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Dyspnea Response Following Bilateral Thoracoscopic Staple Lung Volume Reduction Surgery*

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Purpose: Lung volume reduction surgery (LVRS) has shown promise for treating patients with severe emphysema in recent clinical trials. However, response following surgery is difficult to assess due to frequent discrepancies between subjective and objective outcomes. We evaluated the relationship between improvement in dyspnea and pulmonary function response in 145 consecutive patients with inhomogeneous emphysema enrolled in a bilateral thoracoscopic lung volume reduction protocol in order to assess predictors of improved dyspnea outcome and correlation of subjective and objective improvement measures.

Materials and methods: Baseline complete pulmonary function testing, spirometry, gas exchange, plethysmography, gas dilution lung volumes, along with resting dyspnea index determinations were performed preoperatively, and repeated short term (mean, 33 days; n=129) and long term (>6 months; mean, 276 days; n=84) following surgery.

Results: Improvement in FEV_1 percent predicted was significantly associated with improvement in dyspnea scores, though considerable variability exists (r=0.04, p<0.01, short term; r=0.4, p=0.1, long term). In this preselected patient group, those with the extreme degrees of hyperinflation may have less improvement in dyspnea following LVRS than those with milder preoperative hyperinflation. Greater improvement in dyspnea short term and long term was seen in patients with lower presenting residual volume/total lung capacity ratios (r=0.4, p=0.02, short term; r=0.4, p<0.05, long term).

Conclusions: Bilateral thoracoscopic staple LVRS results in significant objective and subjective improvement in patients with severe emphysema and hyperinflation. There was considerable variability between improvement in dyspnea and improvement in spirometry, and preoperative predictors of response may differ between these outcome variables. Further studies are needed to define the long-term implications of these findings.   *(CHEST 1997; 112:916-23)*

Key words: dyspnea; lung; LVRS; outcome; reduction; volume

Abbreviations: Dco=diffusion of carbon monoxide; LVRS=lung volume reduction surgery; MMRC=Modified Medical Research Council; RV=residual volume; TLC=total lung capacity

Surgical lung volume reduction procedures to improve pulmonary status are being actively investigated at many centers for patients with severe emphysema.[1-10] Optimization of operative procedures and development of selection criteria for lung volume reduction surgery (LVRS) are evolving based on assessment of postoperative outcomes. Except for a few reports, most initial studies have justifiably focused analysis primarily on objective pulmonary function outcome measures in order to avoid influence of placebo effects that could potentially bias subjective response measures.[1,2,4-7,11-19] However, there are well-documented discrepancies between objective measures of pulmonary function and dyspnea response in patients with emphysema.[1,7,13,19-22] Since LVRS is currently aimed primarily at providing symptomatic relief to severely dyspneic patients,[5,7] variables associated with subjective dyspnea improvement must be determined.

This study focuses attention on semiquantitative subjective dyspnea response in order to determine factors that predict improved postoperative dyspnea outcome. In this study, we evaluated the relationship between improvement in dyspnea and pulmonary function response in 145 consecutive patients enrolled in a study of bilateral thoracoscopic LVRS to determine which patients had optimal dyspnea outcome, and to uncover any correlations between subjective and objective improvement measures.

While these analyses are limited by the subjective nature and simplicity of the modified dyspnea scale scoring system, they provide potential initial insights into factors associated with beneficial LVRS outcome that may be further investigated with more specifically directed studies.

MATERIALS AND METHODS

One hundred forty-five consecutive patients enrolled in a prospective bilateral thoracoscopic staple lung volume reduction protocol were studied. Selection criteria and operative procedures have been described previously.[5,11,23] Informed consent was obtained from all patients. Despite maximal medical management, all patients were markedly symptomatic. Chest radiographs showed hyperexpansion of the thorax with flattening or inversion of the diaphragm.

