Does lobectomy for lung cancer in patients with chronic obstructive pulmonary disease affect lung function? A multicenter national study

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Objective: The purpose of this study was to evaluate the effect of lobectomy on pulmonary function in patients with chronic obstructive pulmonary disease.

Methods: One hundred thirty-seven patients were analyzed; 49 had normal pulmonary function tests, and 88 had chronic obstructive pulmonary disease. Different functional parameter groups were identified: obstructive (forced expiratory volume in 1 second [FEV_1], forced expiratory volume in 1 second/forced vital capacity [FEV_1/FVC], and chronic obstructive pulmonary disease index), hyperinflation (residual volume and functional residual capacity), and diffusion (transfer factor of the lung for carbon monoxide). Also, the ratio between observed and predicted postoperative FEV_1 was calculated.

Results: In patients with preoperative FEV_1 greater than 80% of predicted, postoperative FEV_1/FVC slightly but not significantly decreased, and postoperative FEV_1 significantly decreased. In patients with preoperative FEV_1 less than 65%, postoperative FEV_1 and FEV_1/FVC significantly increased. In patients with preoperative FEV_1/FVC greater than 70%, postoperative FEV_1 and FEV_1/FVC significantly decreased. In patients with preoperative FEV_1/FVC less than 70%, postoperative FEV_1/FVC increased, and FEV_1 remained unchanged. In patients with a chronic obstructive pulmonary disease index greater than 1.5, postoperative FEV_1 and FEV_1/FVC significantly decreased, whereas in patients with a chronic obstructive pulmonary disease index less than 1.5, postoperative FEV_1/FVC significantly increased and FEV_1 remained unchanged. In patients with residual volume and functional residual capacity greater than 115% and transfer factor of the lung for carbon monoxide less than 80% of predicted, postoperative FEV_1 diminished less (not significant) compared with patients who had residual volume and functional residual capacity less than 115% ($P = .0001$). Observed postoperative/predicted postoperative FEV_1 was higher if FEV_1/FVC was less than 55% (1.46), if FEV_1 was less than 80% of predicted (1.21), or if the chronic obstructive pulmonary disease index was less than 1.5 (1.17).

Conclusions: Patients with mild to severe chronic obstructive pulmonary disease could have a better late preservation of pulmonary function after lobectomy than healthy patients.

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Lung cancer remains an important cause of death among smokers, and this condition is often associated with chronic obstructive pulmonary disease (COPD). Surgical resection offers the best chance for curing lung cancer, and lobectomy is the most frequent operation performed. Postoperative respiratory failure is a widely known complication that limits parenchymal resection in patients with COPD; exclusion criteria have been adopted to evaluate these patients, and

Abbreviations and Acronyms

COPD = chronic obstructive pulmonary disease
FEV_1 = forced expiratory volume in 1 second
FEV_1(%) = FEV_1 percentage of predicted
FRC = functional residual capacity
FVC = forced vital capacity
PFT = pulmonary function test
RV = residual volume
TLCO = transfer factor of the lung for carbon monoxide

most of them outline the importance of preoperative forced expiratory volume in 1 second (FEV_1), FEV_1/forced vital capacity (FVC), and transfer factor of the lung for carbon monoxide (TLCO). The 6-minute walking test, Master test, maximum oxygen consumption per unit time test, and prediction of postoperative FEV_1 by different formulas are also used to evaluate postoperative risk.[1] More recently, lung volume reduction surgery and recent reports on COPD patients operated on for lung cancer have revised the lung function evaluation and predictors for COPD patients who are candidates for lung resection.[2-7] Unfortunately, most of these reports on lobectomy in patients with airway obstruction reviewed a limited number of cases, and the selection of operable patients remains a great challenge.[2-7] The goal of this study was to evaluate the effect of lobectomy on pulmonary function in COPD patients.

