

Early post-pneumonectomy complications in the elderly

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Abstract

Objective: The surgical treatment of non-small cell lung cancer (NSCLC) in elderly patients presents a serious challenge to thoracic surgeons. As there is considerable divergence of opinion about both the mortality and morbidity rates, it is important to set guidelines for proper patient selection. **Methods:** Early post-operative complications in 42 patients aged over 70 years who had undergone pneumonectomy because of NSCLC (Group I) were analyzed. The control group (Group II) consisted of 48 patients, also aged over 70 years, but who had undergone lobectomy or wedge resections. In both groups, the pre-operative conditions and 30-day morbidity and mortality were evaluated. **Results:** Postoperative complications occurred significantly more frequently in pneumonectomy patients (78.5%) than in Group II (58%). Transient or long-standing arrhythmias were noted in 20 patients (47.6%) from Group I and in 17 (35.4%) from Group II. Pulmonary complications occurred in 17 patients (40.4%) from Group I and 16 (33.3%) from Group II. The most important factors contributing to post-operative complications in pneumonectomy patients were performance status (WHO), chronic obstructive pulmonary disease (COPD) and elevated level of blood urea nitrogen (BUN). The highest impact on early mortality in pneumonectomy patients was exerted by COPD, arterial hypertension, formation of broncho-pleural fistula (BPF), the need for re-thoracotomy and high level of BUN. **Conclusions:** (1) Pneumonectomy in patients over the age of 70 carries a considerable risk of severe post-operative complications and death, when compared to patients with less extensive pulmonary resections. (2) Elderly patients with impaired Performance Status (WHO 2 or more) and co-existing arterial hypertension, COPD and elevated level of BUN should be considered for pneumonectomy very carefully and cautiously. © 2000 Elsevier Science B.V. All rights reserved.

Keywords: Pneumonectomy; Risk factors; Elderly

1. Introduction

The surgical treatment of non-small cell lung cancer (NSCLC) in the elderly patient still poses a great challenge for thoracic surgeons. Physiological changes in the cardiovascular and respiratory systems connected with aging, the increased frequency of other underlying medical conditions and, more importantly, the surgical procedure itself significantly increase the risk of life-threatening complications. In the relevant literature the rate of overall post-operative complication varies within a narrow range from 60 to 67% [1–3]. However, there is a considerable divergence of opinion about the mortality rate. According to various authors this ranges from 6 to 36% [1,4–7]. Despite refinements in both surgical technique and post-operative care, pneumonectomy still has a higher morbidity and mortality than other major lung resections. Proper identification of the risk-factors for pneumonectomy would set guidelines for

appropriate patient selection for the procedure and should lead to higher success rates.

The aim of this study was to analyze retrospectively early post-operative complications in patients over 70 years of age who had undergone pneumonectomy because of non-small cell lung cancer.

2. Materials and methods

Between March 1996 and April 1998 565 patients with NSCLC underwent surgery in the Department of Thoracic Surgery at the Karol Marcinkowski University of Medical Sciences. Of these, 90 patients (16%) were 70 years of age or older and formed the basis for this study.

Forty-two patients after pneumonectomy (Group I) were compared with 48 patients who underwent other, less extensive, lung parenchyma resections – lobectomies and wedge resections (Group II). In Group I (40 male and two female), 19 left and 23 right pneumonectomies were performed. The patients' ages varied from 70 to 78 years (mean 71.7; SD ± 1.99). In control Group II, 40 lobectomies, four bilobec-

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tomies and four segmentectomies were performed. Here the patients' ages ranged from 70 to 81 years (mean 72.76 years; SD \pm 2.37).

In both groups, before the surgical procedure was carried out, the following routine tests were performed: complete blood count (CBC), sodium and potassium levels, arterial blood gases, glutamic oxaloacetic transaminase (SGOT)–Asp, glutamic pyruvic transaminase (SGPT)–Alt, lactate dehydrogenase (LDH), blood urea nitrogen (BUN) and creatinine levels, chest radiograph, fiberoptic bronchoscopy, echocardiogram (ECG), and abdominal ultrasound. Functional pulmonary tests to measure forced expiratory volume (FEV₁), FEV₁/VC and vital capacity (VC) were performed, using an *abc Pneumo* 2000 spirometer. To meet the qualifying criteria for surgery, a chest computerized tomography (CT) scan was performed routinely and also mediastinoscopy, when necessary. Data concerning the past medical history and the current condition of the patient was obtained during the patient interview. Information sought included a history of smoking, myocardial infarction, angina pectoris, dysrhythmias, tuberculosis, arterial hypertension, chronic obstructive pulmonary disease (COPD), obesity, varicose veins, diabetes, and peptic ulcer. We also evaluated the WHO Performance Status as well as ASA (American Society of Anesthesiology) risk classification.

