Factors associated with perioperative complications after pneumonectomy for primary carcinoma of the lung

Maciej Dancewicz, Janusz Kowalewski*, Janusz Pepliński

Department of Thoracic Surgery and Tumors, Nicolaus Copernicus University,
Collegium Medicum in Bydgoszcz, Centrum Onkologii, Ul. I. Romanowskiej 2, 85-796 Bydgoszcz, Poland

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Abstract

According to the literature patient’s age, nutrition and smoking status, cardiopulmonary comorbidity and surgeon’s experience are the main factors associated with perioperative complications after pulmonary resection. The purpose of the study was to identify the correlation between pre- and intraoperative risk factors and complications after pneumonectomy for primary carcinoma of the lung. Between Sept. 11th 1999 and Dec. 20th 2003 121 standard pneumonectomies were performed in patients with non small-cell lung cancer. Sixteen risk factors noted in the patients before surgery were correlated with complications occurred after pneumonectomy. Overall mortality and morbidity rates were 3.3% and 30.6%, respectively. Twenty patients (16.5%) experienced cardiac rhythm disturbances, six (4.9%) – pleural haematomas, five (4.1%) – main bronchus stump fistulas, four (3.3%) – acute respiratory failure. Chronic obstructive pulmonary disease was correlated with broncho-pleural fistulas and acute respiratory failure after surgery. Chronic coronary disease was associated with postoperative cardiac arrhythmias, whereas postoperative bleeding was correlated with the overweight of the patients. Chronic obstructive pulmonary disease, chronic coronary disease and morbidity and overweight are the risk factors associated with complications after pneumonectomy.

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Keywords: Pneumonectomy; Mortality; Morbidity; Risk factors; Pulmonary complications

1. Introduction

After the first report of pneumonectomy for lung cancer by Graham in 1933, pneumonectomy became the accepted method for the treatment of this tumor [1]. Despite the big progress in thoracic surgery and postoperative care during the last decade, patients undergoing pneumonectomy for lung cancer are still at high risk of the development of postoperative complications: cardiac arrhythmias, acute pulmonary failure, bronchopleural fistula [2–4].

Although operative mortality following pneumonectomy has decreased over the past decades (8% in 1980s, 5% in 1990s) [3,4], pneumonectomy, and especially right pneumonectomy is associated with higher mortality and morbidity rates than other pulmonary resections [5–7]. Some authors proved that cardiopulmonary comorbidity, smoking status, older age, altered pulmonary function tests are of great influence on operative mortality after pulmonary resection [8,9].

The problem is that the lung cancer patients are often elderly smokers suffering from coronary artery disease, diabetes and pulmonary events.

The purpose of this study was to identify correlations between potential perioperative risk factors and postoperative complications in a group of patients undergoing pneumonectomy for non-small-cell lung cancer (NSCLC) and to determine which of these factors independently affect the outcome.

2. Patients and methods

Between 1 September 1999 and 31 December 2003, a total of 1086 procedures of general thoracic surgery were done at the Department of Thoracic Surgery and Tumors, Nicolaus Copernicus University in Bydgoszcz, Poland. A total of 486 (44.8%) of these patients underwent pulmonary resection for lung cancer (125 pneumonectomies, 354 lobectomies or bilobectomies and 7 wedge resections).

We retrospectively reviewed the medical records of 121 patients who underwent a standard pneumonectomy at our institution within this period. Completion (2), sleeve (1) and extended (1) pneumonectomies were excluded from the study. In all the patients, computed tomography of the chest, fiber optic bronchoscopy and pulmonary function tests were assessed preoperatively.

In all the patients, chest physiotherapy was carried on for 4–5 days before surgery. Antibiotic prophylaxis and low-weight heparin were administrated to all the patients routinely.

The following risk factors in perioperative complications after pneumonectomy were taken into consideration: age,
overweight, smoking history, chronic coronary disease, chronic obstructive pulmonary disease (COPD), diabetes, induction chemotherapy, altered pulmonary function tests, a surgeon, side of operation and surgical access, anesthetic time, the way of bronchial stump closure, the histological distribution and TNM staging of the non-small cell lung cancer. The overweight was defined as body mass index (BMI) $\pm 25$ kg/m$^2$, and COPD when pulmonary function tests indicated forced expiratory volume in one second (FEV$_1$) to forced vital capacity (FVC) ratio $<0.7$.

3. Statistical analysis

Univariate analysis was carried out using the $\chi^2$ test in the case of discrete variables, and the Student's $t$- or Mann-Whitney test, in the case of continuous variables. Multivariate analysis was carried out to identify risk factors associated independently with selected complications: acute respiratory failure (ARF), bronchopleural fistula (BPF), hemothorax and arrhythmia. The criterion for the selection of the factors for the model was $P<0.25$ in the univariate analysis. Selected co-variates were analyzed by the stepwise procedure using Generalized Linear Models (GLZ) and/or multivariate logistic regression model (Statistica 6.0; Statsoft, Tulsa, OK). $P$ values less than 0.05 were considered as significant.