Contraindications to surgery included current cigarette smoking, age older than 80 years, severe cardiac disease, history of cancer within the last 5 years, ventilator dependency, or prior thoracic surgery. Relative contraindications included age older than 75 years, severe anxiety or depression, or CO_2 retention (resting $PaCO_2$ >55 mm Hg).[5]

To be accepted for the procedure, the pattern of emphysema on CT scan had to be severe and heterogeneous. Radionuclide lung perfusion scans were also used to confirm the heterogeneous pattern of emphysema.[5,11,23]

All patients underwent complete baseline pulmonary function testing, including the following: spirometry, gas exchange measures (room air arterial blood gas measurement, diffusion of carbon monoxide [Dco]), plethysmography, and gas dilution lung volumes. Maximum inspiratory and expiratory flow volume curves, thoracic gas volume, and airway resistance were measured in a plethysmograph (Collins/Cybermedic Classic TCI and Body Plethysmograph; Warren E. Collins Inc; Braintree, Mass), and compared to predicted values. Resting dyspnea index determinations were performed concurrently using the Modified Medical Research Council (MMRC) dyspnea scale.[24] The modified dyspnea scale scoring used in this study was as follows: grade

0=not troubled with breathlessness except during strenuous exercise; grade 1=troubled by shortness of breath when hurrying on the level or walking up a slight hill; grade 2=walks slower than people of the same age on the level because of breathlessness or has to stop for breath when walking at own pace on the level; grade 3=stops for breath after walking about 100 yards or after a few minutes on the level; and grade 4=too breathless to leave the house or breathless when dressing or undressing. All MMRC scale assessments were performed by one nurse working directly with the patients at the time in a preoperative on-site evaluation and again at the first follow-up visit. Subsequent long-term follow-up MMRC evaluations were filled out by mail. The procedure was explained in detail by the nurse in a uniform manner to all patients. All patients who filled out the MMRC questionnaire by mail were familiar with the process from their prior evaluations at the medical center.

Pulmonary function testing (spirometry) and dyspnea index measurements were repeated short term postoperatively (<120 days, mean [±SD] 33±28 days, n=130), and longer term postoperatively (defined as >6 months, mean [±SD] 276±90 days, n=84).

The relationships between improvement in dyspnea postsurgery and pulmonary function at presentation (short and long term) as well as improvement in dyspnea and improvement in pulmonary function were examined. Change in dyspnea was compared to baseline

Table 1—Length of Stay and Causes of Death Postoperatively Following LVRS

Patient	Cause of Death	Days Postoperative
1	Pulmonary emboli	12
2	Cardiorespiratory arrest	3
3	Respiratory failure	1
4	Respiratory failure	11
5	Acute abdominal event	23
6	ARDS	14

Table 2—Pulmonary Function Following Bilateral LVRS: Long-term Follow-up

Variable	Baseline		Follow-up		% Change	p Value
	Mean	SD	Mean	SD		
Dco	5.37	2.6	8.75	3.8	63	<0.001
% Pred*	28.5	14	46.10	19.2	62	<0.001
FEV₁	0.64	0.27	1.04	0.4	62	<0.001
% Pred	25.4	9.21	40.80	14.4	61	<0.001
FVC	1.99	0.73	2.78	0.8	40	<0.001
% Pred	53.5	14.7	75.10	17.2	40	<0.001
RV	4.52	1.55	3.26	1.2	−28	<0.001
% Pred	201	57	145.8	50.0	−27	<0.001
RV/TLC	0.67	0.09	0.56	0.0	−16	=0.002
TLC	7.1	1.8	5.77	1.6	−19	=0.03
% Pred	124	24	117	26.1	−6	=0.12

*Pred=predicted.

