Evaluation of pulmonary function and exercise tolerance after upper lobectomy for lung cancer in patient with emphysema

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Evaluation of pulmonary function and exercise tolerance after upper lobectomy for lung cancer in patients with emphysema.

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Abstract

**Objective:** The purpose of this study was to evaluate dynamic pulmonary function and exercise tolerance after upper lobectomy for lung cancer in patients with emphysema.

**Methods:** This prospective study enrolled 39 patients with combined lung cancer and emphysema (FEV1/FVC < 70 %). There were twenty one right upper and 18 left upper lobectomies. Preoperative dynamic lung functions, as well as 6 minute walk test were compared with follow up results at 3 months period postoperatively.

**Results:** In our study, the preoperative dynamic lung function test has slightly improved after resection. The mean FEV1 of the 39 patient was 1.5L ± 0.38 (range 0.86 – 2.23) and the mean FEV1 % was 47.34 ± 12.31. The post operative mean FEV1 of the 39 patients was 1.5L ± 0.35 (range 0.91 – 1.96), while the mean FEV1 % was 47.55 ± 24.23 with a Δ + 0.21 %. The mean FVC of the 39 patients before resection was 2.27L ± 0.67 and FVC % was 64.35 ± 4.1, while after resection FVC was 2.04L and FVC % was 58 ± 3.7 with a Δ – 6.35 %. The ratio between FEV1 and FVC has improved from a preoperative mean of 66 % to 73.5 % with Δ + 7.5 %.

Exercise capacity of our patients has slightly decreased than preoperative values, but this was not significant statistically. The mean preoperative 6 minute walk test for all the patients was 543.5 ± 99 (range 300 – 685) meters, the mean postoperative 6 minute walk test was 520.29 ± 92 with a Δ – 4.2 %. The main complication after resection was prolonged air leak > 7 days that was found to be inversely proportion to preoperative FEV1.

**Conclusion:** There is a subgroup of patients with emphysema and low preoperative dynamic lung function who can still undergo anatomical resection for lung cancer. Both FEV1 and FEV1/FVC % slightly improved compared to preoperative values. Both FVC and 6 minute walk test slightly decreased to preoperative value but were not statistically significant.

**Keyword:** Lung cancer, Emphysema, Pulmonary function.
1. Introduction.

Surgery still remains the main curative treatment for early stage non small cell lung cancer [1]. Due to common risk factors in particular tobacco smoking, lung cancer may frequently accompany chronic obstructive pulmonary disease (COPD) [2]. And in this group of patient respiratory limitation preclude many of them to enjoy a potential curative resection. The alternative is comparatively poor when radiotherapy with or without chemotherapy are the treatment strategy [3]. Patients with poor pulmonary function in particular low forced expiratory volume in 1 second were denied lobectomy in favor of a more limited resection or not at all [4,5]. However, it has been the experience of many authors that forced expiratory volume in 1 second does not decrease after lobar resection but may improve in patients with pulmonary emphysema [5,6]. This together with experience gained from lung volume reduction surgery with improvement of pulmonary functions after surgery [7], had encouraged us to expand the indications to surgical resection in lung cancer patients with pulmonary emphysema.

The purpose of this study was to evaluate our experience, post operative pulmonary function, exercise tolerance, and complications in patients with non small cell lung cancer and emphysema who underwent upper lobectomies.

2. Patients and Methods.

Between January 2001 and January 2005 one hundred and fifty four patients underwent resection for lung cancer at Cairo university hospitals. Only thirty nine patients (25 %) were prospectively enrolled in the study as they had combined lung cancer and COPD and met our inclusion criteria. The definition of COPD/Emphysema (FEV1/FVC <0.70) was according to the GOLD criteria [8]. Table 1 shows the exclusion criteria for this study. Twenty one patients underwent right upper lobectomy and 18 underwent left upper lobectomy.

All patients had informed consent. The decision for operability and resectability was determined according to thorough history, clinical examination, chest x-ray, computer tomography scan, fibro-optic bronchoscopy, electrocardiogram, echocardiography, spirometry (portable spirobank, MIR, Rome, Italy), arterial blood gases and 6 minute walk test (6MWT). Quantitative CT scan was used to evaluate regional distribution of ventilatory function in the proposed lobe to be resected in patients with FEV1 < 1.2L. The COPD index was calculated using the formula proposed by Korst and colleagues [6] by adding the preoperative FEV1 (% of predicted in decimal form) to the preoperative ratio of FEV1 to forced vital capacity. This formula was used to grade patients according to their COPD severity and purity. Therefore, the patients with the lowest COPD index are those with the most pure and severe obstructive airway disease.