4. Results

There were 101 men (age 42–75 years, mean $60.0 \pm 8.1$) and 20 women (age 50–72 years, mean $59.5 \pm 4.9$). Eighty-one patients (66.9%) were smokers. The overweight was found in 11 cases (9.1%). The comorbidity was as follows: chronic coronary disease – 41 cases (33.9%), COPD – 13 cases (10.7%), diabetes – 8 (6.6%).

The results of the pulmonary function tests were presented as percent values of predicted values. The average value of vital capacity (VC) and FEV$_1$ was $71.4 \pm 9.9$ and $75.9 \pm 8.3$, respectively.

Induction chemotherapy was given in 19 cases (15.7%) for histologically proved N$_2$ disease. All surgical procedures were performed by four surgeons. The surgeons characteristics and their participation in the procedures are presented in Table 1. Antero-lateral thoracotomy was performed in 110 patients (90.9%) and postero-lateral thoracotomy in 11 patients (9.1%). The procedures were carried out under general anesthesia with double lumen intubation, which lasted from 125 to 285 min. In 54 cases (44.6%) right pneumonectomy and in 67 cases (55.4%) left pneumonectomy was performed. The staplers were used in 102 patients (84.3%) for pulmonary artery closure and in 120 patients (99.2) for bronchial closure. In other cases the pulmonary artery or bronchus were sutured manually (Proline 3.0). In 90 cases (74.4%), the bronchus stump was covered with adjacent mediastinal tissues. Each patient underwent systematic mediastinal nodal dissection.

All the patients remained in the intensive care unit (ICU) for $3.2 \pm 1.1$ days (range from 1 to 35 days) and required mechanical ventilation for $240 \pm 40$ min (range 0–405 min). Chest tube drainage lasted from 1 to 35 days (mean $3.5 \pm 0.5$). Blood transfusion was necessary in 24 patients (19.8%) and reintubation in 13 patients (10.7%).

A complete resection, defined as pathologic demonstration of negative tissue margins was obtained in all the patients.

Squamous cell carcinoma was diagnosed in 99 (81.8%) cases, adenocarcinoma in 20 (16.5%) cases and in 2 patients (1.7%) large cell carcinoma was proved.

Postoperative staging was as follows: stage IA ($n=11$; 9.1%), stage IB ($n=39$; 32.2%), stage II A ($n=5$; 4.1%), stage II B ($n=28$; 23.1%), stage III A ($n=37$; 30.6%), stage III B ($n=1$; 0.8%).

Postoperative complications were defined as those occurring within 30 days after pneumonectomy or before discharge from the hospital. Forty-one such complications were noted in 37 patients (30.6%). The most common were cardiac arrhythmias: ($n=20$; 16.5%), which occurred in 10 patients after left- and in 10 after right pneumonectomy (atrial fibrillation in 11 cases – 55.0%, supraventricular tachycardia in 4 cases – 20.0%, premature ventricular contractions in 3 cases – 15.0% and atrial flutter in 2 cases – 10.0%). Drug therapy was necessary in all 20 patients. Conversion to sinus rhythm was succeeded and no recurrent disturbances were noted.

Reoperations were performed in 12 cases (9.9%): pleural hematoma ($n=6$), bronchopleural stump fistula ($n=5$), chylothorax ($n=1$).

The overall mortality was 3.3% (4 patients): 1 patient (0.8%) died due to acute respiratory failure, 1 due to acute myocardial infarction and 2 (1.6%) after the reoperations for BPF.

In univariate analyses, the factors significantly associated with an increased risk of complications were COPD, altered FEV$_1$ (percent predicted) and overweight (Table 2).

Statistically significant correlation was found between the following variables:
- chronic coronary disease and arrhythmias ($P<0.02898$),
- COPD and acute respiratory failure ($P<0.00966$),
- COPD and bronchopleural fistula ($P<0.03096$),
- altered FEV$_1$, and acute pulmonary failure ($P<0.01322$),
- overweight and hemothorax ($P<0.03411$).

<table>
<thead>
<tr>
<th>Surgeon</th>
<th>Experience (years of practice)</th>
<th>Number of procedures performed per year</th>
<th>Number of pneumonectomies performed (1999–2003)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Surgeon 1</td>
<td>45</td>
<td>106</td>
<td>42</td>
</tr>
<tr>
<td>Surgeon 2</td>
<td>46</td>
<td>95</td>
<td>58</td>
</tr>
<tr>
<td>Surgeon 3</td>
<td>40</td>
<td>69</td>
<td>19</td>
</tr>
<tr>
<td>Surgeon 4</td>
<td>35</td>
<td>41</td>
<td>2</td>
</tr>
</tbody>
</table>
By multivariate analysis COPD, BMI and coronary heart disease were significant predictors of higher morbidity (Table 3).