Pre-operatively, the pathology of the lesion was determined by one of the following methods: sputum cytology, bronchoscopy or transthoracic needle-biopsy.

Antero-lateral muscle-sparing thoracotomy was the operative approach used for all the patients. Anesthesia was performed with a double-lumen Robertshaw intubation tube. For post-operative pain management, we applied either 0.25–0.5% Bupivacaine through an intra-pleural catheter or 0.125–0.25% Bupivacaine in a continuous infusion into the epidural space (at the level of Th5–Th6). Following pneumonectomy every patient was supplied with a water-seal drainage system, whereas after the other resections a suction-drainage system was used. Antibiotic prophylaxis and low-weight heparin were administered to all the patients in both groups.

Examination of the pathological specimens was carried out by the same pathologist. The staging system was estimated according to the American Joint Committee on Cancer (AJCC) classification [8].

Post-operative complications occurring within a 30 day period were evaluated.

2.1. Statistical analysis

The statistical analysis was made with Statistica[®] software. The fractions of patients in both analyzed groups were compared using Fisher's exact test. The normally distributed statistical variables of the two groups were compared using the unpaired *t*-test and those with non-normal distribution by means of the Mann–Whitney test. The impact of individual risk factors on post-operative complications and

on mortality was calculated by means of binary logistic regression. The *P*-value was considered statistically significant if lower than, or equal to 0.05.

3. Results

Statistical analysis of the pre-operative clinical status revealed no significant differences as to underlying clinical conditions in both groups (Table 1). Spirometric values were also not significantly different in two groups; FEV₁: 1.85 \pm 0.32 vs. 1.93 \pm 0.67 and FEV₁/VC: 81.10 \pm 9.60 vs. 80.40 \pm 10.90 (mean \pm SD). The most frequent histologic type of cancer in both groups was squamous cell carcinoma which constituted 55% of Group I and 50% of Group II. However, the cancer stages were different: Stage IA (T1N0M0) was present in control Group II only whereas Stage IIIA (T2N2M0) was present in the majority of Group I patients, i.e. those who underwent pneumonectomies (Table 2). When consecutive seven stages of cancer (from IA to IV) were allocated digits from 1 to 7 and both groups were compared by means of Mann–Whitney test, the difference between two groups was significant (*P* < 0.001).

Postoperative complications occurred in the majority of patients in both groups (Table 3). At least one post-operative complication or death occurred in 33 of 42 patients from Group I (78.5%) and in 28 of 48 patients from Group II (58%). The difference is significant, *P* < 0.01 (Fisher's exact test). The post-operative complications by type are shown in Table 3. The most common complications were transient dysrhythmias. These disturbances included tachycardia (Group I 32%, Group II 7%) and atrial fibrillation

Table 1
Characterization of population by pre-operative assessment criteria

	Group I (n = 42)	Group II (n = 48)	Significance
<i>Underlying conditions^a</i>			
History of myocardial infarction	6	7	NS
Angina pectoris	2	7	NS
Arrhythmia	2	1	NS
Arterial hypertension	20	16	NS
COPD	9	10	NS
Diabetes	1	3	NS
Peptic ulcer	5	8	NS
Tuberculosis	4	6	NS
Varicose veins	9	10	NS
Obesity	3	4	NS
Psychiatric disturbances	1	3	NS
<i>Performance status (WHO)^b</i>			
H1/H2/H3	27/4/1	39/9/0	NS
ASA 1/2/3	10/31/1	10/38/0	NS
FEV ₁ /VC ^c	81.1 \pm 9.6	80.4 \pm 10.9	NS

^a Significance determined by Fisher's exact test.

^b Significance determined by Mann–Whitney test.

^c Significance determined by an unpaired *t*-test.

Table 2
Characterization of population by clinical staging of cancer

	Group I (n = 42)	Group II (n = 48)	Significance (Fisher's exact test)
IA	0	10	$P = 0.001$
IB	10	18	NS
IIA	0	2	NS
IIB	10	8	NS
IIIA	16	3	$P = 0.0002$
IIIB	6	5	NS
IV	0	2	NS

(Group I 47% and Group II 35%). Pulmonary complications were observed in 17 patients in Group I and in 16 patients in Group II. There was a trend ($P = 0.06$) for transient mental disturbances occurring more frequently in Group I. Prolonged drainage problems were noted in three and five patients in Group I and II, respectively. Bronchopleural fistula (BPF) occurred in three patients, all from Group I. Re-thoracotomy for bleeding was performed in three patients after pneumonectomy and in one after lobectomy. Because of this complication, the post-pneumonectomy patients required significantly greater quantities of blood in the post-operative period and their ICU-stay was longer. The 30-day operative mortality was noted only in Group I and included seven patients, followed four right and three left pneumonectomies. The cause of death was BPF in three cases, complications of brain metastases in one and myocardial infarction in one. One patient died due to hemorrhage from major vessels and in one the cause of death was not established.

