Lung Cancer at a University Hospital: Epidemiological and Histological Characteristics of a Recent and a Historical Series

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OBJECTIVE: To describe the clinical, histological, and epidemiological characteristics of patients diagnosed with lung cancer in our hospital over a period of 5 years and compare them with those of historical cases treated at the same hospital.

PATIENTS AND METHODS: The cases of patients diagnosed with lung cancer from January 1998 through December 2002 were studied retrospectively and compared with data published for the period from 1978 through March 1981.

RESULTS: A total of 678 patients (89% men, mean age 67 years) were studied. Fifty-six percent of the men and 38% of the women were smokers (*P*<.001). The most common histological types were squamous cell carcinoma (33%) and adenocarcinoma (30%): squamous carcinoma in men (36%) and adenocarcinoma in women (56%). Metastasis was present in 42% of the patients with non-small cell lung cancer and in 55% of those with small cell lung cancer. In patients with a history of neoplastic disease, laryngeal tumors were most common in patients with squamous carcinoma whereas bladder tumors were the most frequent in patients with adenocarcinoma. The ratio of men to women was lower in the recent series than in the historical one. The percentage of squamous carcinoma was lower and that of adenocarcinoma higher (*P*<.001). The percentage of patients diagnosed with regional involvement was greater in the recent series (*P*<.001).

CONCLUSIONS: Squamous cell carcinoma continues to be the most frequent histological type. Male sex and smoking are associated with squamous carcinoma and female sex is associated with adenocarcinoma. Epidemiological and histological patterns have changed, possibly in relation to changes in smoking habits.

Key words: *Lung cancer. Epidemiology. Histological type.*

Características del cáncer de pulmón en un hospital universitario. Cambios epidemiológicos e histológicos en relación con una serie histórica

OBJETIVO: Describir las características clínicas, histológicas y epidemiológicas de los pacientes diagnosticados de cáncer de pulmón en nuestro hospital durante un período de 5 años y compararlas con las de una serie histórica del mismo centro.

PACIENTES Y MÉTODOS: Se incluyó retrospectivamente a todos los pacientes diagnosticados de cáncer de pulmón desde enero de 1998 hasta diciembre de 2002, y se compararon con los datos obtenidos durante el período comprendido entre enero de 1978 y marzo de 1981.

RESULTADOS: El total de pacientes fue de 678 y la edad media, de 67 años. De los varones (89%), el 56% eran fumadores, y de las mujeres, el 62% eran no fumadoras (p < 0,001). Los tipos histológicos más frecuentes fueron el carcinoma escamoso (33%) y el adenocarcinoma (30%). El carcinoma escamoso fue el más frecuente en varones (36%) y el adenocarcinoma en mujeres (56%). En el momento del diagnóstico presentaban metástasis el 42% de los pacientes con carcinoma no microcítico y el 55% de los microcíticos. Las neoplasias previas más frecuentes fueron la de laringe entre los pacientes con carcinoma escamoso y la de vejiga entre los afectados de adenocarcinoma. Al comparar con la serie histórica observamos que actualmente la relación varón:mujer es menor, la proporción de carcinoma escamoso es inferior y la de adenocarcinoma superior (p < 0,001) y el porcentaje de pacientes diagnosticados en estadio regional es mayor (p < 0,001).

CONCLUSIONES: El tipo histológico más frecuente sigue siendo el carcinoma escamoso. Ser varón y fumador se asocia a carcinoma escamoso, y ser mujer, a adenocarcinoma. En comparación con la serie histórica observamos cambios en las características epidemiológicas e histológicas, posiblemente en relación con las modificaciones en el hábito tabáquico.