Table 3—Pulmonary Function Following Bilateral LVRS: Short-term Follow-up

Variable	Baseline		Follow-up		% Change	p Value
	Mean	SD	Mean	SD		
Dco	5.2	2.6	4.99	3.5	−4	=0.19
% Pred	27.5	13.1	26.00	18.0	−5	=0.15
FEV₁	0.64	0.23	0.96	0.3	50	<0.001
% Pred	24.6	8.5	36.80	15.0	50	<0.001
FVC	1.99	0.70	2.29	0.7	15	<0.001
% Pred	52.7	14.8	61.00	15.0	16	<0.001
RV	4.5	1.3	2.80	1.2	−38	<0.001
% Pred	203	53.9	140	43.0	−31	<0.001
RV/TLC	0.67	0.09	0.54	0.1	−19	<0.001
TLC	7.1	1.6	5.72	1.2	−19	<0.001
% Pred	124.3	23	109	19.0	−12	<0.001
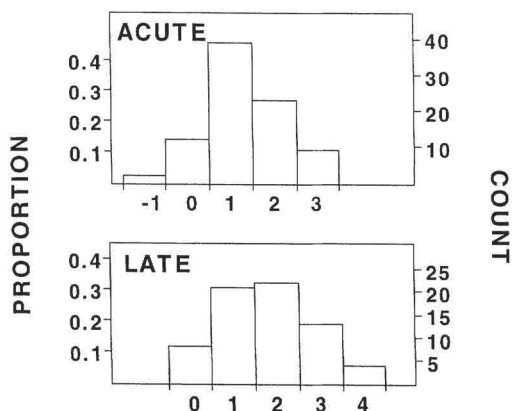
IMPROVEMENT IN DYSPNEA SCORE

FIGURE 1. Distribution of improvement in dyspnea scores short term *(top)* and at long-term follow-up after bilateral LVRS. Proportion of patients improving is shown on left axis, total number on right axis. Baseline dyspnea scores averaged 3.0 ± 0.7 and improved to 1.7 ± 0.8 (mean improvement, 1.3 dyspnea units) short term and improved to an average of 1.3 ± 0.9 (mean improvement, 1.7 dyspnea units) long term.

function and change in objective pulmonary function tests using analysis of variance (for the categorical variable, dyspnea change). Linear regression was used to correlate continuous variable percent change in FEV_1 outcome measures. Two-tailed t tests were used to compare preoperative to postoperative variables.[25]

Operative Procedure

The operative procedures have been described previously.[5,11,23] All patients underwent bilateral video-assisted thoracic surgery under paralyzed (pipecuronium) general anesthesia (isoflurane) using a left-sided double-lumen tube (Mallinckrodt Anesthesia; St. Louis). All the procedures were performed by one surgical group (R.J.M., R.J.F.) with the patient in the lateral decubitus position. The trocar and thoracoscope were placed through the 10th intercostal space in the posterior axillary line. Three additional 1- to 2-cm incisions were made for standard instruments. Patients were turned to the contralateral decubitus position for separate sterile preparation and draping after completion of surgery on the initial side.

The preoperative lung CT scans and ventilation/perfusion scans were used to identify areas of dysfunctional or degenerated lung targeted for resection with the staples.[5,11,23] Ring forceps manipulated the lung into a 60-mm endoscopic stapler (ELC 60; Ethicon; Cincinnati) with bovine pericardium 4, 5 (Peristrips; Biovascular; St. Paul, Minn) or Instat (Johnson and Johnson; New Brunswick, NJ) to buttress the staples. The staples were fired an average of 15 times for bilateral operations. Typically, approximately half of the upper lobe was resected. The chest was drained with two apically placed chest tubes following completion of the procedure. No suction was used on the chest drainage system. Heimlich valves were used for prolonged air leaks (5 days) to facilitate earlier discharge from the hospital. Patients were routinely transferred to the ICU for overnight observation after extubation in the operating room.

