Actual and Predicted Postoperative Changes in Lung Function After Pneumonectomy*
A Retrospective Analysis

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Study objectives: Little is known about long-term effects of pneumonectomy on lung function and exercise tolerance. We evaluated the long-term validity of two formulas frequently used to predict postoperative lung function, as well as trends in postoperative lung function and late postoperative exercise capacity.

Setting: Nonuniversity teaching hospital of Eindhoven, the Netherlands.

Patients: Patients who underwent pneumonectomy between 1993 and 1998 and survived for > 1 year after the operation.

Measurements and results: Lung function and exercise test data of 32 patients were analyzed. Postoperative FVC and FEV₁ according to Kristersson/Olsen (split function of resected lung) and Juhl and Frost (number of segments to be resected) were calculated and compared with observed values measured in the third postoperative year. Calculated values correlated well with observed values, whereas Kristersson/Olsen appeared to be more accurate than Juhl and Frost. When considering trends in FEV₁, we found a mean decline of 44 mL/yr; only three patients (12%) showed a rapid decline of > 100 mL/yr. Of 14 patients (44%), postoperative maximal exercise capacity was impaired due to ventilatory limitation.

Conclusions: The Kristersson/Olsen formula was more accurate in predicting postoperative lung function in the third postoperative year in pneumonectomy patients. Although the annual decline in FEV₁ in these patients is almost the same as in healthy patients without COPD, pneumonectomy has serious implications on exercise capacity in many patients.

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Key words: lung; lung cancer surgery; lung physiology; morbidity; postoperative care

Abbreviations: NSCLC = non-small cell lung cancer; ppo = predicted postoperative; VO₂max = maximal oxygen uptake during exercise; Wmax = workload at maximum exercise

Lung cancer is currently the most common cause of cancer mortality throughout the world. It is the second most frequent type of cancer among men and women.¹² Non-small cell lung cancer (NSCLC) accounts for 80% of all newly diagnosed lung cancers. At present, complete resection offers the best prospects and results in cure in a substantial number of patients with NSCLC. In order to determine whether lung resection is feasible in patients with NSCLC and to what extent, resectable patients need to be carefully screened for their cardiopulmonary reserve. The best and most frequently used indicators for postoperative lung function are the FEV₁, predicted postoperative (ppo),³ ⁶ diffusion capacity of the lung for carbon monoxide ppo,⁶ ⁹ and maximal oxygen uptake (VO₂max) during exercise ppo.⁴ ¹⁰,¹¹ There is consensus in the literature that lobectomy leads to very little permanent functional deficit after 6 months.⁴ Pneumonectomy causes a more permanent deficit that is higher for pulmonary function (ie,
FEV1-ppo (or FVC-ppo) than for exercise capacity (V_{O2,max}). FVC and FEV1 are lowered by approximately 33%, whereas V_{O2,max} is decreased by approximately 20%. However, little is known about long-term (> 1 year postoperative) effects of pneumonectomy on lung function and exercise tolerance.

Several formulas are in use aiming to predict postoperative lung function after resection. In general, these formulas can be divided into two categories. The first category of formulas calculates postoperative FVC and FEV1 by the number of segments to be resected. The second category of formulas includes the function of these segments by measuring their actual perfusion preoperatively. These formulas proved reasonably valid when the predicted lung function was compared with the one measured relatively soon, within 3 months, after the operation. Since recruitment of underperfused or overventilated lung segments may occur after lung resection, especially after pneumonectomy, it is still unclear what the validity of these formulas might be for predicting lung function at a much later stage. Furthermore, these formulas were validated in a small number of patients after pneumonectomy. Nevertheless, they are worldwide accepted in guidelines. Therefore, our main study objective was to investigate the validity of these formulas in pneumonectomy patients surviving for > 2 years after the operation. Subsequently, we studied trends in postoperative lung function and examined the implications of pneumonectomy on exercise capacity in patients surviving for > 1 year after the operation.

Materials and Methods

In a retrospective study, all data of patients who underwent pneumonectomy in a nonuniversity teaching hospital between 1993 and 1998 and survived for > 1 year after the operation were evaluated. Informed consent was obtained.

From the patient records, the following characteristics were gathered: demographic data, tumor histology and stage, date of surgery, site of operation, and presence of COPD, according to American Thoracic Society criteria. We used these data to answer our three research questions.

ppo Lung Function

FEV1-ppo and FVC-ppo were calculated by using the two most commonly used formulas:

\[
\text{FEV1-ppo (or FVC-ppo)} = \text{FEV1 preoperative (or FVC preoperative)} \times (1 - \text{fractional contribution of resected lung segments})
\]

\[
\text{FEV1-ppo (or FVC-ppo)} = \text{FEV1 preoperative (or FVC preoperative)} \times (1 - [S \times 0.0526])
\]

where S is the number of resected lung segments, and each segment accounts for 1/19 of total lung function. The predicted and observed postoperative lung function data measured in the third year after the pneumonectomy were compared. We used the last available data in that third postoperative year for analysis.

