



Original Article

## Poorer Survival in Stage IB Lung Cancer Patients After Pneumonectomy<sup>☆</sup>



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### ARTICLE INFO

#### Article history:

Received 3 July 2014

Accepted 19 September 2014

Available online 25 March 2015

#### Keywords:

Pneumonectomy  
Lobectomy  
Lung neoplasms  
Early stage  
Survival

### ABSTRACT

**Objective:** Pneumonectomy may be needed in exceptional cases in patients with early stage NSCLC, especially in stage IB. The aim of this study was to evaluate whether overall survival in stage IB (T2aN0M0) NSCLC patients is worse after pneumonectomy.

**Methods:** Retrospective study of a series of pathological IB (pIB) patients who underwent either lobectomy or pneumonectomy between 2000 and 2011. The dependent variable was all-cause death. Operative mortality was excluded. The relationship between the age, FEV1%, Charlson index and performance of pneumonectomy variables and the dependent variable were analyzed using a Cox regression. Overall survival for both groups of patients was then plotted in Kaplan–Meier graphs and compared using the log-rank test.

**Results:** A total of 407 cases were analyzed (373 lobectomies and 34 pneumonectomies). According to Cox regression, age, FEV1% and pneumonectomy were associated with poorer survival ( $P < .05$ ). Age-adjusted survival and FEV1% showed diminished survival in patients who underwent pneumonectomy (log-rank,  $P = .0357$ ).

**Conclusions:** In stage pIB NSCLC patients, pneumonectomy is associated with poorer survival compared to lobectomy.

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## La neumonectomía ofrece menor supervivencia a los pacientes con carcinoma de pulmón en estadio patológico IB

### RESUMEN

**Objetivo:** La neumonectomía puede ser necesaria de forma excepcional en pacientes con cáncer de pulmón no microcítico (CPNM) en estadios precoces, algo más frecuentemente en el estadio IB. En este estudio se pretende evaluar si la neumonectomía se asocia con peor supervivencia global en pacientes con CPNM en estadios patológico IB (T2aN0M0).

**Método:** Estudio retrospectivo sobre una población de pacientes con carcinoma de pulmón pIB sometidos a lobectomía pulmonar o neumonectomía entre 2000 y 2011. La variable dependiente es la muerte del paciente por cualquier causa, excluida la mortalidad operatoria. Mediante regresión de Cox se analizó la relación de las variables: edad del paciente, FEV1%, índice de Charlson y neumonectomía sobre la variable dependiente. Se elaboró un gráfico de Kaplan Meier en el que se representó la supervivencia de los pacientes con lobectomía o neumonectomía y se compararon las 2 funciones mediante la prueba log-rank.

#### Palabras clave:

Neumonectomía  
Lobectomía  
Cáncer de pulmón  
Estadio precoz  
Supervivencia

<sup>☆</sup> Please cite this article as: Rodríguez M, Gómez Hernández MT, Novoa NM, Aranda JL, Jiménez MF, Varela G. La neumonectomía ofrece menor supervivencia a los pacientes con carcinoma de pulmón en estadio patológico IB. Arch Bronconeumol. 2015;51:223–226.

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**Resultados:** Se han analizado 407 casos (373 lobectomías y 34 neumonectomías). En la regresión de Cox, la edad, el FEV1% y la neumonectomía se asociaron con una peor supervivencia ( $p < 0,05$ ). La función de supervivencia ajustada para edad y FEV1% demuestra menor supervivencia en los casos intervenidos mediante neumonectomía ( $\log\text{-rank } p = 0,0357$ ).

**Conclusiones:** En los pacientes con estadio patológico IB la neumonectomía se asocia a una menor supervivencia comparada con la lobectomía.

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## Introduction

According to the 7th edition of the TNM classification of lung cancer, stage IB includes tumors 3–5 cm in diameter, with bronchial involvement 2 cm or more distal to the carina, partial pulmonary atelectasis or invasion of the visceral pleura.<sup>1</sup> The surgical approach, therefore, in many tumors classified at this stage will vary, depending on the operating field and the skill of the attending surgeon. In an earlier publication,<sup>2</sup> we reported that 30-day mortality is a poor indicator of pneumonectomy risk, since death due to reasons other than cancer is much greater 6 months after the intervention than at 30 days. The hypothesis of this study is that, when all-cause mortality is taken into account, pneumonectomy in stage IB patients is associated with poorer survival.

