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Pulmonary lobectomy for lung cancer: a prospective study to compare patients with forced expiratory volume in 1 s more or less than 80% of predicted

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Abstract

Objective: To compare post-operative course, lung function and survival of lung cancer patients with a forced expiratory volume in 1 s (FEV1) more or less than 80% of predicted submitted to lobectomy. **Methods**: The data of patients undergoing lobectomy for non small cell carcinoma at the Thoracic Surgery Unit of the Ospedale Maggiore Policlinico of Milan, Italy, were prospectively collected. Inclusion criteria were a radical resectable tumor with size less than 2.5 cm, negative mediastinal nodes, capability to complete pulmonary function tests, Exclusion criteria were FEV1 <40% of predicted, pre- or post-operative chemo or radiotherapy, lobe to be resected receiving more than 30% of the perfusion, incapacity to quit smoking. **Results**: Eighty-eight patients entered the study and were divided into two groups according to their FEV1%: 45 patients were included in control group (mean FEV1: 92.2%) and 42 in chronic obstructive pulmonary disease group (mean FEV1: 64.2%). Post-operative complications, operative mortality and actuarial survival were the same in the 2 groups. Six months after lobectomy, the mean changes in FEV1 were −14.9% for first group and −3.2% for second group ($P < 0.001$). **Conclusion**: Lobectomy for cancer can be performed successfully also in selected patients with chronic obstructive pulmonary disease. Post-operative course and survival of these patients is not different from that of patients with normal FEV1, on the contrary, patients with low FEV1 may lose less pulmonary function or even mend it.

Keywords: Non-small cell lung cancer; Surgery; Obstructive lung disease

1. Introduction

Radical surgical resection offers the best chances to cure patients with non-small cell lung cancer (NSCLC) and anatomic lobectomy is still considered the operation of choice [1,2]. Unfortunately, lung cancer has common etiologic factors with Chronic Obstructive Pulmonary Disease (COPD) and therefore many patients with lung cancer are also affected by respiratory insufficiency that precludes surgical resection [3,4]. Until few years ago, patients with low forced expiratory volume in 1 s (FEV1) were denied lobectomy in favor of a more limited resection [5]. However, it has been our clinical experience that in many COPD patients FEV1 does not decrease after lobar resection. This clinical observation together with the experience acquired in lung volume reduction surgery [6] has led us to extend the indications to surgical resection in lung cancer patients with low FEV1 [7].

The purpose of this prospective study was to compare post-operative course, lung function and survival of NSCLC patients with a FEV1 more or less than 80% of predicted who underwent lobectomy at our Institution.

2. Methods

Between September 1997 and June 1999, the data of patients undergoing lobectomy for NSCLC at the Thoracic Surgery Unit of the Ospedale Maggiore Policlinico, University of Milan, Italy, were prospectively collected. Inclusion criteria were a radical resectable tumor with size less than 2.5 cm, negative mediastinal nodes, capability to complete pulmonary function tests (PFTs). Exclusion criteria were pre- or post-operative chemo or radiotherapy, lobe to be resected receiving more than 30% of the perfusion, incapacity to quit smoking, FEV1 lower than 40% of predicted.

Data collected were age, sex, best pre-operative PFTs, perfusion scan results, best post-operative (6 months) PFTs, post-operative complications, clinical course and survival.

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Table 1
Patients characteristics, preoperative lung function and surgical data

	Control group (FEV1 ≥ 80%)	COPD group (FEV1 < 80%)	*P*
Patients number	45	43	–
Age (mean)	60.3 ± 12.2	66 ± 8.1	0.019[a]
Male/female	27/18	26/17	0.8[b]
Mean pre-operative FEV1 (%)	92.2 ± 9.7	64.2 ± 9.3	0.001[c]
Mean pre-operative FVC (%)	97.6 ± 10.3	78.5 ± 15.1	0.001[c]
FEV1/FVC	0.74 ± 0.09	0.64 ± 0.12	0.001[c]
Upper/lower/middle lobectomy	29/15/1	25/16/2	0.8[b]

[a] Mann–Whitney rank sum test.
[b] *t*-test.
[c] Chi-square test.

Since the differential diagnosis of airway obstruction between asthma and COPD is the assessment of reversibility of impaired expiratory air flow, we collected the data of PFTs after bronchodilator administration. In this paper we consider COPD as a pathophysiologic entity characterized by airflow obstruction, including chronic bronchitis and emphysema. Therefore patients were divided into two groups according to their preoperative FEV1 below or above 80% of predicted according to British Thoracic Society guidelines.

The statistical analysis included chi-square test, *t*-test, Mann–Whitney rank sum test, Pearson product moment correlation, multiple linear regression test, Mantel–Haenszel test and Kaplan–Meier test.

3. Results

Among 96 patients satisfying inclusion criteria one was excluded because the affected lobe received more than 30% of lung perfusion, two because FEV1 was lower than 40% of predicted, and five because post-operative continuation of smoking.