Palabras clave: *Cáncer de pulmón. Epidemiología. Tipos histológicos.*

Introduction

Lung cancer is responsible for the highest mortality rates from cancer both worldwide and within Spain. It is the leading cause of death due to cancer in men and the third most common one in women, after colon and breast cancers.[1]

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Over 90% of lung tumors are classified in 4 well defined histological types: squamous cell—or epidermoid—carcinoma; adenocarcinoma; large cell carcinomas (which are usually classified as non-small cell types); and small cell carcinoma. The first large-scale case-control study in the United States of America, published in 1950, demonstrated a ratio of 16 squamous cell carcinomas to every case of adenocarcinoma.[2] However, studies in recent decades have shown adenocarcinoma to be the most common type in the US at present.[3-5] The main reason for this change in the prevalence of lung cancer seems to be changing smoking habits.[6] The smoking of filtered cigarettes low in nicotine[3] and the increase in the number of female smokers,[7] who have a higher incidence of adenocarcinoma possibly related to hormonal factors,[8] could partially explain the rise in the rate for that histological diagnosis. In Europe, given the heterogeneity of smoking habits in different countries, the patterns vary.[9,10]

The aim of the present study was to describe the clinical, histopathological, and epidemiological characteristics of lung cancer diagnosed in Hospital del Mar, Barcelona, over a 5-year period from January 1998 through December 2002. We also analyzed possible differences from a historical series reported from the same hospital for the period from January 1978 through March 1981.[11]

Patients and Methods

This observational, retrospective study included all cases of primary lung cancer diagnosed from January 1, 1998 through December 31, 2002, based on information from the tumor registry of Hospital del Mar. A total of 678 patients had a diagnosis of lung cancer confirmed by cytology or histology or based on clinical and radiological suspicion.

The following information was obtained from the medical records of each patient: smoking (a patient was classified as an ex-smoker if he or she had quit at least 12 months before diagnosis), cumulative smoking (pack-year index), professional or occupational risk of developing lung cancer, presence of parenchymal lung scarring assessed on a chest radiograph and/or computed tomography scan of the chest, human immunodeficiency virus (HIV) serology, and history of neoplastic disease and type of tumor. If a patient had had a lung neoplasm, the current tumor was considered primary if the histologic type was different from the previous one. Tumor-related variables were as follows: the date when the most reliable diagnosis was reached and the technique used, histologic type, and stage at the time of diagnosis.

The histological typing system of the World Health Organization was used.[12] The most reliable diagnosis was considered to come from histology, provided it was available, in all cases except those in which a carcinoma was thus considered poorly differentiated but cytology was positive for a certain cell type. The cases were distributed in 7 classes: squamous cell carcinoma, adenocarcinoma, small cell carcinoma, large cell carcinoma, poorly differentiated carcinoma, other tumors, and others with no cytological or histological diagnosis available. When we analyzed possible differences from the historical case series, given that the case and control classifications were not fully congruent, only the following comparable histological types were taken into consideration: squamous cell carcinoma, adenocarcinoma, small cell carcinoma, and large cell carcinoma. The classification employed for tumor registration was used in order to facilitate comparison between the 2 series (Table 1).[13] The pre-treatment classification was recorded in all cases except those diagnosed during autopsy.

TABLE 1
Staging, Tumor Registry Classification

Stage	T	N	M
Localized	T1		
	T2	N0	M0
	T3		
Regional	T1	N1	
	T2	N2	
	T3	N3	M0
	T4	Any N	
Disseminated	Any T	Any N	M1

Statistical Analysis

Results are expressed as means (SD) and percentages. The χ^2 or Fisher exact tests and the Student *t* or Mann-Whitney U tests were used for comparisons of 2 variables. When bivariate analysis showed that a variable was at least marginally associated with the presence of 1 of the 2 most common tumor types (either adeno- or squamous cell carcinoma), that variable was entered into multivariate logistic regression analysis. Goodness-of-fit analysis was used to compare the stage of presentation of the various carcinomas to a theoretical population in which all presentations were assumed to be equally probable (33.3%). Statistical significance was set at a value of *P* less than .05.

Results

A total of 678 patients were diagnosed at Hospital del Mar between 1 January 1998 and 31 December 2002. The mean number of patients diagnosed per year was 135.6 (15.5), range, 119-159. Six hundred five (89.2%) of the patients were men and 73 (10.8%) were women (ratio 8:1); the mean age was 67.1 (11.1), range, 33-94. No significant changes in distribution by sex were observed during the study period (*P*=.546).

