

## Original Article

# Prognostic Factors for Survival of Stage IB Upper Lobe Non-small Cell Lung Cancer Patients: A Retrospective Study in Shanghai, China

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## ABSTRACT

**Objective:** To identify clinical and pathologic factors that were associated with the survival of stage IB upper lobe non-small cell lung cancer (NSCLC) patients.

**Methods:** A retrospective study of 147 subjects who had undergone curative resection for stage IB upper lobe NSCLC was performed. Patients who had received any adjuvant or neo-adjuvant chemotherapy were excluded. Survival function curves were estimated using the Kaplan-Meier procedure. Crude and adjusted hazard ratios (HRs) of potential prognostic factors were estimated using Cox proportional hazards models.

**Results:** Five factors, including age, tumor size, histologic grade of differentiation, number of removed superior mediastinal lymph node stations and presence of visceral pleura invasion, were significantly and independently associated with mortality risk. Adjusted HRs were 2.6 [95% confidence interval (95% CI): 1.1–6.5] and 4.6 (95% CI: 1.9–11) for those aged 58–68 years and those >68 years, respectively, relative to those aged <58 years. HRs for those with poorly and moderately differentiated tumors were 6.4 (95% CI: 2.3–18) and 1.4 (95% CI: 0.7–2.8), respectively. HRs for those with tumor size 3.1–5 cm and >5 cm (vs ≤3.0 cm) were 2.3 (95% CI: 1.1–4.9) and 4.3 (95% CI: 1.9–10), respectively. The presence of visceral pleura invasion also increased the risk of mortality (HR=4.0, 95% CI: 1.3–12).

**Conclusion:** Advanced age, larger tumor size, poorly differentiated histology, smaller number of removed superior mediastinal lymph node stations, and presence of visceral pleura invasion were associated with poor survival of surgically treated stage IB upper lobe NSCLC patients.

**Key words:** Non-small cell lung cancer; Stage IB; Prognosis; Lymphadenectomy

## INTRODUCTION

Among all patients with non-small cell lung cancer (NSCLC), those with stage IB accounts for about 20%–30%. Currently, surgery is still the preferred treatment for stage IB NSCLC and is considered to be the only procedure that could potentially cure the condition. However, current long-term survival for patients of stage IB NSCLC is still not optimistic. Despite surgical resection, its 5-year survival rate is only 60%–70%, and nearly half of the patients have died from local recurrence or distant metastasis within 5 years<sup>[1,2]</sup>. Lymph node metastatic is a main pathway for spreading lung cancer and is one of the most important factors affecting the prognosis. In general, lymph node metastasis of lung cancer follows the pathway of lymph drainage: as the metastasis sequence of pulmonary lymph nodes→ hilar lymph nodes→ mediastinal lymph nodes. Upper lobe NSCLC, compared to the middle or lower lobe NSCLC,

tends to have a higher probability of occurring mediastinal lymph node metastasis, and its mediastinal lymph node metastasis is often constricted to regional lymph nodes in superior mediastinum (for right upper lobe NSCLC metastasis more likely to occur at station 4R and for left upper lobe metastasis more likely to occur at station 5)<sup>[3,4]</sup>.

Therefore, it is critical to identify factors that carry an increased risk of mortality in patients with stage IB NSCLC. Based on lymph node metastasis characteristics of upper lobe NSCLC, we analyzed the data from 147 stage IB upper lobe NSCLC patients undergoing complete resection from May 2001 to December 2004 at the Shanghai Chest Hospital retrospectively. We aimed to investigate the clinical and pathological factors related to the prognosis of stage IB upper lobe NSCLC patients.

## MATERIALS AND METHODS

### Case Selection and Inclusion Criteria

One hundred and forty-seven consecutive stage IB upper lobe NSCLC patients undergoing complete resection from May, 2001 to December, 2004 at the Shanghai Chest

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Hospital were included in this study. The inclusion criteria were as follows: 1) participants were Shanghai local residents; 2) their primary lesions were in the left/right upper lobe; 3) all patients had been evaluated by physical examination, chest and brain computed tomographic (CT) scan, ultrasound of the abdomen, bone scan and fiberoptic bronchoscopy prior operation; 4) a complete resection surgery was performed according to the International Association for the Study of Lung Cancer (IASLC) 2005 criteria<sup>[5]</sup>; and 5) the diagnoses were confirmed as non-small cell lung cancer by postoperative pathology as the pathological stage of T2N0M0 (stage IB). Deaths due to non-cancer causes and cases who had received any adjuvant or neo-adjuvant chemotherapy were excluded.