Eighty-eight patients completed the study. Thirty-five were women and 53 men. The mean pre-operative FEV1 was 78.5% of predicted (standard deviation: 16.9, median: 80), the mean pre-operative FVC was 88.7% of predicted (standard deviation: 15.9, median: 90).

The patients were divided into two groups according to their preoperative FEV1 in percent of predicted: the first group, control group, included 45 patients with FEV1 ≥ 80%, while the second group, COPD group, included 43 patients with FEV1 ranging from 79 to 40%. Age and sex distribution of the two groups as PFTs parameters are reported in Table 1.

Fifty-four patients underwent to upper lobectomy, 31 to lower lobectomy and three to middle lobectomy. The distribution of the operations between the two groups were homogeneous (Table 1). Mean post-operative hospital stay was 7.6 days (±2.6 days) in COPD group and 7.4 (±2.5 days) in control group. The difference is not statistically significant. Total morbidity rate was 19.3% with no statistically significant difference between the two groups (Table 2). There was no operative mortality in both groups. Post-operative pathologic staging in control group patients was Ia in 25, Ib in 11, IIa in 2, IIb in 7; in COPD group patients it was Ia in 22, Ib in 14, IIa in 4, IIb in 3. The observational analysis did not show a significant difference in survival between control and COPD group, actuarial survival curves are shown in Fig. 1.

The overall change in FEV1% (delta FEV1%) and FVC% (delta FVC%), six months after lobectomy, were $-9.1 \pm 10.7\%$ (mean ± standard deviation) and $-10.7\% \pm 4.5$ respectively. The correlation analysis between delta FEV1% and pre-operative FEV1% reached a statistical significance ($r = -0.443$, $P = 0.0000343$, power = 0.9), multiple regression analysis revealed that the dependent variable delta FEV1% can be predicted by pre-operative FEV1% ($P = 0.038$) but not by age, per cent of perfusion of resected lobe or preoperative FVC%. Analy-

Table 2
Post-operative complications

Complications	Control group (FEV1 ≥ 80%)	COPD group (FEV1 < 80%)	*P*
Air leaks >7 days	6	7	0.9[a]
Post-operative atelectasis	–	1	–
Post-operative bleeding	–	1	–
Contra-lateral pneumothorax	–	1	–
Atrial fibrillation	1	–	
Total	7	10	0.9[a]

[a] Chi-square test.

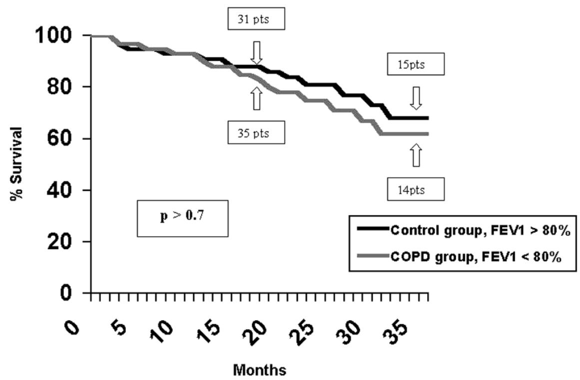

Fig. 1. Actuarial survival of Control and COPD group.

sis of delta FEV1% of the two groups showed a statistically significant lower decrease of FEV1% in COPD group: $-3.2\% \pm 12.8$ versus $-14.9\% \pm 5.2$, $P = 0.001$. Delta FVC% was $-11.6\% \pm 3.6$ in control group and $-9.5\% \pm 5.1$ in COPD group, the difference did not reached statistical significance.

Further stratification of functional data of the COPD group may be useful, and according to the median of preoperative value of FEV1% two subgroups can be identified: mild COPD subgroups of 23 patients with preoperative FEV1% ranging between 79 and 65% of predicted, and severe COPD subgroup of 20 patients with FEV1% ranging between 64 and 40%. Delta FEV1% of mild COPD subgroup was $-8.7\% \pm 6.0$, while delta FEV1% of severe COPD subgroup was $+3.8\% \pm 15.6$, the difference was statistically significant ($P = 0.001$). The two subgroup are not different for type of lobectomy, hospital stay, complication and survival.

4. Discussion

Over the last 40 years several Authors studied morbidity and mortality of patients submitted to pulmonary lobectomy for NSCLC in order to identify a precisely definable point at which the risk of resection is too high [8,9]. Also if several pre-operative function tests such as PFTs, carbon monoxide diffusing capacity, oxygen consumption, 6 min walk test are usually considered to predict post-operative outcome, there is no agreement about the best predictor [10,11]. In our clinical practice for many years we have considered preoperative FEV1 with the commonly accepted lower limit of 1.5 l corresponding to 60–65% of predicted [5] or, more recently, the predicted postoperative FEV1 (ppoFEV1) calculated on the real function of the resected lung segments based on perfusion/ventilation scan accepting a lower limit of 0.8 l corresponding to 30–35% of predicted [12,13]. However, it is a common experience that the ppoFEV1 is often very different from the measured post-operative FEV1, above all in patients affected by COPD with low preoperative FEV1 [14,15]. Moreover, due to the advances in intra- and post-operative care and the experience in lung volume reduction surgery, several patients with a pre-operative FEV1 lower than 1.5 l or a ppoFEV1 lower than 0.8 l currently undergo lobectomy with successful outcome.