A total of 363 (53.8%) patients were smokers at the time of diagnosis, 255 (37.8%) were ex-smokers, and 57 (8.4%) were never smokers. Among the men, 55.8% were smokers and 41.6% were ex-smokers. Among the women, 61.6% were nonsmokers (*P*<.001). The mean number of accumulated pack-years in the series overall (smokers and ex-smokers) was 60.1 (26.5): 60.9 (26.2) for men and 44 (28.2) for women (*P*<.01). The difference was related to the habits of the population of current smokers (men, 62.1 [25.5] pack-years; women, 43.2 [27] pack-years; *P*<.001).

A cytological or histological diagnosis was obtained for 644 patients (95%). In 559 cases (86.8%) primary tumor samples were used. In 79 (12.2%) the samples

came from a site of metastasis, and in 6 (0.9%) they were taken during autopsy. The mean age of these patients was 66.7 (10.9) years. In the 34 remaining patients (5%) whose diagnosis was based on clinical or radiological presentation, the mean age was 74.8 (11.8) years (*P*<.001).

The most common histological types were squamous cell carcinoma (225 patients [33.2%)]) and adenocarcinoma (202 [29.8%]). Small cell carcinoma was diagnosed in 89 patients (13.1%) and large cell carcinoma in 30 (4.4%). The diagnosis was poorly differentiated carcinoma for 91 patients (13.4%). In those cases the diagnosis was exclusively by cytology for 71 patients (78%). No significant changes in the percentages of any histological type were observed over the period of the study (Figure 1).

Squamous cell carcinoma, with a total of 219 cases (36.2%), was the most common type of lung tumor in men; adenocarcinoma was diagnosed in 161 patients (26.6%), small cell carcinoma in 82 (13.6%), and poorly differentiated carcinoma in 78 (12.9%). Among women, adenocarcinoma was the most common malignant tumor. Of the 73 women with lung tumors, 41 (56.2%) had adenocarcinoma, 13 (17.8%) had poorly differentiated carcinoma, 7 (9.6%) had small cell carcinoma, and 6 (8.2%) had squamous cell carcinoma (*P*<.001) (Figure 2).

Among men with squamous cell carcinoma, there were 216 smokers or ex-smokers (98.6%) and 3 (1.36%) were nonsmokers. Among men with adenocarcinoma, 156 (96.9%) were smokers or ex-smokers and only 3 (1.86%) were nonsmokers. In our patient population, adjusting for age and pack-year index, the variables that were associated with greater risk of squamous cell carcinoma were male sex (odds ratio [OR], 3.79; 95% confidence interval [CI], 1.42-10.13; *P*=.008) and smoking more than 80 pack-years (OR, 3.7; 95% CI, 1.18-11.54; *P*=.02). Among women with adenocarcinoma, 14 (34.1%) were smokers at the time of diagnosis and 27 (65.8%) had never smoked. After adjusting for age and cigarette consumption (pack-years), the probability of having adenocarcinoma was greater among women (OR, 2.88; 95% CI, 1.46-5.66; *P*=.002) (Table 2).

TABLE 2
Risk Factors: Squamous Cell and Adenocarcinoma*

	OR	95% CI	*P*
Squamous cell carcinoma			
Sex, male	3.79	1.42-10.13	.008
Pack-years			
1-79	2.55	0.84-7.70	.097
≥80	3.70	1.18-11.54	.024
Age	1.02	1.00-1.03	.044
Adenocarcinoma			
Sex, female	2.88	1.46-5.66	.002
Pack-years			
1-79	0.67	0.31-1.46	.316
≥80	0.63	0.27-1.47	.284
Age	0.98	0.97-1.00	.050

*Logistic regression analysis. CI indicates confidence interval; OR, odds ratio.

