



## Original Article

## Changes in Clinical Presentation and Staging of Lung Cancer Over Two Decades<sup>☆</sup>



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## ABSTRACT

**Introduction:** Important clinical and epidemiological changes have been observed in lung cancer (LC) in our healthcare area compared to the previous decade. In the last 10 years, specific LC care circuits have been implemented and the active search for cases has been stepped up. The aim of this study was to analyze the progress of these changes over the last 20 years.

**Methods:** This is a retrospective study comparing clinical and epidemiological changes between 2 historical cohorts of LC patients (1992–1994 [group 1, 164 patients] and 2004–2006 [group 2, 250 patients]) and a current group from the period 2011–2012 (group 3, 209 patients).

**Results:** Two hundred and nine (209) LC patients were included in group 3 (2011–2012 period). After comparing groups 3 and 2, a non-significant rise in smoking was observed in women (59% vs 41%,  $P=.25$ ), while the prevalence of adenocarcinoma was unchanged (45% vs 44%,  $P=.9$ ). The main changes observed were the increase in cases with previous malignancies (23% vs 16%,  $P=.04$ ), the rise in patients with no associated LC symptoms (33% vs 16%,  $P<.001$ ), and an increased number of localized NSCLC (non-small cell LC) diagnoses (42% vs 24% in series 2,  $P<.001$  and 14.2% in series 1,  $P<.001$ ).

**Conclusions:** The number of LC patients diagnosed in localized stages has increased significantly. Furthermore, the number of patients with no symptoms associated with LC and with a history of previous malignancy was significantly increased.

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### Cambios en el estadio y presentación clínica del cáncer de pulmón a lo largo de dos décadas

## RESUMEN

**Introducción:** En la pasada década observamos que en nuestra área sanitaria se produjeron importantes cambios clínico-epidemiológicos en el cáncer de pulmón (CP) con respecto a la década anterior. En los últimos 10 años se han puesto en marcha circuitos asistenciales específicos de CP y se ha intensificado la búsqueda activa de casos. El presente estudio fue realizado para analizar la evolución de dichos cambios 20 años después.

**Metodología:** Estudio retrospectivo en el que se comparan aspectos clínico-epidemiológicos de 2 series históricas de pacientes con CP (periodo 1992–1994 [serie 1, 164 pacientes] y periodo 2004–2006 [serie 2, 250 pacientes]) con una serie actual correspondiente al periodo 2011–2012 (serie 3, 209 pacientes).

## Palabras clave:

Cáncer broncogénico

Cambios epidemiológicos

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Estadio tumoral

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**Resultados:** Se incluyeron 209 pacientes del periodo 2011–2012 (serie 3). Al comparar las series 3 y 2 se observa un aumento no significativo de la frecuencia de tabaquismo en la mujer (59% vs 41%,  $p=0$ ) y se mantiene la frecuencia de adenocarcinoma (45% vs 44%  $p=0$ ). Los principales cambios observados fueron el incremento de casos con neoplasias previas (23% vs 16%,  $p=0$ ), de pacientes sin clínica relacionada de CP (33% vs 16%,  $p<0$ ) y los diagnósticos de CPNM (CP no microcítico) en estadios localizados (42% vs 24% en serie 2,  $p<0$  y 14% en serie 1,  $p<0$ ).

**Conclusiones:** Se ha incrementado significativamente el número de pacientes diagnosticados en estadios localizados. También han aumentado los pacientes sin clínica relacionada con CP y con el antecedente de cáncer previo.