Trends in Postoperative Lung Function

If more than two postoperative lung function tests were available, the changes in postoperative lung function over time were analyzed. These lung function tests had to be done at least > 6 months postoperatively and with a minimum interval of 12 months between the first and last available test.

Exercise Capacity

The preoperative and postoperative maximal incremental exercise test results, performed according to European Respiratory Society criteria, were compared. The postoperative test had to be done > 1 year after the operation. Ventilatory limitation of exercise capacity was defined as follows: (1) P_{CO2} at maximum exercise being > 45 mm Hg or, (2) ventilation at maximum exercise ≥ 37.5 × FEV1.

Statistics

Statistical software (SPSS 9.0; SPSS; Chicago, IL) was used for statistical analysis. For the evaluation of the two formulas for predicting postoperative lung function, scatterplots were made and regression analysis performed with the ppo lung function as the independent variable and the observed postoperative lung function as the dependent variable. Long-term trends in lung function after pneumonectomy were studied by linear regression analysis.

Results

Patients

From 1993 until 1998, 76 patients underwent pneumonectomy in our hospital. Forty-four patients were excluded from the study, 17 patients because of missing data, 26 patients died within 1 year after the operation, and 1 patient refused to participate. Table 1 presents initial patient characteristics of the 32 included patients compared to the dropouts and the total patient group. There were no statistical significant differences between the groups. Figure 1 shows a schematic overview of evaluable postoperative data and dropouts for each separate research question.

The diagnosis of lung malignancy was confirmed histologically in 31 patients; 1 patient underwent pneumonectomy because of an abscess with persisting empyema. Of all 31 malignant tumors, 20 were squamous cell carcinoma, 7 were adenocarcinoma, 2 were large cell undifferentiated carcinoma, 1 was adenocystic carcinoma, and 1 was a carcinoid tumor. Adjuvant radiotherapy was administered to 10 patients, 9 patients because of residual disease and 1
FEV1 by both formulas correlates well with the after pneumonectomy, calculation of ppo FVC and FEV1. Furthermore, the formula by Juhl and Frost 13 pre-
termination (R2) was higher for the Kristersson/Olsen formula than the Juhl and Frost formula. This indicates that the formula by Kristersson et al12 and Olsen et al14 was more accurate in predicting postoperative FVC and FEV1 than the formula by Juhl and Frost13 for the investigated postoperative year. Additionally, the formula by Juhl and Frost13 predicted postoperative FEV1 roughly 300 mL lower than the Kristersson/Olsen formula.

Predicting Postoperative Lung Function

Scatterplots of predicted lung function data according to both formulas vs observed postoperative lung function data obtained in the third year after pneumonectomy are depicted in Figures 2, 3, as well as the results of the linear regression analysis. These figures show that in patients surviving for > 2 years after pneumonectomy, calculation of ppo FVC and FEV1 by both formulas correlates well with the observed postoperative FVC and FEV1. Linear regression analysis showed that the coefficient of determination (R2) was higher for the Kristersson/Olsen formula than the Juhl and Frost formula. This indicates that the formula by Kristersson et al12 and Olsen et al14 was more accurate in predicting postoperative FVC and FEV1 than the formula by Juhl and Frost13 for the investigated postoperative year. Furthermore, the formula by Juhl and Frost13 predicted postoperative FEV1 roughly 300 mL lower than the Kristersson/Olsen formula.

Trends in Postoperative Lung Function

Long-term postoperative changes in lung function of individual patients could be analyzed in 26 patients. The number of postoperative lung function tests varied between 3 tests and 12 tests (mean, 7 tests), and the mean time interval between the operation and most recent lung function test over which trends were analyzed was 9.9 ± 63.0 months (± SD). The mean annual decline in FEV1 was 44 mL. Of 26 patients, 6 patients had improvement in FEV1 postoperatively, 10 patients had a decline of 0 to 50 mL/yr in FEV1, 7 patients had a decline of 50 to 100 mL/yr in FEV1, and 3 patients had a decline > 100 mL/yr in FEV1.

Exercise Capacity

Table 2 shows the results of the preoperative and postoperative exercise tests. These were available in 17 of 32 patients, with a mean time interval between the operation and the postoperative exercise test of 38 ± 21.4 months (range, 12 to 77 months). Decreases in workload at maximum exercise (Wmax) and V02max were 27% and 30%, respectively. Preoperatively, maximal exercise tolerance was restricted due to a limited ventilatory capacity in 4 of these 17 patients, whereas postoperatively this was the case in 5 of these 17 patients. In all cases, it was concluded that maximal exercise was restricted due to a limited ventilatory capacity because Pco2 exceeded the 45 mm Hg limit at maximum exercise.