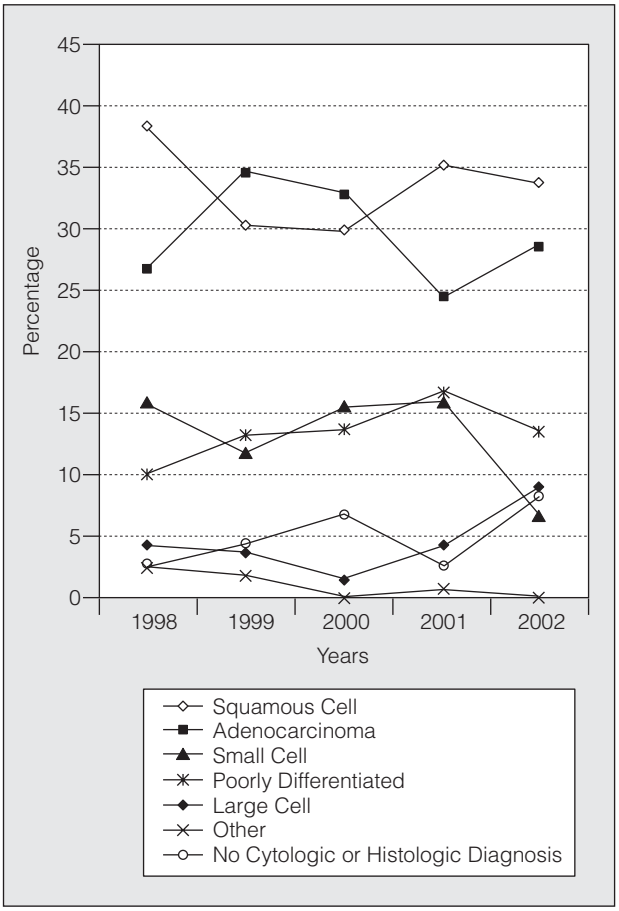

Figure 1. Evolution of the different histological diagnoses during the study period (January 1998 through December 2002).

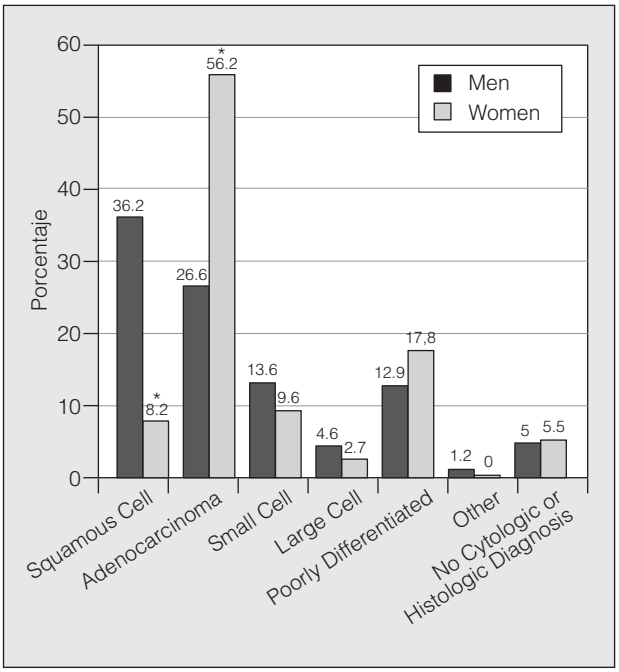

Figure 2. Distribution of histological types by sex. *P<.001.

TABLE 3
Stages, Non-Small Cell Carcinomas*

Carcinoma	Localized	Regional	Disseminated	Total	*P*†
Squamous	56 (25.1)	101 (45.3)	66 (29.6)	223	.001
Adenocarcinoma	49 (24.5)	55 (27.5)	96 (48.0)	200	<.001
Large cell	2 (6.9)	13 (44.8)	14 (48.3)	29	.010
Poorly differentiated	9 (9.9)	27 (29.7)	55 (60.4)	91	<.001

*Data are expressed as numbers, with percentages between parentheses. Goodness-of-fit analysis.
†In comparison with a theoretical distribution that assumes that the 3 stages are all equally probable.

TABLE 4
Histological Typing: Comparison Between the 2 Series*

Carcinoma	Historical Series	Current Series
Squamous cell	63 (60.50)	225 (41.20)
Adenocarcinoma	15 (14.40)	202 (36.90)
Small cell	21 (20.10)	89 (16.30)
Large cell	5 (4.80)	30 (5.50)

*Data are expressed as numbers, with percentages between parentheses.
P<.001, χ^2 test.

TABLE 5
Stages, Non-Small Cell Carcinomas: Comparison Between the 2 Series*

Carcinoma	Historical Series	Current Series
Localized	21 (22.30)	126 (21.70)
Regional	11 (11.70)	207 (35.70)
Disseminated	62 (65.90)	247 (42.50)

*Data are expressed as numbers, with percentages between parentheses.
P<.001, χ^2 test.