Materials and Methods

This was a retrospective, multicenter national study. Data from 7 Italian hospitals with thoracic surgery experience (including lung transplantation, lung volume reduction surgery, or both) were collected. All patients with at least 1 preoperative and 1 postoperative pulmonary function evaluation who underwent lobectomy for lung cancer from March 1997 to March 2003 were considered; usually no more than a 6-month period was analyzed for each center. Postoperative pulmonary function tests (PFTs) were performed not earlier than the third postoperative month and not later than the 15th month. Patients who received any adjuvant or neoadjuvant therapy were not considered eligible for this study. One hundred thirty-seven patients met the criteria (35 women and 102 men); 49 had normal static and dynamic pulmonary function, according to European Respiratory Society 1993, whereas 88 had COPD ranging from grade 1 to 3 according to Global Initiative on Obstructive Lung Disease guidelines. Hyperinflation was considered if residual volume (RV) and functional residual capacity (FRC) were greater than 115% of predicted and vital capacity was in the normal limit, and impairment of gas transfer was defined as TLCO less than 80% of predicted. PFTs were performed in different laboratories by using the European Respiratory Society 1993 predicting values. All tests were performed with the same methods, and static volumes were measured by the nitrogen washout method. Patients were evaluated by radiograph and computed tomographic scan to stage the tumor, to ascertain the presence of a flattening diaphragm, and to distinguish bullous from nonbullous emphysema.

TABLE 1. Study population

Variable	COPD (88 patients)	Normal (49 patients)	*P* value
FVC%	96 ± 17	102 ± 16	$P = .04$
FEV_1(%)	63 ± 8	98 ± 15	$P = .00001$
FEV_1/FVC	58 ± 8	76 ± 5	$P = .00001$
COPD index	1.28 ± 0.26	1.71 ± 0.23	$P = .00001$
RV%	117 ± 26	103 ± 27	$P = .001$
TLC%	100 ± 13	99 ± 13	$P = .6$
TLCO%	69 ± 17	85 ± 22	$P = .00001$
Pao_2-pre (mm Hg)	80 ± 9	84 ± 8	$P = .01$
$Paco_2$-post (mm Hg)	36 ± 5	39 ± 3	$P = .002$

COPD, Chronic obstructive pulmonary disease; *FVC,* forced vital capacity; *FEV_1(%),* forced expiratory volume in 1 second percentage of predicted; *RV,* residual volume; *TLC,* total lung capacity; *TLCO,* transfer factor of the lung for carbon monoxide.

Ninety-two patients underwent upper lobectomy, 37 underwent lower lobectomy, and 8 underwent middle lobectomy; 17% of these patients had bullous emphysema, and 32% had diaphragmatic flattening. Thirty-one had squamous cell cancer, 72 had adenocarcinoma, 5 had small cell lung cancers, and 4 had carcinoid tumors. In 25 patients, histologic results were not available or were uncertain.

In all patients, the observed postoperative FEV_1 was compared with the predicted postoperative FEV_1 by the observed postoperative/predicted postoperative FEV_1 ratio. The predicted postoperative FEV_1 value was calculated with the following equation:

$$\text{Predicted postperative } FEV_1 = \text{Preoperative } FEV_1 \times (\text{No. of segments remaining}/\text{Total no. of segments})$$

The COPD index was calculated according to Korst and associates[5] to evaluate the severity and purity of obstructive airway disease; the preoperative FEV_1 (percentage of predicted in decimal form; FEV_1%) was added to the preoperative ratio of FEV_1 to FVC. Patients with the lowest COPD index are those with the most severe airway obstruction. Patients with a COPD index greater than 1.5 do not have obstructive diseases.

The mean age of COPD patients was 68 ± 15 years, and the mean age of non-COPD patients was 66 ± 13 years (mean ± SD). FEV_1 ranged from 980 mL (34% of predicted) to 4050 mL (115% of predicted) in the entire study population. Preoperative functional data in healthy and COPD patients are shown in Table 1.