Comments

This study shows that calculation of FVC-ppo and FEV1-ppo by both the Kristersson/Olsen and the Juhl and Frost formula correlated well with the

Table 1—Initial Patient Characteristics of Included Patients and Total Patient Group*

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Study Group</th>
<th>Dropouts</th>
<th>Total Group</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patients, No.</td>
<td>32</td>
<td>35</td>
<td>67†</td>
</tr>
<tr>
<td>Male/female gender, No.</td>
<td>24/8</td>
<td>32/3</td>
<td>56/11</td>
</tr>
<tr>
<td>Mean age, yr (range)†</td>
<td>62.4 (42–75)</td>
<td>62.1 (37–76)</td>
<td>62.3 (37–76)</td>
</tr>
<tr>
<td>Median survival, mo postoperative (range)‡</td>
<td>64.5 (19–110)</td>
<td>6.0 (1–21)</td>
<td>19.0 (1–110)</td>
</tr>
<tr>
<td>With COPD, No.†</td>
<td>9</td>
<td>11</td>
<td>20</td>
</tr>
<tr>
<td>Right/left pneumonectomy, No.</td>
<td>13/19</td>
<td>18/17</td>
<td>31/36</td>
</tr>
<tr>
<td>Preoperative lung function data</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Patients, No.</td>
<td>32</td>
<td></td>
<td>67†</td>
</tr>
<tr>
<td>FVC, L</td>
<td>3.41 ± 0.8</td>
<td>3.39 ± 1.0</td>
<td>3.40 ± 0.9</td>
</tr>
<tr>
<td>FVC % predicted</td>
<td>89.8 ± 14.3</td>
<td>84.9 ± 19.1</td>
<td>87.2 ± 17.0</td>
</tr>
<tr>
<td>FEV1, L</td>
<td>2.48 ± 0.7</td>
<td>2.44 ± 0.7</td>
<td>2.46 ± 0.7</td>
</tr>
<tr>
<td>FEV1 % predicted</td>
<td>83.5 ± 18.9</td>
<td>78.7 ± 18.8</td>
<td>81.0 ± 18.9</td>
</tr>
<tr>
<td>FEV1/FVC</td>
<td>69.0 ± 11.3</td>
<td>70.2 ± 9.6</td>
<td>69.5 ± 10.4</td>
</tr>
</tbody>
</table>

*Data are presented as mean ± SEM unless otherwise indicated; n = 32.
†At time of surgery.
‡Of which complete preoperative data could be obtained (n = 67); nine missing because of missing data.
observed postoperative FVC and FEV₁ in the third year (mean, 31.4 ± 3.7 months) after pneumonectomy. The formula by Kristersson/Olsen appeared to be more accurate in predicting postoperative FVC and FEV₁ than the formula by Juhl and Frost. Roughly seen, the formula by Juhl and Frost estimated FEV₁-ppo in the third postoperative year approximately 300 mL lower than the formula by Kristersson/Olsen. When considering the long-term trend in lung function, we found that the mean decrease in FEV₁ was approximately 44 mL/yr. Only three patients showed a rapid decline of > 100 mL/yr. No evidence for regeneration capacity in pneumonectomy patients could be detected. Finally, pneumonectomy appears to lower Wmax at least by 27% and VO₂max by 30%. At least 40% of the patients experience impaired maximum exercise capacity due to ventilatory limitation.

The lower postoperative FVC and FEV₁ predicted by the Juhl and Frost formula compared to the observed FVC and FEV₁ might be explained by the fact that this formula does not take into account the function of the segments that will be removed. Zeiher et al. found this underestimation of FEV₁-ppo to be approximately 500 mL at 7.2 months (mean) [range, 24 days to 5 years] after pneumonectomy. In our study, we found an underestimation of FEV₁-ppo of 225 mL, indicating further decrease in FEV₁ in this period of time or a better prediction of FEV₁-ppo by the Juhl and Frost formula a few years after pneumonectomy. Bolliger et al. recently found that both predictions of postoperative cardiopulmonary function by perfusion scan and quantitative CT scan (6 months postoperatively) were useful irrespective of the extent of resection. Unfortunately, we did not choose the use of quantitative CT scan for long-term prediction in our study, which would be very interesting to do.