Preoperative patients' data were collected as regards age, sex, smoking history, medications and others. All patients were subjected to a brief rehabilitation program ranging from 2 weeks to 6 weeks preoperatively. This was also continued in the post operative period for 6 weeks and composed of inhaled bronchodilators, inhaled steroids, smoking cessation program, physiotherapy, incentive spirometry and daily exercise.

Follow up of the patients included post operative spirometry and 6MWT at 3 months range (2-5) postoperatively.
3. Statistical Analysis

Computations were performed using Microsoft Office Excel 2003 version 11. Data are expressed as mean ± standard deviation (SD) with range in brackets. Comparison of mean values was done with the paired t-student test.

4. Results

Thirty nine patients underwent upper lobectomy for combined lung cancer and emphysema. They were divided into 2 groups twenty one patient underwent right upper lobectomy and eighteen underwent left upper lobectomy. There were 36 males and 3 females with a mean age of 63.75 ± 8.3. More than 70 % were smokers (30/39). All patients were subjected to posterolateral thoractomy, careful mediastinal lymph node dissection and proper pathological staging was evaluated and revealed. T1N0 in 8 patients (20.5 %), T1N1 in 7 patients (17.9 %), T2N0 in 8 patients (20.5 %) and T2N1 in 16 patients (41 %). Squamous cell carcinoma was diagnosed in 76.9 % of patients (30/39), adenocarcinoma was diagnosed in 17.9 % of patients (7/39) and 5.1 % of patients had large cell carcinoma (2/39).

There was no 30 days operative mortality. The main post operative morbidity was prolonged air leak >7 days, which occurred in 30 % of our patients (12/39), six patients on each group and these patients had FEV1 < 1.2L. Superficial wound infection occurred in 5.1 % of our patients (2/39).

In our study, the preoperative dynamic lung function tests have slightly improved after resection. The mean preoperative FEV1 of the 39 patient was 1.51 ± 0.38 (range 0.86 – 2.23) and the mean FEV1 % was 47.34 ± 12.31. The post operative mean FEV1 of the 39 patients was 1.5 ± 0.35 (range 0.91 – 1.96), while the mean FEV1 % was 47.55 ± 24.23 with a Δ + 0.21 %. The mean FEV % before right upper lobectomy was 47.2 ± 11.52, while after resection was 47.9 ± 10.55 with a Δ + 0.7 %. The mean FEV1 % before left upper lobectomy was 47.4 ± 13.51, while after resection was 47.1 ± 11.2 with a Δ − 0.3 %.

The mean FVC % of the 39 before resection was 64.35 ± 4.1, while after resection was 58 ± 3.7 with a Δ − 6.35 %. The mean FVC % before right upper lobectomy was 63.76 ± 4.5, while after resection was 57.2 ± 4 with a Δ − 6.56 %. The mean FVC % before left upper lobectomy was 65 ± 3.6, while after resection was 59.11 ± 3.1 with a Δ − 5.89 % (Table 3 and 4).

The mean preoperative 6 minute walk test for all the patients was 543.5 ± 99 (range 300 – 685) meters, the mean postoperative shuttle walk test was 520.29 ± 92 with a Δ − 4.2 % (Table 5).
5. Discussion

An estimated 20% of patients with bronchogenic carcinoma have pulmonary dysfunction sufficiently severe to be considered inoperable by conventional criteria [8]. The major concern for this group of patients is the postoperative mechanical ventilation or mortality. A secondary consideration is the potential for long-term postoperative respiratory morbidity. These risks can be estimated by evaluating the anatomic location of the lung cancer, as well as the physiology of the underlying emphysema.

Anatomically, resection of the dysfunctional apical lung tissue is relatively well tolerated because the apical portions contribute little or nothing to gas exchange. In selected patients, reducing the overall lung volume by resecting the apex has several beneficial effects. First, the decreased volume of lung tissue allows the distended chest wall and diaphragm to return to more normal anatomic positions. This in turn results in a significant improvement in ventilatory mechanics. Second, the smaller lung more effectively tethers the small airways, which results in improved expiratory airflow. Thus, the patient with apical emphysema and a lung cancer in the upper lobe is a potential candidate for surgical resection [9].

Physiologically, several functional factors have been studied as predictors of outcome after pulmonary resection. Preoperative evaluation usually includes tests such as spirometry, blood gas analysis, DLCO and prediction of postoperative pulmonary function, by means of split lung function perfusion scanning or quantitative CT scan and by calculating the contribution of the resected segments to total lung function [10,11]. In our study we used quantitative CT measurement of lung attenuation to assess the extent and the regional distribution of emphysema. Previous studies have proved that prediction of split lung function by quantitative CT scan is similar to results obtained from quantitative radionuclide pulmonary perfusion scintigraphy. Specific tests are also used to assess exercise capacity and to identify parameters that seem to be associated with postoperative outcome, such as maximum oxygen consumption and blood oxygen desaturation.