Rehabilitation

Patients did not receive preoperative rehabilitation at the Medical Center prior to LVRS. All patients underwent a similar regimen of pulmonary rehabilitation at Chapman Medical Center beginning immediately following hospital discharge. The rehabilitation consisted of a 10-day outpatient regimen involving a multidisciplinary approach with nursing, respiratory, dietary, nutritional, psychosocial, occupational, and physical therapy. Patient education, physical exercise (walking, flexibility, and strengthening), self-monitoring, breathing retraining, and bronchial hygeine instruction were included.
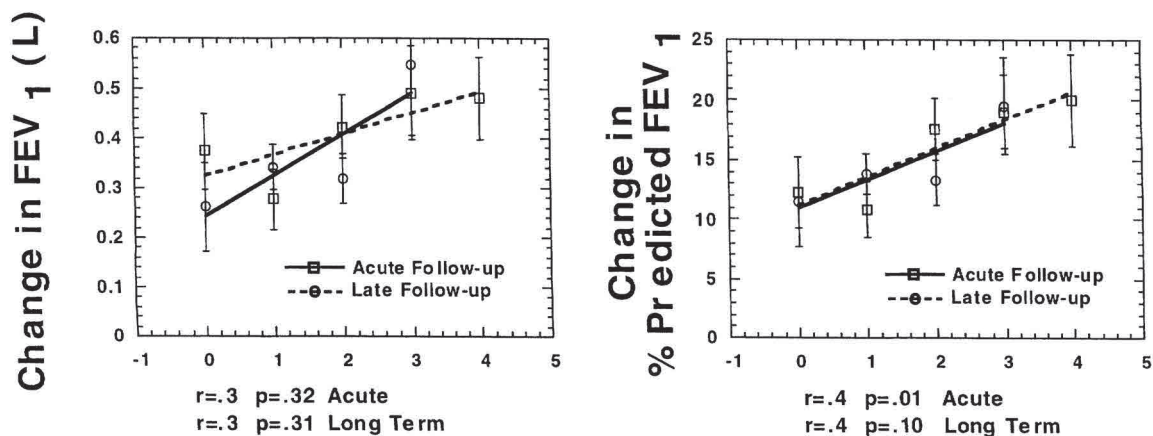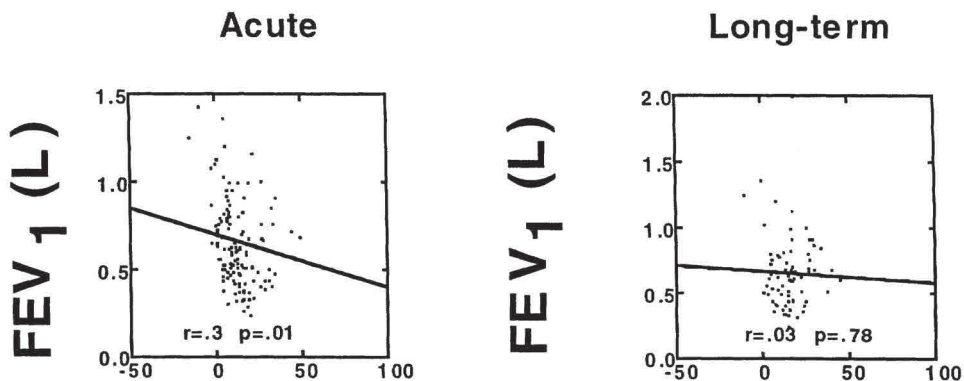

