



# Assessing the prognostic impact of the International Association for the Study of Lung Cancer proposed definitions of complete, uncertain, and incomplete resection in non-small cell lung cancer surgery



Matteo Gagliasso<sup>a</sup>, Giuseppe Migliaretti<sup>b</sup>, Francesco Ardisson<sup>a,\*</sup>

<sup>a</sup> University of Torino, Department of Oncology, Thoracic Surgery Unit, San Luigi Hospital, Regione Gonzole 10, 10043 Orbassano, Torino, Italy

<sup>b</sup> University of Torino, Department of Clinical & Biological Sciences, Statistical Unit, San Luigi Hospital, Regione Gonzole 10, 10043 Orbassano, Torino, Italy

## ARTICLE INFO

### Keywords:

Non-small cell lung cancer  
Surgery  
Incomplete resection  
Residual disease  
Survival

## ABSTRACT

**Objective:** The aim of this study was to assess the prognostic impact of the definitions of complete, uncertain, and incomplete resection in non-small cell lung cancer (NSCLC) surgery, as proposed by the International Association for the Study of Lung Cancer (IASLC).

**Patients and methods:** Single institution retrospective study of consecutive patients undergoing surgery for NSCLC between 1998 and 2007. Complete resection was defined by absence of gross and microscopic residual disease; systematic nodal dissection; no extracapsular extension in distal lymph nodes; and negativity of the highest mediastinal node removed. An uncertain resection was defined by free resection margins, but one of the following applied: lymph node evaluation less rigorous than systematic nodal dissection; positivity of the highest mediastinal node removed; presence of carcinoma in situ at the bronchial margin; positive pleural lavage cytology. A resection was defined incomplete by presence of residual disease; extracapsular extension in distal lymph nodes; positive cytology of pleural or pericardial effusions. Follow-up was complete and all patients were followed up until death or for a minimum period of 5 years. Overall survival (OS) was analyzed using Kaplan-Meier method, log rank test, and Cox proportional hazards model.

**Results:** A total of 1277 patients were identified. One thousand and three patients (78.5%) underwent complete resection, 185 (14.5%) underwent uncertain resection, and 89 (7.0%) underwent incomplete resection. Both uncertain and incomplete resection were associated with significantly worse OS when compared with complete resection (hazard ratio: 1.69 and 3.18, respectively; both  $p = 0.0001$ ). Median OS and 5-year survival rate were 80.1, 39.9, 17.3 months and 58.8%, 37.3%, 15.7% in patients undergoing complete, uncertain, and incomplete resection, respectively.

**Conclusion:** The present analysis suggests that in patients undergoing surgery for NSCLC, the IASLC definitions of complete, uncertain, and incomplete resection are associated with statistically significant differences in survival.

## 1. Introduction

In patients with non-small cell lung cancer (NSCLC), in the absence of distant metastasis, complete surgical resection continues to be the mainstay therapeutic modality. However, controversy exists about the definition of complete resection in NSCLC surgery [1–4] and inconsistencies regarding the impact of incomplete resection on prognosis further complicate matters [5–7]. In 2005, the International Association for the Study of Lung Cancer (IASLC) proposed several criteria to define complete and incomplete resection in NSCLC surgery taking into account pertinent literature and incorporating the concept of systematic nodal dissection [8]. Besides, a third category of uncertain resection

was added.

To our knowledge, no studies have specifically addressed the prognostic significance of the IASLC proposed definitions. Thus, we conducted a retrospective study evaluating the prognostic impact of these definitions in conjunction with other established clinicopathologic prognostic factors in a series of 1277 consecutive patients undergoing surgery for NSCLC.

\* Corresponding author.

E-mail addresses: [matteo.gagliasso@gmail.com](mailto:matteo.gagliasso@gmail.com) (M. Gagliasso), [giuseppe.migliaretti@unito.it](mailto:giuseppe.migliaretti@unito.it) (G. Migliaretti), [francesco.ardissone@unito.it](mailto:francesco.ardissone@unito.it) (F. Ardisson).

## 2. Patients and methods

### 2.1. Data retrieval

The study protocol was approved by the Institutional Review Board with a waiver of patient consent. We performed a retrospective analysis on a prospectively computerized database including all consecutive NSCLC patients who underwent thoracotomy for a planned resection between January 1998 and December 2007 in our institution. The following exclusions were made: patients proved to have not resectable lesions at the time of exploration, and patients receiving pulmonary resection for carcinoid tumors.

### 2.2. Data variables

The demographic and clinical variables considered were patient age, patient gender, and comorbidity. The modified Charlson Comorbidity Index (CCI) [9] was used as a measure of comorbidity and each patient was categorized in one of three comorbidity grades: 0, 1–2, and 3 or more.