This prompted us to prospectively collect pre-operative and post-operative data of patients undergoing lobectomy for NSCLC, including COPD patients. Despite several efforts, some disagreement still surround the term of COPD: practically we consider COPD a functional disorder so that its presence and severity are determined by PFTs. The test most commonly used to assess ventilatory function for COPD is FEV1 and its ratio to the FVC. In this study we consider COPD patient who has a FEV1 <80% of predicted.

We excluded from the study patients with a FEV1 lower than 40% because, if pure emphysematous patients, they are usually better treated by cancer resection associated with bilateral lung volume reduction, on the contrary, in case of pure bronchitic patients the operative risk is too high. We also excluded patients with NSCLC diameter higher of 2.5 cm (volume: 8 ml) in order to avoid relevant influence of lung mass on PFTs and lung scan.

Patients were divided into two groups according to their FEV1 more or less than 80% of predicted. While in the former we observed a consistent decrease in post-operative FEV1% (delta FEV1: −14.9%), in the latter the post-operative FEV1% decreased lightly (delta FEV1: −3.2%) and the difference was highly statistically significant.

In these COPD patients any trial of predicting the post-operative FEV1% according to the commonly accepted formulas would have been wrong.

Recently, while we were prospectively collecting our data, a couple of interesting retrospective studies have been published on this topic. They studied the post-operative changes in FEV1 of patients with emphysema submitted to lobectomy and confirmed our results [16,17]. In order to identify patients who improve or at least do not decrease their FEV1 after lobectomy two indexes were proposed. Korst and coworkers [16] utilized a 'COPD index' to grade severity and purity of airway disease. It was calculated by adding the pre-operative FEV1 (% of predicted in decimal form) to the pre-operative ratio of FEV1 to FVC. Carretta and coworkers [17], on the other side, used a radiological grading based on chest X-ray and CT scan. Both indexes tend to identify patients with pure obstructive pulmonary disease that can well-tolerate resection of some lung parenchyma. This is what we learned from lung volume reduction surgery in emphysematous patients [18]. In fact, in Carretta's patients, measured post-operative FVC increased, as increases after lung volume reduction in pure emphysematous patients. On the contrary, in our COPD group we observed a decrease of post-operative FVC not statistically different from control group. This may suggest that in our COPD group patients emphysema is not pure and/or that functioning lung tissue as well as emphysematous tissue were resected. Nevertheless, according to our results, lobectomy in these patients can be successful and this fact may result more evident observing the stratification if COPD group in two subgroup. In our opinion, even if emphysema does not appear to be the only responsible for expiratory airflow obstruction, resection of some lung tissue may increase lung elastic recoil and decrease critical transmural pressure in selected patients [19,20].

We noted in COPD group patients a high standard deviation in FEV1 change after lobectomy. Therefore, we divided COPD group patients into two subgroups according to the median of change FEV1% (−6%) and we applied the Korst COPD index. In the subgroup with high decrease in FEV1% the COPD index was 1.35, while in the other it was 1.15. The difference is statistically significant ($P < 0.001$, power: 0.95). In our patients the COPD index proved useful in identifying those patients whose FEV1 decrease lightly or increase after lobectomy.

Although the obstructive pulmonary disease and the changes in FEV1 of COPD group patients are not homogeneous, their post-operative outcome was not significantly different from that of control group patients, also as hospital stay and post-operative complications. Three years survival was the same in both groups of patients and no patient needed long term oxygen therapy. Several patients of COPD group referred a subjective improvement in shortness of breath and all regained a normal lifestyle after operation. These results in terms of survival and quality of life after lobectomy in patients with low FEV1 are encouraging. For many years these patients were believed to have a shorter life expectancy after lung resection for cancer [5].

However, our results need to be evaluated with criticism. We must underline that even if the patients included in our study had small lesions (<2.5 cm), all them underwent perfusion scan before operation, in order to avoid to resect a lobe receiving more than 30% of total perfusion.

In conclusion, our study confirms that lobectomy for cancer can be performed successfully in selected patients with low FEV1. Differently from previous studies which tried to identify pure emphysematous patients to get satisfactory results, we found that also in patients with ‘not pure COPD’ post-operative FEV1 does not decrease significantly or even increases. Post-operative course and survival of these patients are not different from that of patients with FEV1 more than 80% of predicted.

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