Improvement in Dyspnea Score

FIGURE 2. Relationship between change in FEV_1 from baseline following LVRS vs short term (solid line) and long term (dotted line) improvement in dyspnea scores. *Left:* change in FEV_1 in liters following surgery (y-axis) vs improvement in dyspnea score (x-axis). *Right:* change in percent predicted FEV_1 following surgery (y-axis) vs improvement in dyspnea score (x-axis). Due to large individual variability in dyspnea and FEV_1 response, the association is statistically significant only between change in percent predicted FEV_1 and improvement in dyspnea.
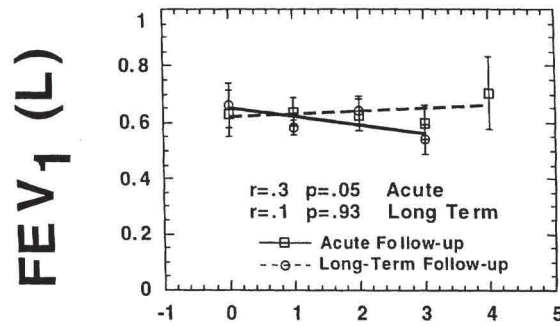
FIGURE 3. *Top:* relationship between baseline FEV_1 vs short-term (solid line) and long-term (dotted line) improvement in dyspnea scores. Change in FEV_1 is shown in liters following surgery (y-axis) vs improvement in dyspnea score (x-axis). *Bottom:* correlation between baseline FEV_1 and improvement in percent predicted FEV_1 as the outcome measure. *Bottom left:* short-term change in FEV_1 following surgery (y-axis) vs improvement in percent predicted FEV_1 (x-axis). *Bottom right:* long-term follow-up change in FEV_1 vs improvement in percent predicted FEV_1.

RESULTS

The mean length of stay for the 139 surviving patients was 8.8 ± 5.6 days (mean$\pm$SD) (range=3 to 49 days). There were six deaths (4.2% operative mortality). Causes of death are summarized in Table 1. Clinical follow-up is available for all patients. Short-term follow-up pulmonary function tests are available for 130 of 139 (94%) surviving patients and showed a mean increase in postoperative FEV_1 of 50% from baseline (Table 2). Spirometry and lung volumes improved significantly at the time of short-term follow-up as summarized in Table 2. D_{CO} did not change at short-term follow-up. Long-term follow up pulmonary function tests were available for 84 (65%) patients and continued to show similar improvement in objective lung function results (Ta-

ble 3). Though only modest changes in D_{CO} were seen, improvement was statistically significant at the time of long-term follow-up.

Baseline dyspnea scores averaged 3.0 ± 0.7 (mean$\pm$SD) and improved to 1.7 ± 0.8 short term ($p<0.0001$) and 1.3 ± 0.9 long term ($p<0.0001$ compared to baseline). Distribution of dyspnea score improvement short term and long term is shown in Figure 1.

Baseline FEV_1 was weakly associated with resting dyspnea score ($r=0.27$, $p=0.06$). Improvement in FEV_1 was associated with improvement in the dyspnea score ($r=0.3$, $p=0.3$, both short and long term) though considerable individual variability was seen between FEV_1 and dyspnea response (Fig 2). When improvement in FEV_1 was measured as change in FEV_1 percent predicted, the correlation with im-

provement in dyspnea scores was closer (r=0.4, p<0.01, short term; r=0.4, p=0.1, long term) (Fig 2).

Baseline FEV_1 did correlate weakly with improvement in dyspnea score short term (r=0.3, p<0.05, short term), with a tendency toward greater improvement in those with lower initial FEV_1. However, this relationship was not seen at long-term follow-up (r=0.1, p=0.9, long term) (Fig 3). A similar pattern was seen when change in FEV_1 was examined as the outcome variable (Fig 3).

When the relationship between presenting measures of hyperinflation and dyspnea response was examined, there were definite trends toward decreased dyspnea response in patients with the greatest degrees of hyperexpansion. At long-term follow-up, baseline residual volume (RV) was neg-

atively associated with improvement in dyspnea score (r=0.4, p<0.05), with a tendency toward greater improvement in those with lower initial RVs (Fig 4). A trend toward greater improvement in FEV_1 was also seen in patients with lower RVs (Fig 4). Greater improvement in dyspnea short and long term was seen in patients with lower presenting RV/total lung capacity (TLC) ratios (r=0.4, p=0.02, short term; r=0.4, p<0.05, long term) (Fig 5).

A similar but not statistically significant trend toward decreased dyspnea response was seen in patients with higher preoperative TLC and trapped gas volumes (Fig 6).

