Long-term Survival Following Pneumonectomy for Non-Small Cell Lung Cancer*

Clinical Implications for Follow-up Care

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Background: **The aim of this study was to determine the risk of overall death in long-term survivors (> 5 years) after pneumonectomy for non-small cell lung cancer (NSCLC), and to establish the optimal follow-up strategy for these patients.**

Methods: **We analyzed a single-center experience with 94 long-term survivors who underwent pneumonectomy (group A) for NSCLC between January 1992 and December 2000. Prospective tumor registry data were compared with data for 147 long-term survivors who underwent lobectomy (group B) during the same period.**

Results: **Clinical characteristics at the time of operation differed between the two groups with more squamous histology, larger tumor size, and more advanced stage in group A compared with group B. During follow-up, late lung cancer relapses were rare in both groups (2.1% vs 1.4%), and second primary malignancies were less frequent in group A (2.1% vs 9.5%, p = 0.032). The overall 10-year survival rate was lower in group A than in group B (67.3% vs 82.8%); however, there was no significant difference in lung cancer-specific survival (93.5% vs 95.1%). Intercurrent disease was the leading cause of death in group A (14 patients, 14.9%), most commonly respiratory failure resulting from community-acquired pneumonia.**

Conclusion: **Late cancer relapse or second primary malignancies were rare in long-term survivors after pneumonectomy, but the overall mortality remained high as a result of intercurrent diseases. Continued surveillance should focus on prevention, early detection and aggressive management of intercurrent disease during follow-up care of these patients.**

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Key words: long-term survivors; lung cancer; outcome; pneumonectomy

Abbreviations: NSCLC = non-small cell lung cancer; SPLC = second primary lung cancer

In the United States, primary lung cancer is expected to be diagnosed in an estimated 210,000 people in 2007, and approximately 31,000 patients will become long-term survivors every year.[1] These long-term survivors may succumb to late cancer recurrence, second primary malignancy, or intercurrent disease including cardiopulmonary disorders that are, in part, a consequence of pulmonary resection and/or chemoradiation.

For decades, pneumonectomy has been the operation of choice to treat centrally located or locally

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advanced tumors; however, it is also known to cause impaired function and decreased 5-year survival compared with lobectomy.[2] Although shortened survival is partly explained by oncologic factors, premature death from adverse physiologic effects appears to be a major factor. There is considerable information on the outcome of pneumonectomy within the first 5 years after surgery, but relatively little information is available concerning the long-term outcome of such patients beyond 5 years.

This study focuses on the clinical outcome of patients who survive for ≥ 5 years after pneumonectomy for non-small cell lung cancer (NSCLC). Our primary objectives were to quantify the risk of death in long-term survivors after pneumonectomy, and to apply the results to our daily practice in the follow-up care of such patients.

Materials and Methods

A retrospective study was conducted on NSCLC patients who underwent pneumonectomy at our institute between January 1992 and December 2000. During this period, 628 consecutive patients underwent complete resection for NSCLC by the same surgical team. Of these, long-term survivors (> 5 years) were selected for the study from our prospective tumor registry database. We examined 94 of these patients 5 years after pneumonectomy (group A). Patients were evaluated for demographic, surgical, and pathologic variables, and were compared with 147 long-term survivors who underwent lobectomy (group B) during the same period.

Patient evaluation included medical history, physical examination, chest radiography, and blood tests. CT scans of the chest and upper abdomen, abdominal sonography, and bone scintigraphy were performed routinely. Cervical mediastinoscopy was performed in patients with suspected N3 disease. On thoracotomy, the extent of the primary lesion was carefully assessed, and systematic dissection of all hilar and mediastinal lymph nodes was performed in every case. Until the mid-1990s, we favored pneumonectomy over sleeve lobectomy because we considered the oncologic advantage of the latter to be unclear, especially for central tumors with suspicious hilar node metastasis in patients with sufficient pulmonary reserve. Histologic type, location and size of the tumor, status of bronchial resection margin, and visceral pleural invasion were recorded in a prospective manner. Pathologists examined every dissected node during and/or after surgery. Pathologic staging was performed according to the International Staging System for Lung Cancer.[3]

Follow-up was achieved through regular clinic visits until the patient's death. Patients were examined at 3-month intervals for 2 years and typically at 6-month intervals thereafter. The evaluation included physical examination, chest radiography, and measurement of tumor markers. In addition, chest CT scan, abdominal sonography, and bone scintigraphy were performed at 6-month intervals for 5 years and subsequently at 1-year intervals.

We define multiple primary lung cancers as tumors that are anatomically separate and histologically different.[4] When the tumors are histologically the same, they must have no systemic metastases or mediastinal spread. For metachronous tumors with the same histology, the disease-free interval should be at least 2 years.

Survival was calculated by the Kaplan-Meier method, and differences in survival were determined by log-rank analysis. We define death as lung cancer specific when the cause of death was either a locoreginal recurrence or distant metastasis. Deaths due to noncancer or unknown causes were considered to be cancer-unrelated deaths. Cox proportional hazards model was used to examine and adjust for the effects of pneumonectomy and other covariates on overall survival. Statistical difference was considered to be significant if the p value was < 0.05.

Results

Clinical Characteristics

Clinical characteristics of patients in groups A and B are compared in Table 1. The median age at the time of surgery was similar between the two groups. There were no significant differences in FEV_1 and lobe involvement. In group A, the incidence of squamous cell carcinoma was higher than in group B (64 patients [68.1%] vs 52 patients [35.4%]) and the mean tumor size was larger (4.2 ± 0.2 cm vs 3.4 ± 0.2 cm [± SEM]). The number of patients with an advanced stage of disease was greater in group A (for stage ≥ II, 61.7% vs 27.9%), and therefore more patients underwent adjuvant therapy than in group B.

Table 1—*Clinical Characteristics of the Patients

Variables	Group A (n = 94)	Group B (n = 147)	p Value
Median age (range), yr	58.0 (35–76)	58.0 (10–79)	ns
Sex, No. (%)			0.005
Male	79 (84.0)	94 (63.9)	
Female	15 (16.0)	53 (36.1)	
FEV_1, % predicted†	82.6 ± 1.9	98.6 ± 8.0	ns
Primary site, No. (%)			ns
Right upper lobe	22 (23.4)	47 (32.0)	
Right middle lobe	7 (7.4)	9 (6.1)	
Right lower lobe	18 (19.1)	41 (27.9)	
Lelt upper lobe	26 (27.7)	33 (22.4)	
Left lower lobe	18 (19.1)	17 (11.6)	
Other	3 (3.3)‡	0 (0.0)	
Histology, No. (%)			0.000
Squamous	64 (68.1)	52 (35.4)	
Nonsquamous	30 (31.9)	95 (64.6)	
Tumor size, cm†	4.2 ± 0.2	3.4 ± 0.2	0.024
Pathology stage, No. (%)			0.000
I	36 (38.3)	106 (72.1)	
II	27 (28.7)	19 (12.9)	
III	28 (29.8)	22 (15.0)	
IV	3 (1.2)‡	0 (0.0)	
Adjuvant therapy, No. (%)			0.000
None	41 (43.6)	106 (72.1)	
Chemotherapy	5 (5.3)	8 (5.4)	
Radiotherapy	14 (14.9)	14 (9.5)	
Chemoradiation	34 (36.2)	19 (12.9)	

*ns = not significant.
†Mean ± SEM.
‡Satellite nodule in different lobe.