Binary logistic regression analysis revealed that out of pre-operative clinical factors determining the occurrence of post-operative complications (including death) the most significant ones in both groups were WHO performance status and the concentration of BUN above 45 mg/dl (Table 4). Additionally, in pneumonectomy group (Group I) the important factor predictive of post-operative complications was COPD, while in Group II such factors were obesity and trend for angina pectoris.

In Table 5, the results of binary regression analysis are presented concerning the effect of pre-operative and post-operative factors on mortality in pneumonectomy group. As

Table 3
Postoperative complications by type

	Group I (n = 42)	Group II (n = 48)	Significance (Fisher's exact test)
Pulmonary complications	17	16	NS
Supraventricular arrhythmias	20	17	NS
Myocardial infarction	1	0	NS
Broncho-pleural fistula	3	0	NS
Psychiatric disturbances	8	3	$P = 0.06$
Prolonged drainage	3	5	NS
Bleeding (re-thoracotomy)	3	1	NS
Mortality (30 days)	7	0	$P = 0.004$

Table 4
Significance of pre-operative factors determining the occurrence of post-operative complications (including death) as determined by binary logistic regression

Factor	Group I (n = 42)	Group II (n = 48)
Performance status (WHO)	$P = 0.008$	$P = 0.0003$
Angina pectoris	NS	$P = 0.08$
Arterial hypertension	NS	NS
COPD	$P = 0.05$	NS
Obesity	NS	$P = 0.03$
ASA	NS	NS
Staging	NS	NS
Arrhythmia	NS	NS
Diabetes	NS	NS
Tuberculosis	NS	NS
Psychiatric disturbances	NS	NS
Peptic ulcer	NS	NS
Varicose veins	NS	NS
FEV ₁ %VC	NS	NS
BUN > 45 mg/dl	$P = 0.021$	$P = 0.027$

shown, the most important pre-operative factor determining mortality was an increase in BUN, following by arterial hypertension and COPD. Out of post-operative factors, the most significant one was the occurrence of broncho-pleural fistula and the need for re-thoracotomy (bleeding).

4. Discussion

The goal of our study was the analysis of early post-operative complications in patients over 70 years, especially after a pneumonectomy. The patient groups included in this study –

Table 5
Pre-operative and post-operative factors significantly connected with mortality in pneumonectomy group as determined by binary logistic regression

	Significance
<i>Pre-operative factors</i>	
Staging	NS
COPD	$P = 0.05$
Performance status (WHO)	NS
Arterial hypertension	$P = 0.02$
Angina	NS
Arrhythmia	NS
BUN > 45mg%	$P = 0.00001$
FEV ₁ %VC	NS
ASA	NS
<i>Post-operative factors</i>	
Left/right pneumonectomy	NS
Pulmonary complications	NS
Arrhythmia	NS
Myocardial infarction	NS
Psychiatric disturbances	NS
Bronchopleural fistula	$P = 0.0005$
Prolonged drainage	NS
Re-thoracotomy	$P = 0.05$

Group I, after a pneumonectomy, and Group II, after less radical lung parenchyma resections, had shown no statistical differences as to underlying clinical conditions except for staging. This implies that the patient selection for both procedures was adequate. The clinical TNM stage was consistent with the extent of the resection performed.

Both the high post-operative mortality rate in the post-pneumonectomy patients and the markedly lower rate in other cases of lung parenchyma resections carried out in patients over the age of 70 years are similar to those reported by previous authors. They reported post-pneumonectomy mortality rates of 17–37% compared with 10–14% following other pulmonary resections [1,5,7,9]. However, other studies conducted by Kadri and Dussek [4], Swartz et al. [6], Cangemi et al. [10] Kohman [11] and Richelme et al. [12] reported lower rates: 4–11%, as well as no significant differences in the rate of complications between pneumonectomy and lobectomy [13].

Our present study indicates that the risk of life-threatening complications and of death in the elderly patient is greater with the greater extent of the surgery (78.5% in Group I and 58% in Group II). Moreover, all cases of death were observed exclusively in pneumonectomy group (Group I). As mentioned, the pre-operative status of the patients in both groups was equal, except for staging. However, subsequent logistic binary regression analysis revealed that staging did not significantly influence the rate of post-operative complications in both groups as well as mortality in pneumonectomy group (Tables 4 and 5).