#### Follow-up and Measurements

All the 147 stage IB cases were followed up until December 30, 2009. The endpoint mortality data during the follow-up period were obtained from the Shanghai Center for Disease Control and Prevention. The postoperative survival time was calculated as the difference between the surgery date and the date of death. Those who survived beyond December 30, 2009 were censored on that day and their survival time was determined as the difference between December 30, 2009 and the surgery date.

For all enrolled subjects, we collected the following data: hospital admission number, date of surgery, age, gender, tumor size, tumor location, histological type, grade of differentiation, visceral pleural invasion, number of removed lymph nodes, number of removed mediastinal lymph nodes and number of removed superior mediastinal lymph node stations.

#### Statistical Analysis

Survival time curves were estimated using the Kaplan-Meier product method. We calculated the crude

hazard ratios (HRs) of potential prognostic factors using the Cox proportional hazards model. To assess the independent predictive values of potential predictors, we further calculated adjusted HRs after adjusting for other variables using multivariate Cox proportional hazards models. A backward stepwise approach was used to determine the final model which included all significant variables. A *P*-value of less than 0.05 was considered significant. All statistical analyses were performed using SPSS version 15.0 (SPSS Inc., Chicago, IL).

## RESULTS

#### Characteristics of the Study Participants

A total of 147 eligible patients met the inclusion criteria. Their clinical and pathological characteristics are shown in Table 1. Among these eligible patients, 76 cases were in the group of stage IB right upper lobe NSCLC and 71 cases in the group of stage IB left upper lobe NSCLC. The differences between the two groups in age, gender, histological type, grade of differentiation, visceral pleural invasion, and tumor size did not reach a statistical significance. A total of 925 lymph nodes were removed during the surgery in all enrolled patients with an average of 6.29 lymph nodes, and a total of 491 mediastinal lymph nodes (266 and 225 for superior and inferior mediastinal lymph nodes respectively) were removed; the number of cases whose number of removed superior mediastinal lymph node stations was less than 2 amounted to 55, and the number of cases whose number of removed superior mediastinal lymph nodes was not less than 2 amounted to 92. The differences between the two groups in the numbers of removed lymph nodes, and removed mediastinal lymph nodes did not reach a statistical significance. However, the number of removed superior mediastinal lymph node stations was significantly higher in the right upper lobe group than in the left upper lobe group.

**Table 1.** Characteristics of 147 patients with stage IB upper lobe NSCLC

	Number (%)	Right upper lobe		Left upper lobe		<i>P</i>
		Number (%)	Number (%)	Number (%)	Number (%)	
Age, years						0.30
<58	51 (34.7)	30 (39.5)	21 (29.6)			
58–68	56 (38.1)	29 (38.2)	27 (38.0)			
>68	40 (27.2)	17 (22.4)	23 (32.4)			
Sex						0.09
Female	64 (43.5)	28 (36.8)	36 (50.7)			
Male	83 (56.5)	48 (63.2)	35 (49.3)			
Histological type						0.77
Adenocarcinoma	96 (65.3)	50 (65.8)	46 (64.8)			
Squamous	37 (25.2)	20 (26.3)	17 (23.9)			
Adenosquamous	14 (9.5)	6 (7.9)	8 (11.3)			
Grade of differentiation						0.82
Well	74 (50.3)	41 (53.9)	33 (46.5)			
Moderate	53 (36.1)	26 (34.2)	27 (38.0)			
Poor	13 (8.8)	6 (7.9)	7 (9.9)			
Unknown	7 (4.8)	3 (3.9)	4 (5.6)			
Visceral pleura invasion						0.73
Present	129 (87.8)	66 (86.8)	63 (88.7)			
Absent	18 (12.2)	10 (13.2)	8 (11.3)			