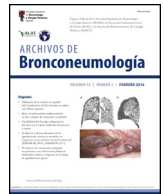


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## Original Article

## Description and Survival of Stage I and II Lung Cancer Patients<sup>☆</sup>

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### ABSTRACT

**Introduction:** The objective of our study was to describe the characteristics of patients diagnosed with stage I and II lung cancer in the health area of A Coruña (Galicia) and to determine their overall survival according to certain variables.

**Methods:** Retrospective case series in patients diagnosed between January 2011 and December 2015 with stage I and II primary lung cancer with a minimum follow-up of 18 months.

**Results:** One hundred and fifty-eight patients were included, 99 at stage I, with a median age of 69 years [range 20–90], predominantly men (81%). Adenocarcinoma was the most common histology (52.9%), followed by epidermoid carcinoma (33.1%). Asymptomatic patients (35.9%) presented more frequently in stage I. Median survival was 57 months (95% CI: 48.1–65.9), with higher survival among women, patients under 70 years of age, and those who received surgical treatment.

**Conclusions:** Early-stage lung cancer in the health area of A Coruña occurs predominantly in men, in advanced age, and with adenocarcinoma histology. Survival was greater among patients with stage I disease, women, individuals aged under 70 years, and those treated surgically. Despite early diagnosis, median survival was less than 5 years.

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## Características al diagnóstico y supervivencia de estadios I y II de cáncer de pulmón

### RESUMEN

**Introducción:** El objetivo de nuestro estudio es detallar las características de los pacientes diagnosticados en estadios I y II de cáncer de pulmón en el área sanitaria de A Coruña (Galicia) y conocer su supervivencia global en función de ciertas variables.

**Métodos:** Serie de casos de carácter retrospectivo en sujetos diagnosticados entre enero de 2011 y diciembre de 2015 de cáncer pulmonar primario en estadios I y II con un seguimiento mínimo de 18 meses.

**Resultados:** Se incluyeron 158 pacientes, 99 en estadio I, con una edad mediana de 69 años [rango 20–90] y mayoritariamente hombres (81%). El adenocarcinoma fue la histología más frecuente (52,9%) por encima del carcinoma epidermoide (33,1%). Los sujetos asintomáticos (35,9%) se presentaron más frecuentemente en estadio I. La mediana de supervivencia fue de 57 meses (IC 95%: 48,1–65,9), con una mayor supervivencia para el sexo femenino, los menores de 70 años y los pacientes que recibieron tratamiento quirúrgico.

#### Palabras clave:

Neoplasias pulmonares

Supervivencia

Neoplasias por tipo histológico

Epidemiología

Diagnóstico precoz

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**Conclusiones:** El cáncer de pulmón en estadios iniciales en el área de sanitaria de A Coruña presenta un predominio de hombres, edad avanzada y mayoritariamente adenocarcinomas. La supervivencia fue mayor en el estadio I, mujeres, menores de 70 años y subsidiarios de tratamiento quirúrgico. Pese a este diagnóstico precoz, la mediana de supervivencia no alcanza los 5 años.

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## Introduction

Lung cancer (LC) is the most common global cause of cancer death in men and the third most common in women.<sup>1</sup> It is the leading cause of cancer death in Spain, where it was estimated that 22,450 new diagnoses would be made in men and 5917 in women by 2015. While mortality in men has fallen slightly in recent years, it is increasing in women, in whom rates have almost doubled in the last decade. In Spain, LC is the third most common tumor in men and the fourth most common in women,<sup>2,3</sup> and its impact on health and social welfare is considerable. Moreover, survival has not increased in the last few years, and the relative 5-year survival is 10.6%.<sup>4</sup>

In recent years, there has been an increase in the incidence of LC among women, and the pattern of predominant histological variants has changed due to changes in the type of tobacco smoked.<sup>5</sup> Squamous cell carcinoma remains the most common histological type only among male smokers.<sup>6</sup> Survival has also improved slightly in certain patient groups, primarily those with mutations that respond to targeted treatments.<sup>7,8</sup>