Treatment variables included induction therapy, year of surgery, surgery, and adjuvant therapy. Surgical procedures were defined as pneumonectomy, lobectomy, segmentectomy, and wedge resection. Bronchial sleeve resections and bilobectomies were grouped under the lobectomy category. Perioperative outcomes included length of hospital stay, postoperative morbidity and mortality. Overall postoperative morbidity was defined as the occurrence of at least one complication within 30 days after surgery or during the hospitalization. Major cardiopulmonary morbidity occurred if one or more than one of the following were present: acute myocardial infarction; cardiac failure requiring inotropic support; haemodynamically unstable arrhythmia requiring treatment; pulmonary embolism; adult respiratory distress syndrome; respiratory failure ( $\text{PaO}_2 < 65 \text{ mmHg}$  and/or  $\text{PaCO}_2 > 45 \text{ mmHg}$ ); pneumonia defined by typical clinical, laboratory, and radiographic features; atelectasis requiring bronchoscopy; bronchopleural fistula. Operative mortality was reported as 30-day mortality, defined as any death occurring within 30 days of surgery; perioperative mortality, defined as any death occurring in hospital or within 30 days of surgery; and 90-day mortality, defined as any death occurring within 90 days of surgery.

Tumor variables considered were histology, tumor size, pT status, pN status, and pTNM stage. Histology subtypes were classified into categories of adenocarcinoma, squamous cell carcinoma, and other histologic types. Patients were initially staged according to the sixth TNM classification and the TNM descriptors were converted to the eighth edition [10]. Intrathoracic lymph node stations were localized according to the Mountain-Dresler map [11].

Finally, operative notes and pathology reports were reviewed and the completeness of resection was determined based on the IASLC proposed criteria [8]. A complete resection required all of the following: absence of gross and microscopic residual disease; systematic nodal dissection including, at least, three nodes removed from pulmonary stations and three removed from mediastinal stations, one of which had to be the subcarinal station; no extracapsular extension in distal lymph nodes; and negativity of the highest mediastinal node removed. An uncertain resection was defined by free resection margins, but one of the following applied: lymph node evaluation less rigorous than systematic nodal dissection; positivity of the highest mediastinal node removed; presence of carcinoma in situ at the bronchial margin; positive pleural lavage cytology. A resection was defined incomplete if any of the following applied: presence of residual disease; extracapsular extension in distal lymph nodes; positive cytology of pleural or pericardial effusions.

### 2.3. Statistical methods

#### 2.3.1. Sample size and power of the study

The power of the study associated with the available sample size was based on the primary endpoint of overall survival (OS) among patients undergoing complete resection in comparison with OS among patients undergoing uncertain or incomplete resection for NSCLC. For an  $\alpha$  value equal to 0.05 level of significance, considering a total of 1277 available patients and an accrual time of 120 months, and assuming a median follow-up time of 66 months and median survival times  $m_1 = 75$  months and  $m_2 = 57$  months among patients undergoing complete resection and patients undergoing uncertain or incomplete resection, respectively (hazard ratio = 1.316), a power  $(1 - \beta)$  92.4% was achieved. The power was estimated assuming a dropout rate  $\phi$  equal to 0.20 (Schoenfeld's formula [12] implemented by the ADDPLAN version 4.0.3 [Adaptive Design and Analyses, AD-DPLAN GmbH, Germany] software).

#### 2.3.2. Statistical analysis

Descriptive statistics were used to describe patient characteristics, surgical treatment and perioperative outcomes, and tumor characteristics. Categorical data were reported as counts and proportions. After being examined for normality with the Shapiro-Wilk test, continuous data used in the study were not symmetrically distributed and were expressed as medians and interquartile ranges, unless otherwise stated. For between-group comparisons, we used the Kruskal-Wallis test for continuous data and the  $\chi^2$  test for categorical data. All variables entered in the study were complete.

The primary endpoint of interest was the impact of the IASLC definitions of complete, uncertain, and incomplete surgical resection on OS, calculated as the difference in months between date of surgery and death from any cause or censored at the date of last contact or the end of the study in September 2013. Follow-up was complete and all patients were followed up until death or for a minimum period of 5 years. Long-term mortality data were collected using a combination of data linkage to civil administrations or direct contact with patients. Survival curves were estimated using the Kaplan-Meier approach and differences between groups were analyzed using the log rank test. Cox proportional hazard regressions were used to estimate crude and adjusted hazard ratios for death and relative 95% confidence intervals in order to assess the significance of covariates included in the models. An  $\alpha$  value equal to 0.05 was used for statistical significance.

Statistical analysis was performed using the IBM SPSS Statistics version 22 (IBM SPSS Inc., USA) software package.

## 3. Results

### 3.1. Patient data

A total of 1277 consecutive patients were included in the final analysis (Fig. 1). One thousand and three patients (78.5%) underwent complete resection, 185 (14.5%) underwent uncertain resection, and 89 (7.0%) underwent incomplete resection. The uncertain resection group included 107 patients in whom lymph node evaluation was less rigorous than systematic nodal dissection; 76 patients in whom the highest mediastinal node removed was positive; and 5 patients in whom the bronchial resection margin showed carcinoma in situ. In 3 patients, the resection fulfilled more than one criteria required to be designated as an uncertain resection. As a matter of fact, during the study period, pleural lavage cytology was not performed. However, at thoracotomy, small amounts of pleural fluid (less than 100 ml) were observed in 125 (9.8%) patients out of 1277 and cytological examination results were positive for malignant cells in 14 (11.2%). These were included in the incomplete resection group ( $n = 89$ ) which also comprised 12 patients with macroscopic residual tumor (mediastinum 7, chest wall 5); 32 patients with microscopic residual tumor (bronchial stump 15, vascular

Download English Version:

<https://daneshyari.com/en/article/5528335>

Download Persian Version:

<https://daneshyari.com/article/5528335>

[Daneshyari.com](https://daneshyari.com)