Statistical analysis included the paired *t* test for comparison of preoperative and postoperative mean values, because the patients were observed before and after a single treatment. Smith's statistical software package version 2.5, 2001 (by G. Smith, Claremont, Calif) was used for all analyses. Statistical methods included multiple comparisons of interrelated parameters, and this may cause problems with determining the appropriate significance level. To overcome this problem, we computed the number of comparisons for each category group (each table) and decreased the significance level by an appro-

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TABLE 2. FEV_1 group data

Variable	FEV_1 <65%	FEV_1 >65% <80%	FEV_1 ≥80%	FEV_1 <80%
FEV_1-pre (%)	56 ± 7	69 ± 3	98 ± 15	63 ± 8
FEV_1-post (%)	64 ± 11	65 ± 17	78 ± 16	65 ± 14
	P = .0004	*P* = .17	*P* = .0001	*P* = .29
FEV_1/FVC-pre	55 ± 10	65 ± 10	70 ± 8	59 ± 11
FEV_1/FVC-post	64 ± 11	66 ± 16	66 ± 10	65 ± 14
	P = .0004	*P* = .7	*P* = .06	*P* = .004
RV-pre (%)	117 ± 27	114 ± 22	108 ± 30	116 ± 24
RV-post (%)	94 ± 18	91 ± 24	84 ± 27	93 ± 20
	P = .0003	*P* = .0003	*P* = .0003	*P* = .00001
Pa_{O_2}-pre (mm Hg)	83 ± 9	79 ± 8	84 ± 8	80 ± 9
Pa_{O_2}-post (mm Hg)	79 ± 9	78 ± 8	83 ± 9	79 ± 9
	P = .7	*P* = .6	*P* = .7	*P* = .5

FEV_1, Forced expiratory volume in 1 second; *FVC*, forced vital capacity; *RV*, residual volume.

TABLE 3. FEV_1/FVC group data

Variable	FEV_1/FVC <55%	FEV_1/FVC >55 <70%	FEV_1/FVC ≥70%	FEV_1/FVC <70%
FEV_1-pre (%)	60 ± 13	76 ± 14	96 ± 21	70 ± 67
FEV_1-post (%)	65 ± 12	69 ± 17	78 ± 16	67 ± 16
	P = .1	*P* = .01	*P* = .00007	*P* = .6
FEV_1/FVC-pre	48 ± 15	63 ± 4	76 ± 5	58 ± 8
FEV_1/FVC-post	67 ± 16	64 ± 14	66 ± 10	65 ± 13
	P = .00002	*P* = .6	*P* = .00001	*P* = .0003
RV-pre (%)	123 ± 25	114 ± 26	103 ± 27	117 ± 26
RV-post (%)	95 ± 18	90 ± 23	84 ± 27	93 ± 20
	P = .00009	*P* = .000001	*P* = .0007	*P* = .000001
Pa_{O_2}-pre (mm Hg)	83 ± 9	79 ± 8	84 ± 8	80 ± 9
Pa_{O_2}-post (mm Hg)	79 ± 9	78 ± 8	83 ± 9	79 ± 9
	P = .09	*P* = .5	*P* = .5	*P* = .4

FEV_1, Forced expiratory volume in 1 second; *FVC*, forced vital capacity; *RV*, residual volume.

priate factor accordingly. In particular, for 4 × 4 comparisons, the significance level was decreased by 20-fold (from .05 to .002), and for 4 × 2 comparisons, the significance level was decreased by 10-fold (from .05 to .005).

Results

Flow volume and blood gas analyses were available in all patients, dynamic and static lung volumes were available in 108 patients, and carbon monoxide diffusion capacity was available in 89 patients. Preoperative chest radiographs and computed tomographic scans were examined in most COPD patients to consider diaphragmatic flattening and bullous emphysema. No postoperative differences were observed with regard to the lobectomy area because upper, lower, or middle lobe resection did not influence the postoperative FEV_1 or FEV_1/FVC change.

Patients were divided into different groups to characterize the grade of airway obstruction, the grade of hyperinflation, and the grade of carbon monoxide diffusion capacity. Changes of functional variables before and after operation were then analyzed.

