Radiol Oncol 1995; 29: 19-24.

Outcome of pneumonectomy for primary non-small cell lung cancer – A ten-year experience

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Between 1982 and 1992, 105 patients with non-small cell lung cancer underwent pneumonectomy and mediastinal node dissection. Thirteen patients (12%) were categorized as pathological stage I, 18 (17%) were categorized as pathological stage II, 63 (60%) were categorized as pathological stage IIIa, and 11 (11%) were categorized as pathological stage IIIb. The overall actuarial 3-year survival rate was 27%. Postpneumonectomy complications occurred in 20 patients. Operative mortality occurred only in 8 pathological stage IIIa male patients (7.6%). No significant differences in operative mortality were noted for the following criteria: age, sex, side of resection, pathological stage, histologic classification, preoperative forced expiratory volume in 1 second (FEVI) of 2.0 L or less, and predicted postoperative FEVI of 1.0 L or less. Of the surviving 97 patients, 3 patients were lost during follow-up, 13 patients (13.8%) died due to pneumonia and/or respiratory failure, and 40 patients (42.6%) died due to distant metastases, with bone as the most common metastatic site, during the mean follow-up time of 39 months. Pathological stage I and stage II patients showed actuarial 3-year survival rates, of 60.0% and 31.3% respectively. The survival rates of stage I and stage II patients were higher than for stage IIIa patients.

Key words: carcinoma non-small-cell lung, lung neoplasms- surgery, penumonectomy, survival rate

Introduction

Surgical resection remains the most curative modality for non-small cell lung carcinoma.[1-3] With improvements in preoperative preparation and postoperative fluid and respiratory therapy, the mortality and morbidity rates for pulmonary surgery have dramatically decreased over the past decade.[4]

In 1933, Graham and Singer reported a successful one-stage pneumonectomy for carcinoma of the lung.[5] In 1950, Churchill and associates reported improved results with lobectomy, which remains the procedure of choice for the majority of patients with carcinoma of the lung.[6]

What is the most appropriate resection for cancer of the lung? That most appropriate procedure is the one that excises all of the carcinoma and preserves as much of the normal tissue as possible. In previous studies, operative

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UDC: 616.24-006.6-089.85

mortality after pneumonectomy has ranged from 6.2% to 12.4%[7-11] and the 5-year survival rate from 8% to 25% for all stages of carcinoma of the lung,[7, 9, 12]

We retrospectively reviewed 105 patients with non-small cell lung cancer who had undergone pneumonectomy, to identify the postoperative morbidity and mortality, factors associated with postoperative mortality, the survival times for various stages, and the outcomes.

Materials and methods

Between 1982 and 1992, 105 patients with non-small cell lung cancer underwent pneumonectomy and mediastinal lymph node dissection in our institute. There were 93 men and 12 women with a mean age of 62.0 years (range, 42 to 72 years).

The patients were categorized as operable with a clinical stage of IIIa or less. Clinical staging was performed using TNM classification.[13] Extensive preoperative evaluations were conducted including plain chest roentgenograms and computed tomographic scans of the chest and abdomen. Clinical N2 disease was defined by the presence of an enlarged mediastinal lymph node greater than 1 cm in diameter. A bone scan and liver sonography were routinely performed for each patient. A computed tomographic scan of the brain was performed if symptoms were present. Mediastinoscopy was performed to rule out N3 disease. All patients received preoperative pulmonary function tests including spirometry, regional pulmonary ventilation and perfusion scan using Xenon-133 gas and Tc-99m MAA, and arterial blood-gas determination.

Pneumonectomy was performed in patients whose tumor was considered to be completely resectable, and was determined by tumor size and local extension. The necessity for pneumonectomy was determined, at the time of operation, by the surgeon. Patients with a completion pneumonectomy were excluded from this study.

Operative mortality was defined as death within 30 days of pneumonectomy or death during hospitalization after pneumonectomy. Risk factors of pneumonectomy were examined, including age, sex, side of resection, pathological stage, histological classification, preoperative FEV1 of 2.0L or less, and predicted postoperative FEV1 of 1.0L or less (using percent perfusion to the uninvolved lung from the Tc-99m MAA perfusion scan study).

All patients were followed until death. There were 3 patients who were lost during follow-up. The mean follow-up time was 39 months (range, 12 to 118 months). The actuarial survival rates of the remaining 94 patients were analyzed by pathological stage.

Statistical analysis

Survival distributions were calculated using the methods of Kaplan and Meier. Differences in operative mortality, based on variable criteria, were calculated using the chi-square test.