For patients with non-small cell carcinomas, staging indicated that 126 (21.4%) had localized disease, 207 (35.1%) had regional spread, and 247 (41.9%) had disseminated disease. Tumor stage could not be established for 9 patients. Stages were significantly different from those predicted for a theoretical population in which all stages were equally probable (Table 2). Squamous cell carcinoma presented mainly as regional disease, adenocarcinoma and poorly differentiated carcinomas as disseminated disease, and large cell carcinomas, which were the least common type, as localized disease. Thirty-nine (43.8%) of the 89 patients with small cell carcinoma had localized disease and 49 (55%) had disseminated disease. For 1 patient, stage could not be determined.

Information on a previous diagnosis of neoplastic disease was obtained for 90 patients (13.3%) who had a total number of 96 tumors (85 patients had a single neoplasm, 4 had 2, and 1 had 3). The most frequent tumors were in the bladder (16) and the larynx (15); following in frequency were colon (11), prostate (11), and skin (10) cancers. The most common previous tumor location was the larynx (9 cases) for patients with squamous cell carcinoma, whereas for those with adenocarcinoma it was the bladder (7 cases).

Scarring of the pulmonary parenchyma was observed in 171 of the 674 patients for whom that information was available (25.3%). No relation between histological type and pulmonary scarring could be found (data not presented).

Occupational or professional risk of lung cancer was present for 40 patients (5.9% of 673 cases in which that information was available). No significant differences between risk exposure and the various histological types could be found (data not shown).

Six patients in the study population were found to be HIV positive. The mean age of those patients was 42.3 (12) years. Four had adenocarcinoma, 1 had squamous cell carcinoma, and 1 had a poorly differentiated carcinoma diagnosed by cytology. The diagnostic stage was regional in 2 of those cases and disseminated in the remaining 4 cases.

The results for the present study were compared with those of a reported historical series diagnosed from January 1978 through March 1981 in the same hospital[11]; the analytical method in the former study was similar to that of the present one. The earlier study included 122 patients with a mean age of 63.6 years (117 men [95.9%] and 5 women). The following noteworthy findings emerged from the comparison:

– The percentage of women with lung cancer increased, to give a male-to-female ratio of 8:1 in the current series in comparison with 23:1 in the historical series (*P*<.05).

– The overall percentage of adenocarcinomas increased, while the percentage of squamous cell carcinomas decreased (*P*<.001) (Table 4).

– Although patients were diagnosed with localized cancers at roughly the same rate in both series—around 22%—we saw an increase in the percentage of regional cancers (*P*<.001) and a decrease in the percentage diagnosed with disseminated disease in the current series (*P*<.001) (Table 5).

Discussion

Studies of the epidemiology of lung cancer in Spain published in recent years have shown that the disease continues to be diagnosed in considerably more men than women.[11,14-17] The percentage of men with lung tumors in our study was 89.2% whereas the percentage of women was 10.8%, and the mean age of patients at the time of diagnosis was 67 years. Those figures are similar to those reported by other authors for Spain.[14-17]

Squamous cell carcinoma continues to be the most common diagnosis, followed closely by adenocarcinoma.

The differences between our observations and those of North American series in which adenocarcinoma is the most common histological type[18] are probably attributable to the still relatively low percentage of women diagnosed in our study and to other unknown factors.

When we considered the relation between sex and smoking habit, we found that men in our series were mostly smokers or ex-smokers and that the most common histological type among them was squamous cell carcinoma. In fact male sex and smoking over 80 pack-years was related to greater likelihood of developing lung cancer. The histologic diagnosis that was most common among women with lung cancer, on the other hand, was adenocarcinoma and most of them had never smoked. Our study design, however, did not allow us to evaluate the role that passive smoking might have played in the history of women who apparently never smoked. Female sex was significantly associated with a greater probability of developing adenocarcinoma according to our results.

The percentage of patients with lung tumors for whom a diagnosis confirmed by cytology or histology is unavailable ranges from 4% to 26% depending on the patient series studied.[14] Such diagnostic information was obtained for the great majority of our patients: only 5% of the cases had diagnoses recorded based only on clinical and radiological findings. It is noteworthy that patients in that group were older. That finding is consistent with reports from other studies,[19] is probably attributable to the comorbidity present in the elderly, and may derive from a more conservative approach to ordering the more invasive complement of tests needed to reach a firm diagnosis.