One of the most common post-pneumonectomy complications was supra-ventricular arrhythmia (SVA). Mitsudomi et al. [2] reported their frequency to be 34% of all post-operative complications. Osaki et al. [3] obtained similar results, namely 24%, in an analysis of 33 patients over 80 years of age who underwent thoracotomy. In a previous study regarding SVA, we observed a rate of 26% which was markedly lower than in the present study [14]. However, the average age of those patients was also lower – 65 years. Contrary to what one may have expected, the arrhythmias did not have an influence on either post-operative mortality or morbidity in patients who died after a pneumonectomy. The association of SVA with morbidity and mortality is a controversial issue in the literature. Some authors [6,11,15,16] claim them to be a prognostic factor of increased mortality whereas others, including us in the present study, do not confirm this [2,7]. However, there is general agreement that SVAs prolong the ICU-stay, thus delaying rehabilitation. This, indirectly, may eventually contribute to the increase in mortality. We strongly believe that intensive post-operative care with immediate treatment of SVAs prevents further severe complications. We mainly used drugs from classes III (amiodarone) or IV (calcium-entry blockers) and/or digitalis in selected cases. When these failed, we performed a cardioversion, if it was not contraindicated. These methods were effective as we were successful in re-storing the sinus rhythm in 85% of the patients.

The rates of various pulmonary complications which we observed were similar to those in the literature. The most frequent were atelectasis and residual pneumothorax. These and other complications did not generally deteriorate into more serious conditions such as lung abscess or empyema. Other authors report rates of these complications ranging from 34 to 43%, which are similar to ours [2,3].

Undoubtedly, the most severe complication following resection for NSCLC is bronchopleural fistula. According to the literature, this complication occurs in a wide range from as little as 0.6% to as much as 30% [2,3,12,16,17]. In our study, BPF only occurred in the pneumonectomy patients (7.7%) and had a significant impact on mortality in that group. The stump was routinely closed with a stapling device (the mechanical suture). An air-leak occurred in one case only and this was corrected by standard hand-suture technique. This patient had no sign of a BPF in the post-operative period. In our department the incidence of BPF in elderly patients after pneumonectomy was significantly higher than in their younger (less than 70 years old) counterparts, where we found it in 2.4% of patients [18]. We believe that the most important factor leading to this complication is the presence of underlying diseases, especially COPD. Chronic inflammatory changes leading to lesions in the mucous membrane disturbed the natural healing process of the stump. Also, the fact that the start of rehabilitation was delayed in these patients may have been a contributory factor.

The frequency of other complications, including post-operative psychiatric disturbances, prolonged bleeding and drainage-time is similar to that reported in the literature [3,5,16,19]. However, we found that psychiatric complications were commoner in Group I (pneumonectomy) than in Group II (less extensive resections). They were usually of a delusional or depressive nature. It is therefore worth considering instituting a psycho-pharmacological preventive programme prior to surgery.

The general status of elderly candidates for NSCLC surgery and their underlying diseases are considered by many authors to be important risk factors [2,5,6]. In our study we observed a significant relationship between performance status and the rate of post-operative complications following both pneumonectomy and lobectomy or pulmonary wedge resections. Furthermore, COPD appeared to be a significant risk factor in pneumonectomy (Group I), while obesity in patients from Group I. This is only in partial agreement with the reports of other authors [1,6]. Some of these state also that ischemic heart disease (IHD) is one of the most predictive risk factors in post-pneumonectomy patients [1,10]. In our study we found no such statistically significant correlation between IHD and higher mortality or morbidity. This may be due to the adequate levels of ICU-care and pharmacological prevention of post-operative cardiac ischemia in our unit.

A useful guide to a patient's general status is the pre-operative assessment described by the American Society

of Anesthesiology (ASA). However, we were not able to find a significant impact of this factor on either morbidity or mortality in both groups.

The BUN level higher than 45 mg/dl (range 46–53 mg/dl) with creatinine levels within the normal range were found in all the patients who died within 30 days after a pneumonectomy. We have not been able to find any reference to this observation in the literature.

Contrary to the literature, we found no association between either which of the lungs, right or left, was operated on or the pre-operative values of pulmonary function tests and higher mortality in post-pneumonectomy patients [1,3,5,7,17]. In our study, the increased BUN level (>45 mg/dl) appeared to be a significant risk factor for post-operative complications in both groups as well as for mortality in pneumonectomy group. Another significant pre-operative factors contributing to mortality in pneumonectomy patients in our study were arterial hypertension and COPD and out of post-operative ones BPF and the need for re-thoracotomy.

We believe that the results of this study, which is still in progress, will be of considerable interest to thoracic surgeons as the number of pneumonectomies in the elderly patients is rising constantly.

5. Conclusions

1. Pneumonectomy in patients over the age of 70 years carries an increased risk of severe post-operative complications including death, compared to patients in the same age group who had undergone less extensive pulmonary resections.
2. The most important factors contributing to post-operative complications in pneumonectomy patients were performance status, chronic obstructive pulmonary disease (COPD) and high level of blood urine nitrogen (BUN).
3. The highest impact on early mortality in pneumonectomy patients was exerted by COPD, arterial hypertension, broncho-pleural fistula, need for re-thoracotomy (bleeding) and elevated BUN.

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