Results

Eighty-four patients (80%) presented with squamous cell carcinoma; 16 patients (15%) presented with adenocarcinoma, 4 patients (4%) presented with adenosquamous carcinoma and 1 patient presented with (1%) large cell carcinoma.

Sixty-nine patients (66%) underwent a left pneumonectomy and 36 patients (34%) underwent a right pneumonectomy. After operation, patients were staged based on pathological examination of the tumor and lymph node mapping. There were 13 patients (12%) categorized as pathological stage I, 18 patients (17%) categorized as stage II, 63 patients (60%) categorized as stage IIIa, and 11 patients (11%) categorized as stage IIIb.

Table 1 shows the complications that occurred in 20 patients and their association with operative mortality.

Table 2 shows the results of various criteria associated with operative mortality. Although all 8 operative deaths (7.6%) occurred in male patients with a pathological stage of IIIa, there

Table 1. Incidence of complications and their association with operative mortality.

Complications (n = 34)	No. of patients (n = 20)	Deaths	
		No.	%
Respiratory causes (35.3%)			
pneumonia	6	4*	67
prolonged ventilation (>24 hrs)	3	0	0
pulmonary edema	2	0	0
bronchopleural fistula	1	1	100
Cardiac causes (29.4%)			
arrhythmia	7	0	0
heart herniation	2	0	0
myocardial infarction	1	1	100
Others (35.3%)			
hemorrhage	2	0	0
chylothorax	2	0	0
stroke	2	1	50
pulmonary embolus	1	1	100
renal failure	1	1*	100
wound infection	2	0	0
recurrent nerve palsy	2	0	0

* one of these four patients had renal failure.

Table 2. Differences in operative mortality for various criteria.

Criteria	No. of deaths	No. of patients	%	P value
Age (years)				
<70	6/90		6.7	NS
≥70	2/15		13.3	
Sex				
Male	8/93		8.6	NS
Female	0/12		0.0	
Side of resection				
Right	4/36		11.1	NS
Left	4/69		5.8	
Staging				
I + II	0/31		0.0	NS
IIIa	8/63		12.7	
Pathology				
Squamous cell ca.	7/84		8.3	NS
Adenocarcinoma	1/16		6.3	
Preop. FEV1				
≥2.0 L	5/44		11.4	NS
<2.0 L	3/23		13.0	
Predicted postop. FEV1				
≥1.0 L	8/65		12.3	NS
<1.0 L	0/2		0.0	

FEV1: forced expiratory volume in 1 second. NS: no significance.

were no significant differences in operative mortality for gender or pathological stage (using the chi-square test).

Actuarial survival was determined for all patients (Figure 1), as well as by pathological stage (Figure 2). The overall survival rate was 27% after 3 years. Patients with pathological stage I, stage II, stage IIIa, and stage IIIb diseases showed 3-year survival rates of 60.0%, 31.3%, 18.2%, and 0%, respectively. The median survival times of patients with pathological stage I, stage II, stage IIIa, and stage IIIb diseases were 3.82 years, 2.66 years, 1.46 years and 0.93 years, respectively.

Among the surviving 94 patients, 13 patients (13.8%) died due to pneumonia without evidence of disease before death, and 40 patients (42.6%) died due to distant metastasis, with bone as the most common metastatic site during the follow-up period.

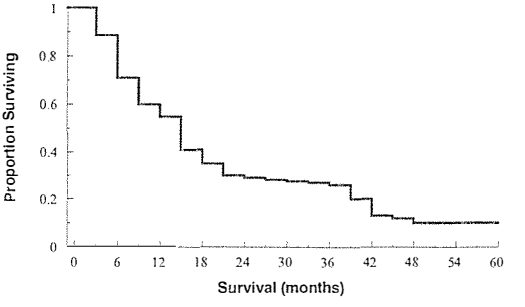

Figure 1. Overall actuarial survival od 94 patients who underwent pneumonectomy for primary non-small cell lung cancer.

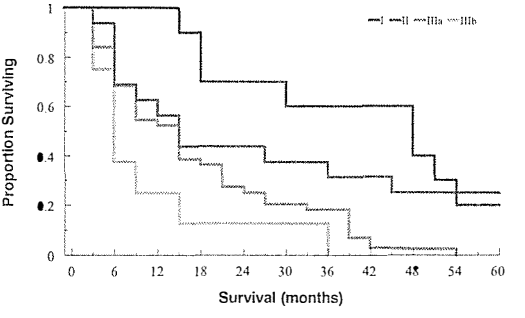

Figure 2. Actuarial survival of 94 patients who underwent pneumonectomy for primary non-small cell lung cancer by pathological stage.