It is worth noting that we found a high percentage of poorly differentiated carcinomas among the cases for whom cytological or histological confirmation was available—such was the diagnosis for nearly 14% of cases with confirmation. This finding may be a result of the large number of patients (78%) for whom only cytology samples were available.

The distribution of tumor extension showed that many patients were in an advanced stage of disease at the time of diagnosis in spite of diagnostic techniques currently available. That observation is similar to those reported by other authors[14,15] and helps to explain the low number of patients who are potentially curable.

Another matter to emphasize is the relation between lung cancer and the previous history of neoplastic diseases. The associations observed with greater frequency were related to smoking, whether as a result of local mechanisms (in the larynx) or systemic ones (in the bladder). These findings are consistent with those of a recent study carried out in the Spanish province of A Coruña.[14] However, an interesting observation from our study is the association between squamous cell lung carcinoma and a history of laryngeal cancer, on the one hand, and between pulmonary adenocarcinoma and a history of bladder cancer on the other. This suggests that genetic and/or environmental factors probably favor the development of certain histological types of cancer that over the years might appear in more than a single location. On the other hand, the high frequency of prostate and colon cancers in our series might be attributable to the prevalence of those tumors in the general population in the relevant age range.

Lung scarring was present in a high percentage of cases (25%), possibly due to the number of patients in our practice area who have had pulmonary tuberculosis with parenchymal sequelae.

No differences in associations between potentially risky occupational exposures and the various histological types were observed, although our study design was not optimal for a careful evaluation of environmental and workplace exposures.

Although the number of HIV-positive patients in our study was small, the epidemiological and histological characteristics and the stage at the time of lung tumor diagnosis for those patients are consistent with findings published elsewhere. Thus, a case-control study by Tirelli et al,[20] in which 36 patients with lung cancer who were HIV-positive were compared with HIV-negative patients, revealed that the seropositive patients developed lung tumors at a younger age, the most common histological type was adenocarcinoma, and stage at time of diagnosis was more advanced.

The comparison of current and historical cases presents a series of well-known limitations.[21] However, in our study the observed changes cannot be considered invalid based on methodological considerations, at least with respect to the variables compared between the 2 series (current and historical).

Comparative analysis allowed us to confirm a change in distribution of histologic diagnoses, specifically the increased percentage of adenocarcinoma and the decrease in the rate of squamous cell carcinoma. The change can be attributed to several factors: the greater number of female smokers and smaller number of male smokers in the general population and changes in smoking habits (the use of low-nicotine and filtered cigarettes, which leads to changes in the manner of inhaling tobacco smoke[10]). The considerable increase in the percentage of cases diagnosed in women in our series in comparison with the historical cases may be attributable partly to the rise in smoking among women. On the other hand, the high rate of adenocarcinoma among nonsmoking females obliges us to look more closely at the role of carcinogens besides those contained in tobacco smoke.

Finally, it is interesting to note that, although more patients in our series were diagnosed in local or regional stages (57.4% vs 34% in the historical series), the change was related to the greater proportion of cases with regional extension rather than to a change in the percentage of patients with localized disease. That finding has therapeutic and prognostic implications.

Recent decades have seen progress in health care provision in Spain, regarding both improved diagnostic procedures and staging and better access to health care

for the population in general. Improvements made in staging methods may have shifted a percentage of patients formerly diagnosed with localized disease to other nonlocalized stages, specifically to those indicating regional spread in our current series. Improvements in the health care system may also explain, at least partially, the lower percentage of patients currently diagnosed with disseminated disease. These factors may account for the higher percentage of patients diagnosed with regional disease in our current series in comparison with the historical cases. However, it is important to remember that increasing the rate of early diagnosis—which improves prognosis in the management of patients with lung cancer—is a problem still pending solution.