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## Introduction

Lung cancer (LC) has the highest incidence and mortality rates in developed countries, probably due to its frequent presentation in advanced stages.<sup>1–3</sup> It is currently the most common malignant tumor among Spanish men, and already ranks third among women.<sup>4–7</sup> According to the Spanish National Institute of Statistics, 21,058 deaths due to LC were recorded in 2011, 3579 of them in women. The latest trends show that while mortality in men remains stable, it has been increasing in women: between 2010 and 2012, mortality in Spain due to LC increased by 12.7% in women compared to 0.2% in men.<sup>4</sup> Recent data indicates that the 5-year survival has remained virtually unchanged in both Europe (13%) and Spain (10.7%).<sup>3</sup> The last 20 years have seen clinical and epidemiological changes that could be explained by the steady increase in the number of women taking up smoking and improvement in diagnostic techniques.<sup>4–15</sup> Until a few years ago, most therapeutic decisions in LC were based on the patient's functional state, TNM staging based on tumor extent (T), lymph nodes (N) and the presence of metastasis (M), and the anatomical and pathological differentiation between small cell lung cancer (SCLC) and non-small cell lung cancer (NSCLC). Since then however, major advances in the development of new imaging techniques such as fused positron emission tomography–computed tomography (PET–CT), sample collection using endobronchial (EBUS) and esophageal ultrasound (EUS), and new approaches in thoracic surgery such as video-assisted thoracoscopic surgery (VATS) have improved disease staging.<sup>15</sup> Care of LC patients has also improved with the introduction of rapid diagnostic units (RDU) and care pathways coordinated with primary care and other departments, with the active involvement of radiologists who report suspected LC cases to the RDU to facilitate patient access.<sup>16–18</sup> To this must be added the case management role of nursing staff, which reinforces the efficacy and sustainability of these units to the clear benefit of the patient.<sup>16–18</sup> These improvements, together with a greater index of suspicion among primary care doctors and more active follow-up of risk groups, justify analysis of the impact of these new developments on the epidemiology, symptoms and staging of LC. The aims of our study, therefore, were to analyze changes in LC stages at diagnosis, patient demographic and clinical characteristics, the radiological forms of presentation and the histological types of LC over the last two decades.

## Methodology

Retrospective, observational study with an analytical component, comparing two historical cohorts of patients diagnosed with LC with a third cohort of patients from the current period. The first cohort consisted of 164 patients reviewed from January 1992 to December 1994 (group 1), the second group included 250 patients reviewed between 2004 and 2006 (group 2) and the current cohort, analyzed between January 2011 and December 2012 (group 3), consisted of 209 patients.

## Patients

Patients were recruited on the basis of pathology reports that were conclusive for LC in patients from the Hospital Xeral (Vigo, Spain) healthcare area, a tertiary hospital with a catchment area of 350,000 inhabitants.

Patient medical records were reviewed and the following variables obtained: age, sex, smoking habits, occupational exposure, neoplastic disease, chronic obstructive pulmonary disease (COPD) and tuberculosis, as well as LC-related symptoms and type of radiological lesion at diagnosis. Tumor characteristics such as histological type and staging were also analyzed. Patients were classified by histological type into squamous cell carcinoma, adenocarcinoma, large cell carcinoma and small cell carcinoma. In the case of non-small cell carcinomas, staging was based on the TNM classification in use at any particular time: stages Ia, Ib, IIa and IIb were defined as localized, stages IIIa and IIIb as regional and stage IV as disseminated. For the purpose of this study, data from the first cohort were obtained and analyzed in 1995, those from the second cohort in 2007 and those from the third cohort in 2013.

## Statistical Analysis

Data were analyzed using two-sided tests;  $P$  values  $<0.05$  were considered significant. Qualitative variables were expressed as percentages and frequencies, and numerical variables as mean  $\pm$  standard deviation (SD). The Chi-square test and Fisher's exact test were used for statistical analysis of qualitative variables. The Student's  $t$ -test was used for comparative analysis of numerical variables if the distribution was normal, otherwise non-parametric techniques were used. Normal distribution was confirmed using the Kolmogorov–Smirnov test. The analyses were performed using the Statistical Package for Social Sciences, version 15.0 (SPSS, Chicago, IL, USA).

## Results

Data from the current cohort of 209 patients studied between 2011 and 2012 were similar to those from previous series: 82% were male, with a mean age of 66 years (Table 1). With respect to smoking habits, 45% of patients in the last group analyzed were active smokers and 43% were former smokers. These findings are similar to those of group 2 (Table 2), maintaining the difference previously found between the two earlier cohorts. A non-significant increase in the percentage of female smokers was found, confirming the trend observed in the comparison between 1994–1996 and 2004–2006 groups (Table 2). Patient histories are shown in Table 1. The significant increase in the number of patients with a prior diagnosis of neoplasia is notable: from 14% to 23% ( $P=.04$ ). The most common types of cancer observed were, in decreasing order: colorectal carcinoma, bladder carcinoma and prostate adenocarcinoma.

The most common LC-related symptoms at diagnosis were still cough and constitutional syndrome (Table 3). In the current cohort,

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