Several functional criteria were associated with operative risk but no cut off value is universally acknowledged. In general practice, a preoperative FEV1 less than 1.5 L or 60% of predicted or a predicted postoperative FEV1 (ppoFEV1) less than 800 mL or 40% of predicted is considered a high risk for lobectomy [12]. Gaensler [13] in 1955 related maximal voluntary ventilation (MVV) lower than 50% of predicted to be associated with an unfavorable outcome. Others [10] noted that ppoFEV1, DLCO, predicted postoperative DLCO (ppoDLCO), and oxygen desaturation during exercise were predictive of postoperative pulmonary complications. They recommended operability if ppoFEV1 was equal or higher than 40% of predicted and inoperability if ppoFEV1 was lower than 30%. Other reports [14, 15] had correlated exercise capacity as a predictor to outcome after resection, maximal oxygen consumption (MVO2) < 10 ml / kg / min had a prohibitive surgical risk, while patients with an MVO2 greater than 20 ml/kg per min had a low risk of postoperative complications after pulmonary resection. Although the 6 minute walk test as a continuous measure was not predictive of surgical outcome, but it was found for instance, if a patient walked less than 250 m on 6 minute walk testing, the overall chance of having a poor outcome was 66% [16].

In our study, patients with emphysema undergoing upper lobectomy for lung cancer and who had a marginal preoperative FEV1 had slight improvement after right upper lobectomy or insignificant reduction after left upper lobectomy of their FEV1 as
compared to preoperative results. There has been a slight improvement of FEV1/FVC % in all patients. These results agree with other reports [4,5,6,18]. FVC value has decreased in our study which point to some functioning lung tissue is most likely being resected. If only nonfunctioning lung is removed, FVC should increase, as it does in the patients undergoing lung volume reduction. This also suggests that functioning lung tissue can be resected and still result in higher FEV1. Second, a rising FEV1 in the face of a falling FVC implies that the actual severity of airway obstruction has somehow improved, possibly related to changes in elastic recoil and closing volumes [5,17].

The mean COPD index of our patient population was 1.2, these values shows improved postoperative FEV1 compared to preoperative FEV1. This has been coined out by other investigators [5, 18] that FEV1/FVC improves if preoperative FEV1 is less than 65% of predicted, if preoperative FEV1/FVC is less than 55%, or if the COPD index is less than 1.5, whereas FEV1/FVC worsens if the preoperative FEV1/FVC is more than 70% and the COPD index is more than 1.5. These values have been met in this study. Our preoperative FEV1 % had a mean of 47 % of predicted, the mean COPD index had a mean of 1.2 and FEV1/FVC was less than 70 %.

Although there has been insignificant reduction in the mean 6MWT of our patient population after resection, the significance of this test has been questioned by some investigators as the absolute distance achieved on a 6 minute walk test should not be used to predict poor surgical outcome in lung cancer patients with borderline lung function, contrary to current recommendations. It is advisable to perform a formal cardiopulmonary exercise test in the assessment of such patients if at all possible, since it can be expressed as a predicted value and has been shown to be a better predictor of poor outcome. As such, the 6MWT walk test should be used with caution, only when the former is not available [16]. The results of other investigators found that COPD patients undergoing lobectomy may be found, 3 months after surgery, to have a persistent, significant exercise capacity loss in the absence of modifications of FEV1.

Like others [19], the main complication in our study was prolonged air leak which was inversely proportion to FEV1 results.

The criticism of our data may be focused on the biased outcome by choosing patients with homogenous emphysema or localized disease confined to the upper lobes, however we have to stress that initially all these patients were denied surgery or offered a more limited resection for an early stage lung cancer that has a better prognosis when anatomically resected. Moreover, a good outcome in this group of patients is not only based on proper selection but also a good rehabilitation program [20] particularly smoking cessation that correlate with deterioration in FEV1 if the patient continue to smoke. In this study we could not use formal cardiopulmonary exercise test and this was due to the absence of this test at our institute. Instead we found that the 6MWT was simple and informative. In this study it was not significantly affected after resection.

In conclusion, the expected change in pulmonary functions in patients with emphysema and marginal preoperative dynamic lung functions after upper lobectomy for lung cancer is minimal or even improves and should encourage anatomical resection in selected group.
6. References


Table 1. Exclusion criteria
Patients who underwent resection other than upper lobectomy

Tumors > 4 cm in size.