REFERENCES

1. Fernández E, González JR, Borrás JM, Moreno V, Sánchez V, Peris M. Recent decline in cancer mortality in Catalonia (Spain). A joinpoint regression analysis. Eur J Cancer. 2001;37:2222-8.
2. Wynder EL, Graham EA. Tobacco smoking as a possible etiologic factor in bronchogenic carcinoma: a study of 684 proved cases. J Am Med Assoc. 1950;143:329-36.
3. Charloux A, Quoix E, Wolkove N, Small D, Pauli G, Kreisman H. The increasing incidence of lung adenocarcinoma. Reality or artefact? A review of the epidemiology of lung adenocarcinoma. Int J Epidemiol. 1997;26:14-23.
4. Valaitis J, Warren S, Gamble D. Increasing incidence of adenocarcinoma of the lung. Cancer. 1981;47:1042-6.
5. Vincent RG, Pickren JW, Lane WW, Bross I, Takita H, Houten L, et al. The changing histopathology of lung cancer: a review of 1682 cases. Cancer. 1977;39:1647-55.
6. Alberg AJ, Samet JM. Epidemiology of lung cancer. Chest. 2003;123 Suppl 1:21-49.
7. Yang P, Cerhan JR, Vierkant RA, Olson E, Vachon CM, Limburg PJ, et al. Adenocarcinoma of the lung is strongly associated with cigarette smoking: further evidence from a prospective study of women. Am J Epidemiol. 2002;156:1114-22.
8. Taioli E, Wynder EL. Re: endocrine factors and adenocarcinoma of the lung in women. J Natl Cancer Inst. 1994;86:869-70.
9. Simonato L, Agudo A, Ahrens W, Benhamou E, Benhamou S, Boffetta P, et al. Lung cancer and cigarette smoking in Europe: an update of risk estimates and an assessment of inter-country heterogeneity. Int J Cancer. 2001;91:876-87.
10. Tyczynski JE, Bray F, Parkin DM. Lung cancer in Europe in 2000; epidemiology, prevention and early detection. Lancet Oncol. 2003;4:45-55.
11. Garcés JM, Guasch I, Planas J, Broquetas J, Drobnic L. Cáncer de pulmón. Análisis clínico de 122 casos. Med Clin (Barc). 1982;79: 441-4.
12. Travis WD, Colby TV, Corrin B, Shimosato Y, Brambilla E. Histological typing of lung and pleural tumours. 3rd ed. Berlin: Springer-Verlag; 1999.
13. Jansen OM, Parkin DM, Maclennan R. Cancer registration: principles and methods. Lyon: International Agency for Research on Cancer, 1991 [IARC scientific publications no. 95]; p. 59.
14. Montero C, Rosales M, Otero I, Blanco M, Rodríguez G, Peterga S, et al. Cáncer de pulmón en el Área sanitaria de A Coruña: incidencia, abordaje clínico y supervivencia. Arch Bronconeumol. 2003;39:209-16.
15. Miravet L, Peláez S, Paradís A, Arnal M, Cabadés F. Estudio epidemiológico del cáncer de pulmón en el norte de la provincia de Castellón. Arch Bronconeumol. 2001;37:298-301.
16. Grupo de estudio del carcinoma broncopulmonar de la SOCALPAR. Incidencia del carcinoma broncopulmonar en Castilla-León durante el año 1997. Estudio multicéntrico de la Sociedad Castellano-Leonesa de Patología Respiratoria (SOCALPAR). Arch Bronconeumol. 2000;36:313-8.
17. Rezola-Solaun R, Sanzo-Ollakarizketa JM. Incidencia, tendencia y supervivencia del cáncer de pulmón por tipo histológico en Guipúzcoa (1983-1992). Rev Clin Esp. 1999;199:208-14.
18. Hoffman PC, Mauer AM, Vokes E. Lung cancer. Lancet. 2000; 355:479-85.
19. Brown JS, Eraut D, Trask C, Davison AG. Age and the treatment of lung cancer. Thorax. 1996;51:564-8.
20. Tirelli U, Spina M, Sandri S, Serraino D, Gobitti C, Fasan M. Lung carcinoma in 36 patients with human immunodeficiency virus infection. The Italian Cooperative Group on AIDS and tumors. Cancer. 2000;88:563-9.
21. Baker SG, Lindeman KS. Rethinking historical controls. Biostatistics. 2001;2:383-96.