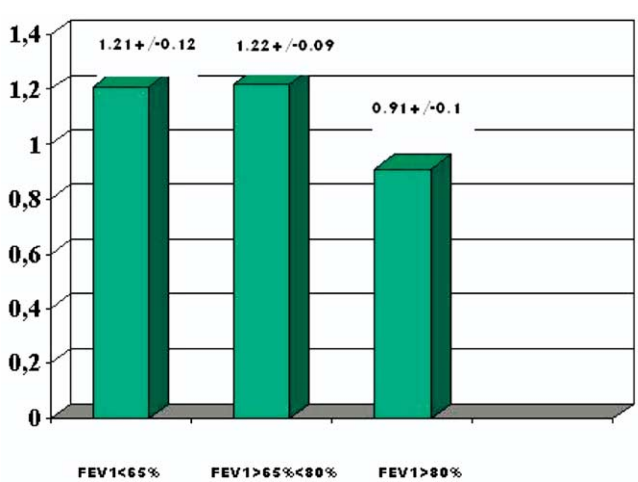

Figure 1. Observed postoperative/predicted postoperative FEV_1 ratio according to FEV_1(%).

Obstructive Parameters (FEV_1[%], FEV_1/FVC, and COPD Index)

We analyzed patients by considering 3 airway obstruction parameters: FEV_1(%), FEV_1/FVC, and COPD index. For FEV_1(%), FEV_1 group 1 included 65 patients with an FEV_1 of 80% or more; FEV_1 group 2 included 72 patients with FEV_1 less than 80%; FEV_1 subgroup 2a included 37 patients with FEV_1 less than 65%; and FEV subgroup 2b included 35 patients with FEV_1 between 65% and 79%. Among patients in FEV_1 group 1, the postoperative FEV_1/FVC slightly but not significantly decreased, whereas FEV_1 significantly decreased and Pa_{O_2} remained unchanged. In FEV_1 group 2, FEV_1/FVC significantly increased, and FEV_1 and Pa_{O_2} remained mostly unchanged. In FEV_1 subgroup 2a, FEV_1/FVC and FEV_1 significantly increased, whereas in FEV_1 subgroup 2b, both FEV_1/FVC and FEV_1 remained unchanged. RV significantly decreased on postoperative follow-up in all groups examined (Table 2). The observed postoperative/predicted postoperative ratio for FEV_1 in FEV_1 group 1 was lower (0.91 ± SD 0.1) than in

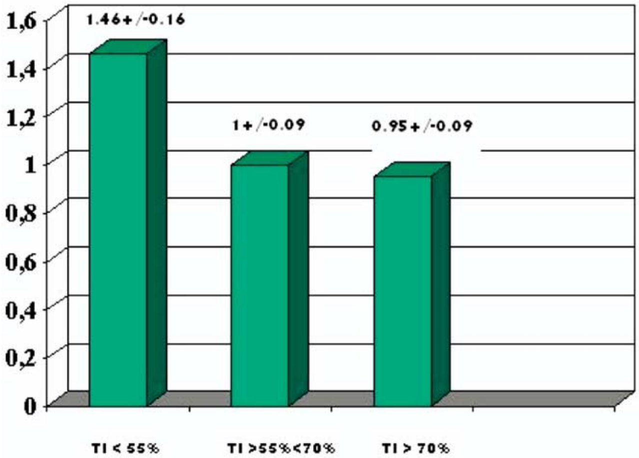

Figure 2. Observed postoperative/predicted postoperative FEV_1 ratio according to TI. ***TI,*** **FEV_1/FVC.**

FEV_1 group 2a (1.21 ± SD 0.12) and FEV_1 group 2b (1.22 ± SD 0.09; Figure 1).

For FEV_1/FVC, FEV_1/FVC group 1 included 49 patients with FEV_1/FVC greater than 70%; FEV_1/FVC group 2 included 88 patients with FEV_1/FVC less than 70%; FEV_1/FVC subgroup 2a included 29 patients with FEV_1/FVC less than 55%; and FEV_1/FVC subgroup 2b included 59 patients with FEV_1/FVC between 55% and 69%. In FEV_1/FVC group 1, FEV_1 and FEV_1/FVC significantly decreased, whereas PaO_2 remained unchanged; in FEV_1/FVC group 2, FEV_1 and PaO_2 remained mostly unchanged, whereas FEV_1/FVC significantly increased. It is interesting to note that in FEV_1/FVC subgroup 2a, FEV_1 slightly increased (not significant) and FEV_1/FVC significantly increased, but in FEV_1/FVC subgroup 2b, FEV_1 decreased and FEV_1/FVC remained unchanged (Table 3). The observed postoperative/predicted postoperative ratio for FEV_1 in FEV_1/FVC subgroup 2a was significantly higher (1.46 ± SD 0.16) than in FEV_1/FVC subgroup 2b (1 ± SD 0.09) and FEV_1/FVC group 1 (0.95 ± SD 0.09; Figure 2).