Discussion

Most surgeons agree that pneumonectomy, for patients with non-small cell lung cancer, should be used only for extensive tumors that cannot be removed by lobectomy, or sleeve lobectomy.[14, 15] In this study, the patients who underwent pneumonectomy showed a predicted postoperative FEV1 equal to or greater than o.8 L (the preoperative FEV1 multiplied by the percent of perfusion of the uninvolved lung). In an experimental clinical study, Adams et al showed the importance of cardiopulmonary reserve as a determinant of risk.[16] Ventilation perfusion studies, using Xenon-133 gas and Tc-99 m MAA showed good reliability for calculating predicted lung function.[17, 18] These predictors are very useful clinically because regional and overall pulmonary functions remain stable after pneumonectomy.[19]

At the time of operation, if a (bi-) lobectomy or a sleeve resection was determined to be insufficient for removing the local disease, a pneumonectomy was performed. We traced the medical records of the patients who had undergone pneumonectomy and found that the procedure was performed if the following criteria were present: (1) tumor encroaching to the pulmonary aftery, (2) tumor invasion into the hilar area, (3) tumor invasion into the main bronchus, and (4) tumor invasion into the interlobar fissure.

Our study showed an operative mortality rate of 7.6%, which is in accordance with the results of Ginsberg et al (6.2%),[7] Patel et al (8.6%),[11], and Putnam et al (8%).[20] Various risk factors of pneumonectomy have been studied. Didolkar et al found that advanced age was associated with an increased mortality rate in pulmonary resection for lung cancer,[21] however, this factor was not suggested in the study by Patel et al[11] or in our study. This may be due to a patient group with a limited number subjects aged 70 or above; 14.3% in our study and 16% in the study of Patel et al.[11] Our report, unlike that of Weiss,[10] did not find that women fare better after resection. This may be due to the fact that the number of male patients (93 patients) greatly surpassed the number of female patients (12 patients) in our study. The side of resection was not related to mortality, although Higgins et al[22] and Harmon et al[23] suggested that right pneumonectomy is more hazardous in terms of bronchopleural fistula and empyema. In our study, although all eight operative mortalities occurred in pathological stage IIIa, there was no statistical significance when compared to stages I and II. This may be due to a greater percentage of patients (60%) in pathological stage IIIa. We found that no single variable enables the clinician to predict operative moratlity after pneumonectomy, and patients should not be excluded from pneumonectomy on the basis of any single criterion.

The complications after pneumonectomy were variable, and some were associated with mortality. In our study, although all patients received prophylactic antibiotics, pneumonia developed in 6 patients. Among them, four patients died due to respiratory failure. Cardiac arrhythmia was the most common complication, occurring in 7 patients (35%), but was not associated with mortality. Wahi et al reported that patients who developed atrial arrhythmia had a longer stay in the intensive care unit and a longer postoperative hospital stay.[4] The cause of the abnormal rhythm is unknown. Mediastinal shift, hypoxia, abnormal pH of the blood, as well as other factors, have been implicated but none have been proven. Shields suggested prophylactic digitalization for older patients undergoing pneumonectomy.[24]

We found that the most significant factor for determining long term survival of patients undergoing pneumonectomy is the pathological stage. Patients categorized as pathological stage I or stage II showed a better 3-year survival rate than those with stage IIIa (60% or 31.3% vs 18.2%). We did not stratify the survival time of the various subtypes of pathological stage IIIa by T and N status. Wilkins and co-workers found a significant correlation for survival time and lymph node status in pneumonectomy-treated patients. Patients with uninvolved nodes had a better 5-year survival rate than those with

involved nodes (42.1 % vs 16.3 %).[3] Putnam et al found that patients classified as pathological stage I, stage II, stage IIIa showed 3-year survival rates of 45 %, 47 %, and 24 %, respectively. In addition, no patient in pathological stage III with a percent predicted FVC of 64 % or less survived more than 1.3 years, compared with a 26 % survival rate after 3 years for other pathological stage III patients ($P = 0.009$).[20] Further multivariate studies may be needed to clarify the significant factors that determine the survival of the pneumonectomy-treated patient.

The fate o patients after pneumonectomy has seldom been reported. Ogilvie and coworkers studied patients with lung cancer 10 years after pneumonectomy, and found that patients had a poorer ventilatory capacity and a higher incidence of cor pulmonale than those patients with lung cancer 1 year after pneumonectomy.[25] In our study, we found that 13.6 % of the patients died due to pneumonia and/or respiratory failure during a mean follow-up time of 39 months. A management strategy that includes prevention of pulmonary infection, respiratory exercise, prohibition of smoking and regular expectoration should be considered during follow-up. The benefit of adjuvant therapy for the various stages of patients after pneumonectomy remains to be verified.

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