Data from the United States suggest that approximately 57% of LCs are diagnosed when the disease has already metastasized, and 22% of cases have regional lymph node dissemination at diagnosis. Only 16% are diagnosed when the tumor is still confined to the primary site.<sup>9</sup> In the Corunna healthcare area, 21% of cases are diagnosed in stages I and II. Symptoms are not only rare in early-stage disease, they are also non-specific, particularly in the early stages. This leads to a significant delay in diagnosis, as other more common diseases are generally ruled out first. It is therefore unusual for LC to be diagnosed in stage I or II, and these stages are generally discovered incidentally during differential diagnosis for other diseases.<sup>10</sup> Consequently, 5-year survival in this type of cancer, at less than 15% worldwide, remains low.<sup>5</sup> In the United States, 5-year survival in localized disease is 55.6%.<sup>9</sup> Screening programs among smokers have been proposed in an attempt to improve survival, but the risk-benefit ratio is unclear, and currently screening is not systematically offered by the public health system of any European country.<sup>10-15</sup>

Given the lack of evidence in stage I and II LC patients, our objective was to determine their characteristics at diagnosis and to analyze survival.

## Methods

This retrospective case series includes all patients diagnosed with stage I and II LC between January 2011 and December 2015 in the Corunna healthcare area (Galicia, Spain). Patient inclusion concluded in December 2015, to allow for a minimum follow-up of 1.5 years after diagnosis (until June 30, 2017). The reference hospital is the Complejo Hospitalario Universitario de A Coruña (CHUAC), which has a catchment area of 584,283 inhabitants.<sup>16</sup>

The study included all cases managed medically in the CHUAC LC clinic with a final diagnosis of stage IA, IB, IIA or IIB LC, according to the 7th edition of the TNM classification.<sup>17</sup> Histopathological diagnosis was confirmed for all patients, except for 1 from whom insufficient sample material for histological study was obtained, but whose clinical and radiological picture were consistent with a diagnosis of LC. Staging was performed from clinical history,

biochemistry, chest-abdomen CT and PET. EBUS/EUS was used when positive mediastinal lymphadenopathies were observed on a PET (SUV > 2.5).

The following variables were collected from the electronic medical records: date of birth, sex, age at diagnosis, smoking habit (smoker/former smoker/never smoker), time since smoking cessation, tobacco consumption (pack-years), presence of COPD, reason for referral (symptoms/follow-up of respiratory disease/purely incidental), symptoms at diagnosis (none/cough/dyspnea/hemoptysis/constitutional syndrome/other), diagnostic test prompting suspicion (chest X-ray/CT/other), stage at diagnosis (IA, IB, IIA, and IIB), histological type (squamous cell/adenocarcinoma/small cell/large cell/other), treatment (surgery/chemotherapy/radiation therapy), and vital status of the patient (date of death/survival). As the reason leading to diagnosis in patients with early-stage disease was considered pertinent to this research, patients were classified as follows: (a) patients investigated for LC due to symptoms consistent with the disease, (b) patients monitored for respiratory disease, or (c) patients diagnosed with cancer by chance (incidental finding). In the latter group, the test prompting the diagnosis was not related with LC (i.e., symptoms may have been present, but this was not why the cancer was detected).

The date of death was obtained using Document Management program of the Corunna healthcare area. This system records the date of death of inhabitants in the healthcare area, although with some delay. The electronic medical records do not include the date of death if death occurs outside the hospital setting. Inclusion ended on December 31, 2015, so survival data of all patients are up-to-date. COPD was diagnosed as an FEV1/FVC ratio of <70% in a post-bronchodilator spirometry.

Bearing in mind the current debate on implementing population screening for LC, we also included a dichotomous variable: meets screening criteria according to the current US criteria, yes/no (smoker or former smoker <15 years, ≥55 and <80 years of age, and cumulative tobacco consumption of ≥30 pack-years).<sup>18</sup>

Exclusion criteria were: stage at diagnosis greater than IIB, no clinical/pathological confirmation of LC, and patients whose first consultation was in the CHUAC but who were subsequently managed in another healthcare area.

Statistical analysis was performed using SPSS 20.0. The  $\chi^2$ -test was used to determine a possible association between qualitative variables. Survival analysis was performed using Kaplan-Meier curves and survival functions were compared using the log-rank test to estimate *p*. Statistical significance was set at *p* < 0.05.

## Results

In total, 158 patients were included in the study, 99 at stage I and 59 at stage II; 81% were men and the median age at diagnosis was 69 years (mean age, 68 years). No statistically significant differences between sex and age were found for stage at diagnosis. The predominant histology was adenocarcinoma (52.9%) (Table 1), which was the histological type most frequently diagnosed in women (73.3%) vs 48% in men, and mainly in individuals under the age of 70 years (62.2%). In patients older than 70 years, adenocarcinoma and squamous cell carcinoma occurred at similar rates.

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