COPD index group 1 included 52 patients with an index greater than 1.5, and COPD index group 2 included 85 patients with an index less than 1.5. In COPD group 1, FEV_1/FVC and

TABLE 4. COPD index group data

Variable	COPD index <1.5	COPD index >1.5
FEV_1-pre (%)	65 ± 10	99 ± 17
FEV_1-post (%)	66 ± 15	77 ± 16
	P = .6	*P* = .000001
FEV_1/FVC-pre	58 ± 10	72 ± 8
FEV_1/FVC-post	65 ± 13	65.9 ± 10
	P = .0001	*P* = .001
RV-pre (%)	116 ± 23	109 ± 37
RV-post (%)	93 ± 20	84 ± 27
	P = .000001	*P* = .0002
PaO_2-pre (mm Hg)	79.9 ± 9	85 ± 8
PaO_2-post (mm Hg)	79.5 ± 9	83 ± 9
	P = .7	*P* = .2

COPD, Chronic obstructive pulmonary disease; *FEV_1*, forced expiratory volume in 1 second; *FVC,* forced vital capacity; *RV,* residual volume.

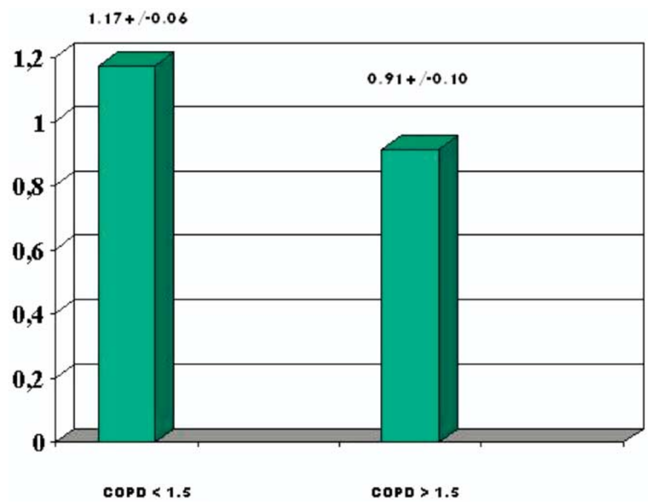

Figure 3. Observed postoperative/predicted postoperative FEV_1 ratio according to COPD index.

TABLE 5. RV group data

Variable	RV <115%	RV >115%
FEV_1-pre (%)	89 ± 21	73.8 ± 19
FEV_1-post (%)	79 ± 17	67 ± 14
	P = .007	*P* = .06
FEV_1/FVC-pre	69 ± 12	59 ± 10
FEV_1/FVC-post	68.9 ± 10	60 ± 11
	P = .1	*P* = .06
RV-pre (%)	91 ± 16	133 ± 22
RV-post (%)	78 ± 22	104 ± 18
	P = .0006	*P* = .00001
Observed postop/predicted postop FEV_1	1.02 ± 0.084	1.08 ± 0.091
PaO_2-pre (mm Hg)	84 ± 9	81 ± 10
PaO_2-post (mm Hg)	80 ± 8	81 ± 9
	P = .06	*P* = .1

RV, Residual volume; *FEV_1*, forced expiratory volume in 1 second; *FVC,* forced vital capacity.