## Method

### Study Population

A retrospective review was performed of patients undergoing pulmonary lobectomy or pneumonectomy for pathological stage IB (pIB) lung cancer in our hospital between January 2000 and December 2011. Information was retrieved from a prospective, computerized double entry database. To ensure maximum homogeneity, patients who had received induction chemotherapy were excluded, even if their definitive staging was pT1-2aN0M0, since in most cases indication for induction chemotherapy was based on a clinical classification of N2. Stage pIB patients who received adjuvant chemotherapy were included in the study, irrespective of the indication for chemotherapy.

### Patient Screening Criteria

Before surgery, all patients underwent the same tests: physical examination, complete blood count and serum biochemistry, electrocardiogram, chest X-ray, computed tomography (CT) of the chest and abdomen, and bronchoscopy. PET-CT was performed in all patients included since 2007. Invasive mediastinal staging (by mediastinoscopy or endobronchial ultrasound since 2009) was performed if mediastinal lymphadenopathies >1 cm were seen on CT and if the mediastinal PET-CT was positive. All patients performed lung function tests; from 2009 onwards DLCO was routinely included.<sup>3</sup> Cardiac risk was evaluated according to criteria previously published by our group.<sup>4</sup> Patients with any neurological signs or symptoms on clinical examination underwent head CT, although this was not routinely ordered. Patients were classified for this study according to the TNM classification, 7th edition.<sup>1</sup> Age was not a contraindication for patients with an indication for pneumonectomy who met screening criteria after individual discussion of the case by a multidisciplinary committee.

### Perioperative Treatment and Follow-up

The surgical approach in all cases was muscle-sparing posterior thoracotomy, or either video-assisted or non-video-assisted axillary thoracotomy. The same group of anesthetists and thoracic

surgeons were responsible for all anesthetic and surgical procedures, respectively. Systematic mediastinal lymphadenectomy was performed in all cases, based on current clinical guidelines.<sup>5</sup> Antibiotic prophylaxis consisted of a single dose of 1500 mg cefuroxime that could be repeated after 6 h if surgery was prolonged. Patients were extubated before they left the operating room, and after a few hours in the reanimation unit were transferred to the thoracic surgery ward. Bupivacaine and fentanyl were administered as postoperative analgesia via a thoracic epidural catheter for the first 3 days. After catheter withdrawal, analgesia consisted of oral non-steroidal anti-inflammatories and paracetamol.

A single face-to-face visit was performed 1 month after surgery, and all other follow-up contact was made in the form of telephone calls to the patient or family members. If contact with the patient was lost, the date of death was retrieved from hospital records or treating physicians in the corresponding hospital.

### Variables Analyzed

Independent variables included were type of resection (pneumonectomy or other), patient age, preoperative FEV1%, and Charlson index.<sup>6</sup> The latter was not recorded prospectively; instead, it was calculated retrospectively from variables recorded in the database that provided all the necessary variables. DLCO was only recorded routinely after 2009,<sup>3</sup> so it was not included in the analysis. The dependent variable was all-cause death, excluding postoperative death (death within the first 30 days or any time before hospital discharge after the procedure).

### Data Analysis

A Cox's regression model with bootstrap resampling with 100 replicates was used to examine associations between independent variables and survival. Age- and FEV1%-adjusted survival functions were constructed for patients undergoing pneumonectomy or lobectomy, and a log-rank test was performed to estimate the *P*-value of the differences between both functions. Data were analyzed using Stata/IC 13 software (StataCorp, Texas, USA).

## Results

A total of 407 patients (373 lobectomies and 34 pneumonectomies) were included in the study. Four patients died during surgery (0.98%; 1 pneumonectomy and 3 lobectomies).

At the time of starting this study, 212 patients had died; 195 (47.9%) remained alive. Causes of death were as follows: lung cancer, 112 cases; other cancer, 10; lung problems, 14; heart problems, 11; stroke, 6; other diseases, 12. In 47 cases (11.5%), cause of death was unknown.

Continuous variables are described in Table 1. Patients undergoing pneumonectomy were slightly younger than the lobectomized patients.

Cox's regression analysis (Table 2) shows that age, FEV1%, and undergoing pneumonectomy are associated with poorer survival. Age-adjusted survival function and FEV1% are shown in Fig. 1. *P*-Value in the log-rank test was .0357.

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