The multivariate analysis does not confirm FEV₁ as an independent risk factor for ARF.

There were no statistically significant correlations between any in the postoperative complications noted and the following variables: age and smoking status of the patients, diabetes, VC, induction chemotherapy, the surgeon, side of resection, surgical access, anesthetic time, TNM staging and histological type of the cancer.

5. Discussion

The study presents a postoperative course of a group of patients after standard pneumonectomy for NSCLC and estimated preoperative and intraoperative variables as possible factors of postoperative complications.

The results of the study showed that COPD, overweight, and chronic coronary disease were independent predictors of postpneumonectomy complications. The similar opinion is presented by others [9], who proved, that heart diseases and low FEV₁ were the predictors of such complications or indicate that the most important factors contributing to post-operative complications in pneumonectomy patients are COPD, performance status and the age over 70 years [10]. In addition, the development of postpneumonectomy complications was related to high mortality rate and prolonged ICU and hospital stay [11]. However, these authors proved additionally that prolonged anesthetic time and no covered bronchial stump were the predictors of such complications. We did not find these correlations in our series.

The rate of the complications after pneumonectomy presented in the literature varies from 11 to 49% [5,6,9]. The level of 30.6% noted in our group is high and indicates that despite careful preoperative care and experienced surgical team pneumonectomy is a hazardous procedure.

Pneumonia after pneumonectomy is a very dangerous complication which occurred in 3.3–21.8% of patients [8,9]. We noted only 3 cases (2.5%) of pneumonia in our patients.

Table 3

Results of the multivariate analyses of selected complications (only statistically significant risk factors are shown)

<table>
<thead>
<tr>
<th>Complication</th>
<th>ARF</th>
<th>BPF</th>
<th>Hemmothorax</th>
<th>Arrhythmia</th>
</tr>
</thead>
<tbody>
<tr>
<td>Risk factor</td>
<td>COPD</td>
<td>COPD</td>
<td>BMI</td>
<td>CHD</td>
</tr>
<tr>
<td>OR</td>
<td>9.64</td>
<td>10.06</td>
<td>8.14</td>
<td>2.89</td>
</tr>
<tr>
<td>+95 CI</td>
<td>1.21</td>
<td>1.21</td>
<td>0.91</td>
<td>1.08</td>
</tr>
<tr>
<td>–95 CI</td>
<td>76.90</td>
<td>83.71</td>
<td>72.90</td>
<td>7.78</td>
</tr>
<tr>
<td>P-value</td>
<td>0.0308</td>
<td>0.0310</td>
<td>0.0149</td>
<td>0.0274</td>
</tr>
</tbody>
</table>

We did not observe postpneumonectomy pulmonary edema in our group, which is observed in 1–5% of patients in other papers [4,9].

The results of the pulmonary function tests are particularly important in patients who are candidates for pneumonectomy [5,11]. Some authors are of the opinion that altered FEV₁ is the most important factor in predicting morbidity and mortality after pulmonary resection [2,9]. Contrary to the literature we found no significant association between the low values of FEV₁, and frequency of acute postoperative respiratory failure as well as bronchopleural fistulas, but these complications were correlated with COPD.

Our data confirm that patients should be carefully selected for pneumonectomy especially with respect to their pulmonary function.

BPF is a devastating postoperative complication with a high mortality rate [7,9]. This complication occurred in 5 of our patients (4.1%), and despite the myoplasty and intensive care, 2 of them died (40%). The rate of BPF after pneumonectomy varies from 2.9 to 6.9% [4,7]. The bronchial stump coverage plays an important role in preventing from this complication [9]. Usually adjacent mediastinal tissues are used for this purpose. Sometimes a myoplasty or thoracoplasty is performed [7]. However, we did not find any correlations between the way of bronchial stump closure and postoperative complications (especially BPF). In

Table 2

Correlations between the risk factors and complications after pneumonectomy (the univariate analysis). The risk factors included in the final models of the multivariate analyses are in bold.