TABLE 6. FRC group data

Variable	FRC <115%	FRC >115%
FEV_1-pre (%)	87 ± 20	79 ± 24
FEV_1-post (%)	74 ± 17	72 ± 16
	P = .0005	P = .07
FEV_1/FVC-pre	70 ± 12	60 ± 11
FEV_1/FVC-post	68 ± 11	61 ± 11
	P = .3	P = .6
RV-pre (%)	88.9 ± 14	119 ± 4
RV-post (%)	76 ± 22	103 ± 14
	P = .0004	P = .00001
Observed postop/predicted postop FEV_1	1.03 ± 0.089	1.04 ± 0.082
Pa_{O_2}-pre (mm Hg)	83 ± 9	81 ± 9
Pa_{O_2}-post (mm Hg)	80 ± 10	82 ± 10
	P = .1	P = .5

FRC, Functional residual capacity; *FEV_1,* forced expiratory volume in 1 second; *FVC,* forced vital capacity; *RV,* residual volume.

TABLE 7. TLCO group data

Variable	DLCO<80%	DLCO>80%
FEV_1-pre (%)	68 ± 15	96 ± 20
FEV_1-post (%)	63 ± 14	83 ± 15
	P = .07	P = .003
FEV_1/FVC-pre	58 ± 12	70 ± 9
FEV_1/FVC-post	60 ± 13	69 ± 8
	P = .4	P = .6
Observed postop/predicted postop FEV_1	1.07 ± 0.1	1.02 ± 0.08
Pa_{O_2}-pre (mm Hg)	78 ± 8	84 ± 8
Pa_{O_2}-post (mm Hg)	79 ± 9	81 ± 9
	P = .5	P = .1

TLCO, Transfer factor of the lung for carbon monoxide; *DLCO,* carbon monoxide diffusion in the lung; *FEV_1,* forced expiratory volume in 1 second; *FVC,* forced vital capacity.

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FEV_1 significantly decreased, whereas in COPD group 2, FEV_1/FVC significantly increased, and FEV_1 remained unchanged (Table 4). The observed postoperative/predicted postoperative ratio for FEV_1 in group 2 (1.17 ± SD 0.06) was higher than in group 1 (0.91 ± SD 0.1; Figure 3).

Hyperinflation Parameters (RV and FRC)

RV group 1 included 53 patients with RV greater than 115%, and RV group 2 included 55 patients with RV less than 115%. In RV group 1, FEV_1 slightly (P = .06) decreased, and FEV_1/FVC remained unchanged; in RV group 2, FEV_1 significantly decreased, and FEV_1/FVC remained unchanged (Table 5).

FRC group 1 included 55 patients with FRC greater than 115%, and FRC group 2 included 53 patients with FRC less than 115%. In FRC group 1, FEV_1 and FEV_1/FVC remained statistically unchanged, whereas in FRC group 2, FEV_1 decreased, and FEV_1/FVC remained unchanged (Table 6).

Alveolar Diffusion Parameter (TLCO)

TLCO group 1 included 35 patients with a TLCO of 80% or more, and TLCO group 2 included 54 patients with a TLCO less than 80%. In TLCO group 1, FEV_1 significantly decreased, whereas FEV_1/FVC did not change; in TLCO group 2, FEV_1 decreased, and FEV_1/FVC increased, but these differences were not significant (Table 7).

Discussion

Our results suggest that pulmonary function after lobectomy improves—or at least diminishes less—in COPD patients as compared with non-COPD patients and that this phenomenon is more evident in patients with more severe airway obstruction and hyperinflation. In particular, some of the preoperative functional parameters seem to be good predictors of late postoperative function improvement (or minimal change). FEV_1/FVC improves if preoperative FEV_1 is less than 65% of predicted, if preoperative FEV_1/FVC is less than 55%, or if the COPD index is less than 1.5, whereas FEV_1/FVC worsens if the preoperative FEV_1/FVC is more than 70% and the COPD index is more than 1.5. FEV_1 improves only if the preoperative FEV_1 is less than 65%; it always worsens when airway flow indexes, diffusion capacity, and RV or FRC are in the normal range. Neither obstruction parameters (FEV_1 and FEV_1/FVC) nor diffusion capacity provides information on postoperative RV changes, because this index always worsens after operation and seems unrelated to these indexes. No change was observed before and after operation regarding oxygen exchange, and these data are unrelated to the preoperative functional data. It is interesting to note that the observed postoperative FEV_1 is better than the predicted postoperative FEV_1 if FEV_1/FVC is less than 70%, if FEV_1 is less than 80% of predicted, or if the COPD index is less than 1.5. TLCO and RV do not influence these variations. An important and practical consideration is that the predicted postoperative FEV_1 underestimates the observed postoperative FEV_1 by approximately 45% if the preoperative FEV_1/FVC is less than 55% and by approximately 20% if the preoperative FEV_1 is less than 80% of predicted.