Despite the negative association between severity of hyperinflation and dyspnea response, some patients with severe hyperinflation improved substantially. There were 36 patients with preoperative
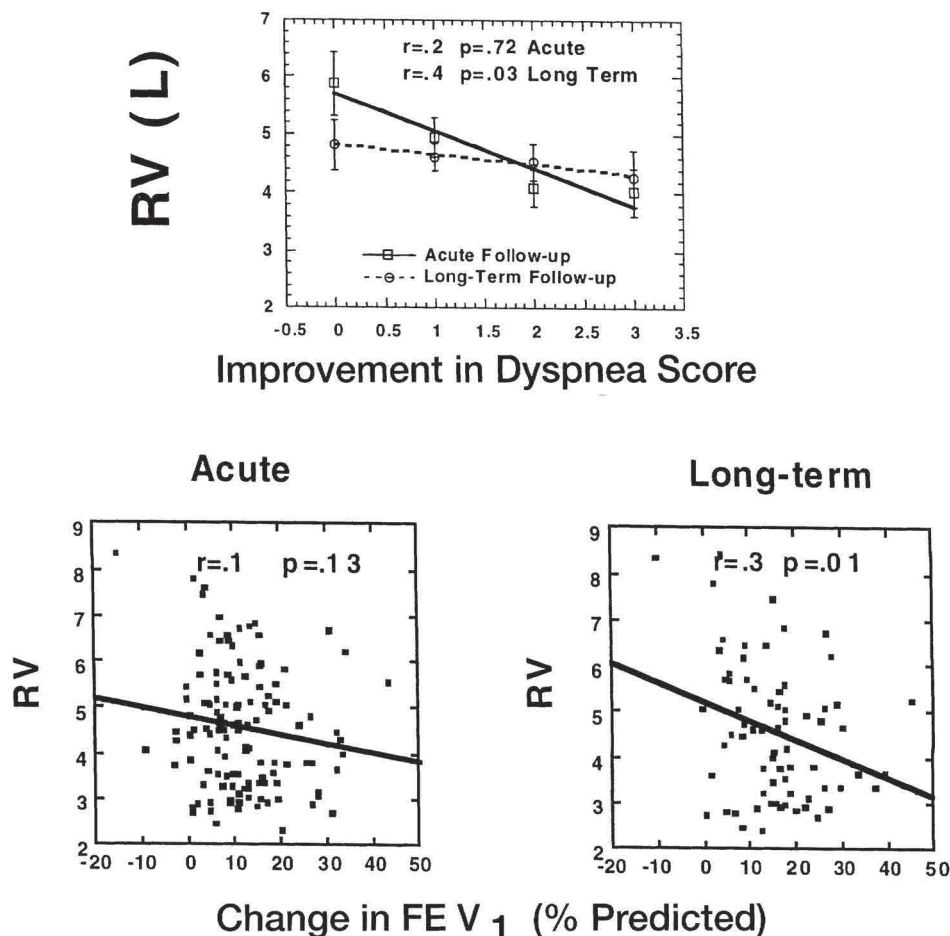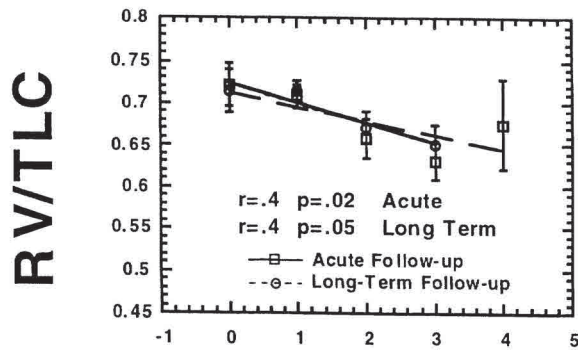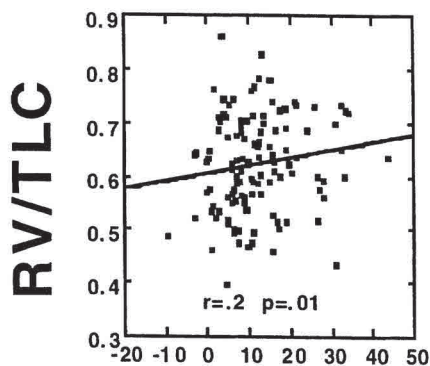