Segmental or lobar collapse before surgery.

Incapacity to quit smoking after surgery.

Failed or refused to comply with rehabilitation program.

Post operative empyema.

Poor lung expansion after resection.

Walking distance < 300 meters preoperative

Table 2. Patients' characteristics

<table>
<thead>
<tr>
<th></th>
<th>Rt. Upper lobectomy (n=21)</th>
<th>Left upper lobectomy (n=18)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>62.1 ± 9.8</td>
<td>65.4 ± 7.9</td>
<td>NS</td>
</tr>
<tr>
<td>Sex</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>19 (90.4 %)</td>
<td>17 (94.4 %)</td>
<td>NS</td>
</tr>
<tr>
<td>Female</td>
<td>2</td>
<td>1</td>
<td>NS</td>
</tr>
<tr>
<td>Body mass Index</td>
<td>22.7 ± 2.9</td>
<td>21.6 ± 2.3</td>
<td>NS</td>
</tr>
<tr>
<td>Smoking</td>
<td>16 (76.1 %)</td>
<td>14 (77.7 %)</td>
<td>NS</td>
</tr>
<tr>
<td>Bronchodilators</td>
<td>12 (57.1 %)</td>
<td>10 (55.5 %)</td>
<td>NS</td>
</tr>
<tr>
<td>Preoperative pulmonary function tests</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>FEV1</td>
<td>1.51±0.4 (0.94-2.23)</td>
<td>1.51±0.37 (1.1-2.1)</td>
<td>NS</td>
</tr>
<tr>
<td></td>
<td>47.22 % ± 11.52</td>
<td>47.48 % ± 13.51</td>
<td></td>
</tr>
<tr>
<td>FVC</td>
<td>2.23±0.73 (1.22-3.71)</td>
<td>2.31±0.62 (1.33-3.38)</td>
<td>NS</td>
</tr>
<tr>
<td></td>
<td>63.76 % ± 4.55</td>
<td>65 % ± 3.6</td>
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<tr>
<td>Arterial Blood gases</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>PaO2</td>
<td>82 ± 11</td>
<td>83 ± 13</td>
<td>NS</td>
</tr>
<tr>
<td>PaCO2</td>
<td>40 ± 5</td>
<td>39 ± 3</td>
<td>NS</td>
</tr>
<tr>
<td>Pre operative 6 MWT</td>
<td>561 ± 91 (480 – 685)</td>
<td>526 ± 106 (300 – 680)</td>
<td>NS</td>
</tr>
</tbody>
</table>

FEV1: forced expiratory volume in 1 sec, FVC: forced vital capacity, 6 MWT: 6 min walk test.

Table 3. Comparison between % of predicted of pre and postoperative dynamic lung functions after RUL
<table>
<thead>
<tr>
<th></th>
<th>Preoperative RUL</th>
<th>Postoperative RUL</th>
<th>Δ %</th>
</tr>
</thead>
<tbody>
<tr>
<td>FEV1 %</td>
<td>47.2</td>
<td>47.9</td>
<td>+ 0.7</td>
</tr>
<tr>
<td>FVC %</td>
<td>63.7</td>
<td>57.2</td>
<td>- 6.5</td>
</tr>
<tr>
<td>FVE1/FVC %</td>
<td>67.2</td>
<td>76</td>
<td>+ 8.8</td>
</tr>
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</table>

RUL: right upper lobectomy.

Table 4. Comparison between % of predicted of pre and postoperative dynamic lung functions after LUL

<table>
<thead>
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<th>Preoperative LUL</th>
<th>Postoperative LUL</th>
<th>Δ %</th>
</tr>
</thead>
<tbody>
<tr>
<td>FEV1 %</td>
<td>47.4</td>
<td>47.1</td>
<td>- 0.3</td>
</tr>
<tr>
<td>FVC %</td>
<td>65</td>
<td>59.1</td>
<td>- 5.9</td>
</tr>
<tr>
<td>FVE1/FVC %</td>
<td>64.9</td>
<td>71.2</td>
<td>+ 6.3</td>
</tr>
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</table>

LUL: left upper lobectomy.

Table 5. Comparison between pre and postoperative 6MWT

<table>
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<th>Preoperative value</th>
<th>Postoperative value</th>
<th>Δ %</th>
</tr>
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<tr>
<td>6MWT walk test</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Right Upper lobectomy</td>
<td>561 ± 91</td>
<td>529.5 ± 99</td>
<td>- 3.5</td>
</tr>
<tr>
<td>Left upper lobectomy</td>
<td>526 ± 106</td>
<td>511 ± 87</td>
<td>- 2.5</td>
</tr>
</tbody>
</table>

6 minute walk test.