Preoperative evaluation for lung resection in lung carcinoma has been well studied, and many reports have been published to evaluate the early and late operative risk for patients with obstructive airway diseases.[8-11] Advances in anesthesia and intensive care management can improve survival in some patients, but respiratory impairment in the long term remains a problem. Although many PFTs and exercise tests have been used to evaluate risk among these patients, obstructive indexes such as FEV_1 and FEV_1/FVC are still the most used criteria to exclude these patients from surgery. In general practice, a preoperative FEV_1 less than 1.5 L or 60% of predicted or a predicted postoperative FEV_1 less than 800 mL or 40% of predicted is considered a high risk for lobectomy.[1] Lung volume reduction surgery has demonstrated that lung function and dyspnea can improve after removal of portions of the lung parenchyma in patients with emphysema. Pulmonary nodule resection and lung volume reduction are feasible and are associated with minimal morbidity and significant improvement in pulmonary function.[12-17]

These data suggest that limited parenchymal resection, as well as lobectomy, might be beneficial for preserving lung function in patients with COPD. Previous investigators have demonstrated the feasibility of limited resection in patients with respiratory impairment.[18-21] Errett and colleagues[21] noted little difference in postoperative outcome in individuals with moderate airflow obstruction (mean FEV_1 of 1.56 L); Miller and Hatcher[19] noted little perioperative difficulty in individuals with severe airflow obstruction (FEV_1 less than 1.0 L) who underwent limited resection. More recently, it has been reported that pulmonary function might remain unchanged or even improve after lobectomy in COPD patients.[2-5] Korst and colleagues[5] reported that the mean change in FEV_1 after lobectomy was +3.7% among patients with a preoperative FEV_1 of less than or equal to 60% of predicted and was −15.7% for patients with a mean preoperative FEV_1 of 69% of predicted. Sekine and associates[2] documented that the postoperative ventilatory function in COPD patients who had lower or middle/lower lobectomies was better preserved than predicted.

The most important consideration from our study, as well as from other similar studies,[2-5] is that some patients will have improved obstructive indexes after lobectomy: the increase of FEV_1/FVC means that airway caliber or elastic recoil improves after resection. Our patients were identified retrospectively; therefore, we cannot know the precise nature of COPD and of the lung tissue resected (apart from the presence of bullae in a small group), but the consistent number of our sample implies that these results are not attributable to lung volume reduction surgery. Nevertheless, we can speculate that the mechanism of this airway improvement could be the relief of hyperinflation and/or chest wall mechanics, although this improvement should not be related to emphysematous lungs. Resection of a dead space in case of local pulmonary artery involvement could be another way to explain functional amelioration in some cases.

This study has several limitations. We analyzed only patients who had been discharged from the hospital, so we did not consider early postoperative mortality or early functional impairment. Furthermore, this was a retrospective study limited to the involvement of 7 different hospitals and selection of patients from different periods. Patients with available postoperative PFTs over a limited period (from the 3rd to 15th postoperative months) and in a consecutive temporal selection were involved. Patients first referred to the respiratory specialist always performed postoperative PFTs, but patients referred to a surgeon usually did not perform postoperative PFTs. Therefore, the selection criteria are related to the specialist who first visited the patient, and this was usually related to the practitioner who addressed the patient for further evaluation of a pulmonary lesion.

In conclusion, patients with mild to severe COPD could present a better late preservation of pulmonary function after lobectomy compared with healthy patients. This minimal deterioration or improvement of airway function seems to be related to preoperative obstructive indexes.

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