FIGURE 4. *Top:* relationship between baseline RV vs short-term (solid line) and long-term (dotted line) improvement in dyspnea scores. Change in RV is shown in liters following surgery (y-axis) vs improvement in dyspnea score (x-axis). *Bottom:* correlation between baseline RV and improvement in percent predicted RV as the outcome measure. *Bottom left:* short-term change in RV following surgery (y-axis) vs improvement in percent predicted RV (x-axis). *Bottom right:* change in RV vs long-term improvement in percent predicted RV. A significant trend toward greater improvement in dyspnea and FEV_1 long term was seen in patients with lower baseline RV.
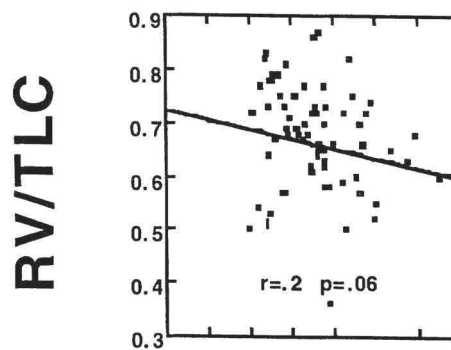
FIGURE 5. *Top:* relationship between baseline RV/TLC ratio vs short-term (solid line) and long-term (dotted line) improvement in dyspnea scores. Change in RV/TLC ratio is shown in liters following surgery (y-axis) vs improvement in dyspnea score (x-axis). *Bottom:* correlation between baseline RV/TLC ratio and improvement in percent predicted RV/TLC ratio. *Bottom left:* change in RV/TLC ratio following surgery (y-axis) short term vs improvement in percent predicted RV/TLC ratio (x-axis). *Bottom right:* long-term change in RV/TLC ratio vs improvement in percent predicted RV/TLC ratio.

RV/TLC >0.7. Of those patients, 8 of 36 (22%) improved by two or more dyspnea scores.

Thirty-seven patients (28% of operative patients) had minimal or no improvement in FEV_1 postoperatively (defined as <10% increase in FEV_1). Yet, 10 of those 37 patients (27%) improved by two or more dyspnea scores.

DISCUSSION

This study was undertaken to investigate semi-quantitative dyspnea response to LVRS. Preoperatively, dyspnea scores were significantly associated with baseline FEV_1. However, as expected, there was considerable variability between individual resting dyspnea scores and baseline FEV_1.

Evaluated as a group, improvement in dyspnea scores postoperatively was also loosely associated with improvement in FEV_1, and more closely with improvement in FEV_1 percent predicted. Again considerable individual variability was seen between dyspnea and FEV_1 improvement.

A substantial fraction (27%) of patients with minimal improvement in FEV_1 had marked improvement (>2 U) in dyspnea scores. This may be the result of placebo effect or from physiologic response not reflected in FEV_1 changes. This subgroup of patients with limited FEV_1 response and marked dyspnea improvement illustrates potential limitations of using objective improvement in FEV_1 as the sole outcome measure, and difficulties in developing absolute selection criteria cutoffs.
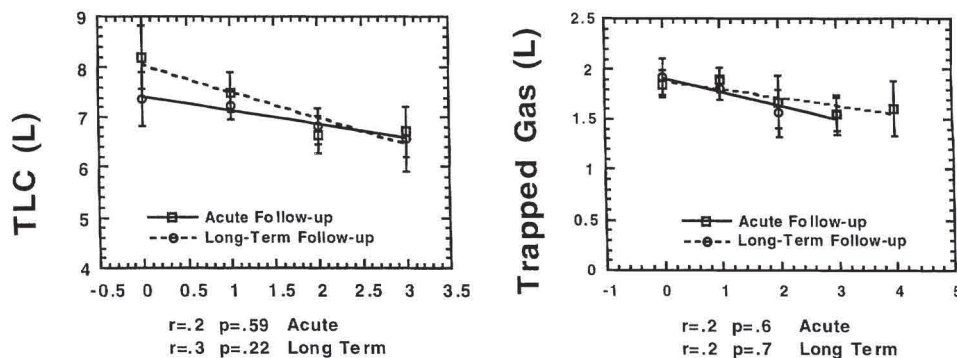
Improvement in Dyspnea Score