<table>
<thead>
<tr>
<th>Complications</th>
<th>Acute respiratory failure (P)</th>
<th>BPF (P)</th>
<th>Hemmothorax (P)</th>
<th>Arrhythmias (P)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>0.49584</td>
<td>0.45218</td>
<td>0.45892</td>
<td>0.25469</td>
</tr>
<tr>
<td>Smoking status</td>
<td>0.46386</td>
<td>0.73610</td>
<td>0.07264</td>
<td>0.45896</td>
</tr>
<tr>
<td>BMI</td>
<td>0.52011</td>
<td>0.47018</td>
<td>0.03411</td>
<td>0.31435</td>
</tr>
<tr>
<td>Chronic coronary disease</td>
<td>0.70263</td>
<td>0.76793</td>
<td>0.97667</td>
<td>0.02898</td>
</tr>
<tr>
<td>COPD</td>
<td>0.00966</td>
<td>0.03096</td>
<td>0.38336</td>
<td>0.96841</td>
</tr>
<tr>
<td>Diabetes</td>
<td>0.14326</td>
<td>0.09887</td>
<td>0.12665</td>
<td>0.09812</td>
</tr>
<tr>
<td>FEV₁</td>
<td>0.01322</td>
<td>0.65821</td>
<td>0.08421</td>
<td>0.85421</td>
</tr>
<tr>
<td>VC</td>
<td>0.09755</td>
<td>0.25489</td>
<td>0.85545</td>
<td>0.56981</td>
</tr>
<tr>
<td>Induction chemotherapy</td>
<td>0.30474</td>
<td>0.44860</td>
<td>0.40447</td>
<td>0.42065</td>
</tr>
<tr>
<td>The surgeon</td>
<td>0.78542</td>
<td>0.08652</td>
<td>0.09854</td>
<td>0.45218</td>
</tr>
<tr>
<td>Side of resection</td>
<td>0.80545</td>
<td>0.38336</td>
<td>0.48524</td>
<td>0.44860</td>
</tr>
<tr>
<td>Surgical access</td>
<td>0.98745</td>
<td>0.45218</td>
<td>0.09651</td>
<td>0.73610</td>
</tr>
<tr>
<td>Anesthetic time</td>
<td>0.09651</td>
<td>0.07264</td>
<td>0.78542</td>
<td>0.65821</td>
</tr>
<tr>
<td>Bronchial stump coverage</td>
<td>0.48524</td>
<td>0.40447</td>
<td>0.94348</td>
<td>0.25489</td>
</tr>
<tr>
<td>TNM staging</td>
<td>0.94348</td>
<td>0.46385</td>
<td>0.53658</td>
<td>0.70790</td>
</tr>
<tr>
<td>Histological distribution</td>
<td>0.54211</td>
<td>0.14369</td>
<td>0.54862</td>
<td>0.21586</td>
</tr>
</tbody>
</table>

BMI, body mass index; COPD, chronic obstructive pulmonary disease; FEV₁, forced expiratory volume in 1 s; VC, vital capacity.
our series this complication did not occur more frequently after right pneumonectomy, which is often emphasized by others [6,7]. The induction chemotherapy remained without statistically significant influence on postoperative course in our patients.

Arrhythmias after pneumonectomy are common complications and varied from 12.3 to 34.0% [2,7,9,12,13]. Some authors believed, however, that they could be managed easily and were not closely related to higher mortality [13]. Others proved, that they significantly altered postoperative outcome and mortality after lung surgery [12].

Right pneumonectomy versus left pneumonectomy was identified as a strong predisposing factor for the establishment of postpneumonectomy cardiac rhythm disturbances [12].

Despite the relatively high frequency of cardiac rhythm disturbances we did not use prophylactic digitalization of our patients. This policy is similar to that presented by others [13], who found no proven benefit from this practice. Rapid drug therapy occurred to be a sufficient tool against cardiac rhythm disturbances in our patients.

Surprisingly, the rate of squamous-cell carcinoma was over 80% in our group, whereas in other papers it was found only in 53% [7] or 55% [10] of cases. In recent series, adenocarcinoma was the predominant tumor histology, occurring in 56.7% [14]. It may indicate the different distribution of histology in our patient population.

The predominant stage of NSCLC in our patients was I and II (68.6%). Although these data are similar to other reports (64% of pneumonectomy patients in stage I and II) [9], in many papers the majority of patients (from 46 to 70.8%) undergoing pneumonectomy had clinical stage III before treatment [7,14,15].

We are aware of the necessity of performing sleeve lobectomy whenever possible but often central localization of the tumor (81.8% of squamous cell carcinoma in our group) makes it impossible.

This study showed an association between some preoperative variables and complications after pneumonectomy. Based on the present report careful attention should be paid to patients with COPD and low FEV1. In these patients acute respiratory failure and BPF may occur more often after pneumonectomy. Therefore, we modified our pulmonary preventive program for these patients prior to surgery. Chronic coronary disease increases the risk of postoperative arrhythmias, whereas overweight of the patient increases the frequency of bleeding after pneumonectomy.

Although our study is limited by its retrospection, it has allowed us to analyze the predicting factors of complications after a relatively uniform surgical procedure: a standard pneumonectomy.

References