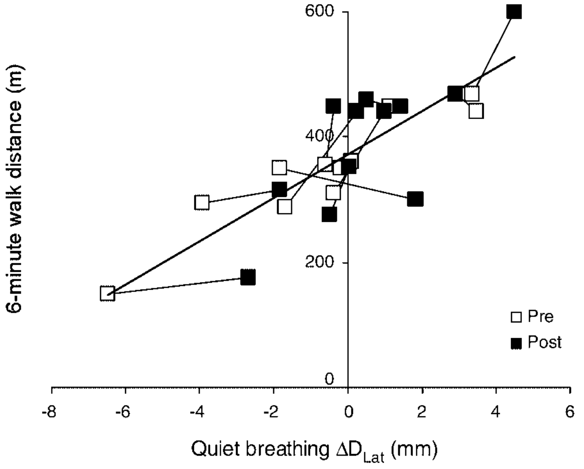

Figure 7. The positive relationship between 6-min walk distance and change in lateral diameter (ΔD_{Lat}) during quiet breathing is shown before and after LVRS ($R^2 = 0.69$, $p < 0.001$). The relationship did not change after surgery, but the increase in ΔD_{Lat}, meaning less paradoxical indrawing of the lateral rib cage during inspiration, was associated with increased 6-min walk distance. Data from one patient with only a post-LVRS ΔD_{Lat} measurement are also plotted.

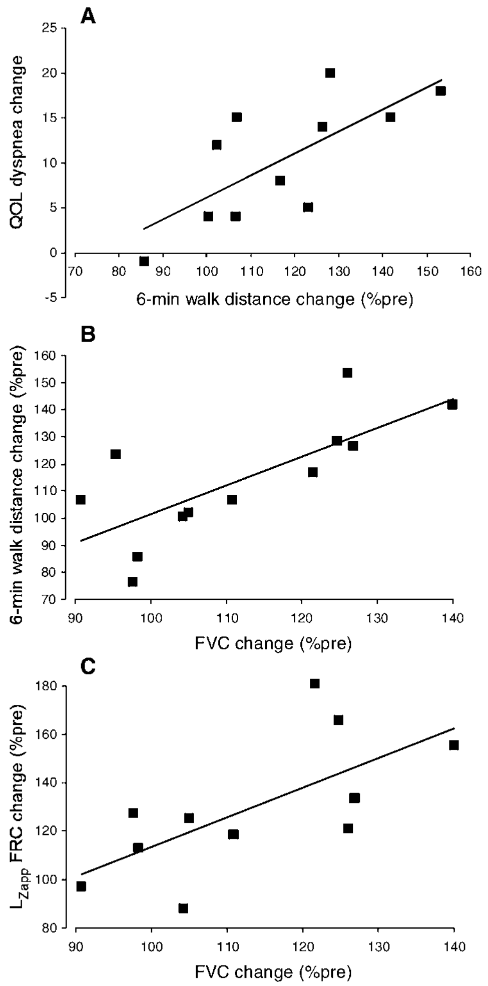

Figure 8. (*A*) Change in patient quality-of-life (QOL) score for dyspnea was linearly related to change in 6-min walk distance after surgery ($R^2 = 0.52$, $p = 0.012$). (*B*) Change in 6-min walk distance was linearly related to change in FVC after LVRS ($R^2 = 0.56$, $p = 0.005$). (*C*) Change in L_{Zapp} at FRC was linearly related to change in FVC ($R^2 = 0.45$, $p = 0.023$). *Straight lines* represent linear regressions.

A further limitation of this study was that we did not study the effect of preoperative pulmonary rehabilitation on inspiratory muscle firing rates and diaphragm mechanics. Nevertheless, pulmonary rehabilitation may improve exercise capacity and quality of life measures, but it has no effect on pulmonary function (34).

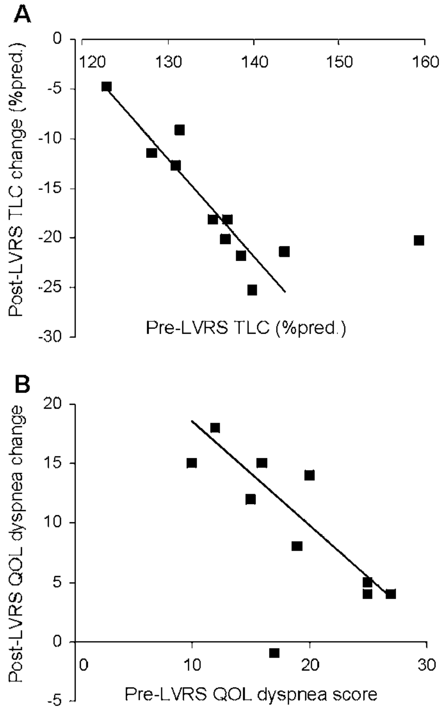

Figure 9. Change in TLC (*A*) and QOL score for dyspnea (*B*) after surgery were linearly related to their values before surgery (R^2 = 0.50, 0.51; p = 0.015, 0.014, respectively). There was one outlier in the TLC data and one in the QOL data (not the same subject), and, if these are excluded, R^2 = 0.86 and 0.81 (p < 0.001) for TLC and QOL score for dyspnea, respectively. *Straight lines* represent linear regressions without the outliers.

At a given L_{Di}, absolute lung volume was decreased after surgery (Figure 3) suggesting that rib cage volume had also decreased (8), although the cross-sectional area of the lower rib cage was not significantly decreased. The firing rate of diaphragmatic motor units during quiet breathing decreased after LVRS, probably because the diaphragm was operating at a longer length. The length–tension relationship of the diaphragm is shifted in patients with COPD compared with normal subjects and there is evidence that after LVRS, the relationship returns toward that for healthy subjects (20, 21, 40). Patients with COPD have chronic adaptations of the diaphragm, with reduced length and/or number of sarcomeres in series (41), and changes in fiber type composition (42, 43). After LVRS, the rat diaphragm undergoes remodeling, increasing the number of sarcomeres in series (44). Other changes post-LVRS may also contribute to a reduced load on the diaphragm, such as decreased intrinsic positive end-expiratory pressure (45), resulting in reduced neural drive.

The patients with COPD significantly improved in QOL and distance walked in the exercise test after LVRS. The improvement in QOL scores for dyspnea correlated best with increases in 6-min walk distance, which in turn was best predicted by the increase in FVC after surgery. The patients in whom FVC increased the most after surgery also had the greatest increase in L_{Zapp} at FRC. In addition, the decrease in firing rate of diaphragm motor units was related to the increase in L_{Zapp} at end inspiration after surgery. The data suggest that after LVRS, improvements in quality of life and exercise performance are associated with improvements in diaphragm function, with reduced neural drive, and increased reserve capacity for shortening. Improvements in diaphragm function are a result of improved lung volumes. Other studies have shown that increased end-expiratory volume or reduced inspiratory capacity are the best predictors for increased breathing discomfort in patients with COPD (46, 47). In the present patients, the reduction in QOL scores for dyspnea after LVRS may, therefore, be a result of improved diaphragm function with reduced lung volume.

This study has confirmed previous reports that patients with COPD have shortened diaphragms and reduced zones of apposition against their rib cages, requiring high firing rates in diaphragm and scalene motor units. We report for the first time that patients with COPD have reduced firing rates of motor units in the diaphragm and scalenes after LVRS. This reduction in neural drive was accompanied by an increase in L_{Di} and L_{Zapp}. This improved diaphragm function is likely to contribute to improved quality of life after surgery, especially in dyspnea and exercise capacity.

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