FIGURE 6. *Left:* relationship between baseline TLC vs short-term (solid line) and long-term (dotted line) improvement in dyspnea scores. Preoperative TLC in liters (y-axis) vs improvement in dyspnea score (x-axis) is shown. *Right:* relationship between baseline trapped gas volume in liters (measured as the differences between plethysmographic and helium dilution functional residual capacity) vs short-term (solid line) and long-term (dotted line) improvement in dyspnea scores. The trends are not statistically significant.

In this preselected patient group (required to have hyperinflation), those with the greatest degrees of preoperative hyperinflation (assessed as RV, TLC, or RV/TLC ratios) appeared to have less improvement in dyspnea following LVRS than those with lesser degrees of hyperinflation. This somewhat surprising result contrasts with a more general lack of correlation between presenting physiologic function and improvement following LVRS when change in FEV_1 is used as the primary outcome variable in this patient series. The negative correlation between hyperinflation and dyspnea response in this study could be artifactual, given the relatively weak associations seen. However, in the extremes of hyperinflation, both improvement in dyspnea and FEV_1 appear slightly reduced. These findings could reflect the degree of underlying emphysema and the amount of functional lung available postoperatively. Such findings could suggest that there may be limits on the severity of preoperative disease for optimal response.

Despite the trend toward reduced dyspnea response with greater degrees of hyperinflation, >25% of patients with the highest degrees of hyperinflation did improve significantly in dyspnea scores and objective pulmonary function measures. Thus, it remains difficult to set firm limits on hyperinflation for selection criteria from these data.

The findings of this study are limited by the fact that the MMRC dyspnea scale is subjective and relatively simplistic. Other dyspnea indexes with more specific applicability toward LVRS patients may yield different results. O'Donnell et al[19] investigated associations between relief of dyspnea follow-ing LVRS and bullectomy in eight patients and pulmonary function using transitional dyspnea index measurements. They found very close correlation between improvement in transitional dyspnea index and change in FVC (r=0.94, p<0.05) or change in FEV_1 (r=0.77, p<0.05) in independent analyses. It is uncertain why they found much closer association between subjective and objective response than was seen in our study. Use of the transitional dyspnea index rather than the modified dyspnea index may explain some of the differences. Additionally, there were a very small number of patients described by O'Donnell et al[19] with some undergoing decompressive bullectomy that may have increased the observed correlations. Future studies using multiple subjective outcome measurement tools may be needed to clarify these issues.

The preselection of patients based on specific radiographic and pulmonary function criteria for inclusion in our study protocol[5,11] narrows the range of disease presentation of patients enrolled. This could predispose to misleading apparent relationships between presenting variables and outcomes due to the limited parameter ranges for the study variables. Finally, the proportion of patients missing long-term follow-up in this study may also have biased results in our study. Patients in this study did not undergo rehabilitation until the postoperative period. Thus, effects of postoperative rehabilitation would be included in the overall protocol subjective response assessment of these patients. Different results may be seen in programs involving preoperative rehabilitation.

Despite these limitations, some trends appear to

emerge from this study. Overall, dyspnea improvement was associated with improvement in FEV_1 following LVRS. However, the correlation was weak, with considerable individual variability between dyspnea response and spirometry improvement. Therefore, careful evaluation of subjective and objective outcomes will be needed to assess LVRS response. If these findings are confirmed in future studies, selection criteria may need to incorporate these factors into the decision-making process regarding optimal surgical candates.

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