In healthy nonsmokers, FEV₁ physiologically decreases with approximately 30 mL/yr. In current, male, heavy cigarette smokers (> 25 cigarettes per day), this decline is approximately 60 mL/yr. The mean annual decline in FEV₁ was 44 mL in our study.
study. No clear correlation between the amount of decline and presence of COPD, adjuvant radiotherapy, or adjuvant chemotherapy could be detected. When looking at the patients individually, we found that 6 of 26 patients showed an improvement in their FEV1 in time after their pneumonectomy, whereas 3 patients showed a rapid deterioration of their FEV1. One of the possible explanations for these findings might be the past and current smoking status of the patients. Unfortunately, we were not able to determine the exact past and current smoking status in our patients because of the retrospective nature of our study. A possible explanation for the improvement in FEV1 we observed in six of our patients might be a better treatment of an underlying obstructive pulmonary disease or the occurrence of recruitment and distention of alveoli and capillaries after pneumonectomy. Some investigators have suggested that this might be the main adaptive mechanism of the lung to the new situation after pneumonectomy. Laros found that because of recruitment and alveolar distention, the vital capacity increased slightly during the first few years after pneumonectomy.
In our study, Wmax and VO₂max decreased 27% and 30%, respectively, at approximately 38 months after the operation. Probably this decrease is an underestimation of the real decrease because nine patients postoperatively could not be tested due to death or shortness of breath. Our data compare well with those of Nugent et al., who found that pneumonectomy was associated with impaired exercise performance and reduced VO₂max by 28% 6 months after the operation. Others found reductions of 16% and 20% at 6 months after the operation. These results suggest that long-term exercise performance might already be predicted at 6 months postoperatively.

Only 17 of the 32 patients were able to perform a postoperative exercise test, of which 5 patients were found to be ventilatory limited to exercise. When taking into account the 15 patients who were not available for postoperative exercise testing, we believe the actual number of ventilatory limited patients might be higher. Of these 15 patients, 5 patients were not able to perform this test because of poor lung function and shortness of breath, indicating that exercise limitation might be due to ventilatory problems. Six patients, including four patients who underwent preoperative ventilatory limited exercise tests, died before having performed a postoperative exercise test. Death was attributed to respiratory failure in four of these six patients also, indicating ventilatory limitation postoperatively. Adding these 9 patients without a postoperative exercise test to the 5 patients with a postoperative exercise test results in 14 of 32 patients (44%) probably being ventilatory limited to exercise after pneumonectomy. Two of these nine patients also experienced cardiac comorbidity, besides their pulmonary limitations, which probably contributed to their limited exercise capacity. The preoperative FVC and FEV₁ of the patients in whom it was proven that ventilatory problems were the reason for postoperative exercise limitation. The preoperative lung function results in these nine patients were worse, which makes it very likely that these nine patients also had ventilatory limitation as a reason for a restricted exercise capacity.

When considering our results, it might be argued that our results are biased because of missing data. Because we found no indications for selective drop out when comparing the final study group and the dropout group on their initial patient characteristics, we have no indication that this might be the case. This study was conducted solely to answer our three research questions in long-term survivors. Also, compared to previous studies, we were able to include a relatively large number of patients, which make our results more robust. Nevertheless, because of the retrospective character of this study, our results need to be confirmed by a prospective study.

In conclusion, this study showed that the Kristersson/Olsen formula was a better predictor of postoperative FVC and FEV₁ than the Juhl and Frost formula in patients surviving for > 2 years after pneumonectomy. Secondly, the annual decline in FEV₁ in these patients is almost the same as in healthy patients without COPD. Finally, we found that Wmax > 1 year after pneumonectomy (mean interval of 38 months) decreased by 27% and VO₂max decreased by 30%, at least. Knowledge of these changes in lung function and exercise tolerance in these patients is extremely useful for the preoperative assessment and counseling of patients who are eligible for pneumonectomy.

### References


### Table 2—Mean Maximum Incremental Exercise Test Results

<table>
<thead>
<tr>
<th>Variables</th>
<th>Preoperative</th>
<th>Postoperative</th>
</tr>
</thead>
<tbody>
<tr>
<td>Wmax, W</td>
<td>123.6 ± 22</td>
<td>90 ± 24.2</td>
</tr>
<tr>
<td>Wmax, % predicted</td>
<td>102.1 ± 19.8</td>
<td>75.5 ± 17.3</td>
</tr>
<tr>
<td>VO₂max, nL/kg/min†</td>
<td>20.3 ± 4</td>
<td>14.2 ± 3.8</td>
</tr>
<tr>
<td>VO₂max, % predicted†</td>
<td>75.4 ± 16.9</td>
<td>53.6 ± 14.7</td>
</tr>
<tr>
<td>Dyspnea index</td>
<td>0.57 ± 0.15</td>
<td>0.67 ± 0.17</td>
</tr>
</tbody>
</table>

Ventilatory limited, No. 4 5

Dyspnea index 0.57

Data are presented as mean ± SEM unless otherwise indicated; n = 17.

†n = 16 because of defective equipment.
28 Laros CD. Lung function data on 123 persons followed up for 20 years after total pneumonectomy. Respiration 1982; 43: 81–87