ORIGINAL ARTICLE

Analysis of Lung Cancer in a Reference Hospital in the City of Santa Fe with a Follow-Up of 21 Years

Análisis del cáncer de pulmón en un hospital de referencia de la ciudad de Santa Fe en 21 años de seguimiento

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ABSTRACT

Lung cancer (LC) is a neoplasm with a poor prognosis, it is the third leading cause of cancer death and the highest mortality worldwide.

The objective of the study is to describe the clinical characteristics of patients diagnosed with lung cancer, evaluated over 21 years by the multidisciplinary Committee of a hospital in the city of Santa Fe, Argentina (MCLC) and the comparative analysis between the first period from 2001 to 2011 (p1) and the second (p2) between 2012 and 2022.

It is a descriptive, observational and retrospective study. A total of 416 adult patients of both sexes with a diagnosis of lung cancer between June 2001 and July 2022 were studied, 211 patients in the first decade and 205 in the second. 65 patients with clinical radiological diagnosis of lung cancer were excluded from the analysis.

The results showed that 294 (70.7%) were male, with a mean age of 60 years. It was observed that 249 patients (80.72%) suffered from one or more comorbidities and the most frequent pathologies were 146 cases of COPD (58.9%, p: 0.05), 19 cases of diabetes (7.7%), 11 patients with chronic liver disease (5%), 23 cases with cardiac disease (9.32%) and 10 patients with chronic kidney disease (4.3%).

Smoking was recorded in 320 patients (81.3%) includes ex-smokers (66.7% of women and 87.1% of men) with a mean of 50 pack-years (3 to 169 p/y). Smoking in general decreased at the expense of men, but there was an increase in smoking in women.

The most frequent histology was adenocarcinoma with 149 cases (35.6%, p: 0.04), followed by squamous or squamous cell carcinoma with 128 cases (30.8%, p: 0.04), 44 cases of small cell neuroendocrine carcinoma or oat cell (10.6%, p: 0.06), 65 undifferentiated (15.6%, p 0.05), 10 large cell carcinoma (2.4% p. 0.12), 7 carcinoid tumors (1.7%, p: 0.15) and other recorded histologies there were 6 cases of mesothelioma (1.44%) and 7 (1.7%) extra tumors pulmonary.

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It is observed that in the second period adenocarcinoma increased significantly from 32.7% to 39.02%, while for epidermoid the cases decreased from 40.7% to 32.8%. An increase from 9.45% to 21.46% was also established for undifferentiated cases and in oat cell histological types no changes were seen (10.9 to 10.2%).

The most used diagnostic methods were bronchoscopy and puncture under CT. A total of 172 endoscopies (41.7%) were performed, which had the highest performance in the ca epidermoid and 110 °CT-guided punctures (26.7%) were performed, with the highest diagnostic yield in adenocarcinoma.

For staging, the TNM edition was used at the time of diagnosis, both sexes were in advanced stages in the main strains of non- small cell neoplasms.

Ninety-two patients (22%) received surgical treatment with curative intent, 292 patients (70%) received cancer treatment based on chemotherapy and/or radiotherapy, and 33 patients (8%) received only palliative treatment.

Key words: Lung cancer; Histological types; Adenocarcinoma

RESUMEN

El cáncer de pulmón es una neoplasia de mal pronóstico. Es la tercera causa de muerte por cáncer y el de mayor mortalidad a nivel mundial.

El objetivo del estudio es describir las características clínicas de los pacientes con diagnóstico de cáncer de pulmón, evaluados a lo largo de 21 años por el Comité multidisciplinario de un hospital de la ciudad de Santa Fe, Argentina y el análisis comparativo entre el primer período del 2001 al 2011 (P1) y el segundo (P2) entre 2012 y 2022.

Es un estudio descriptivo, observacional y retrospectivo. Se analizó un total de 416 pacientes adultos, de ambos sexos con diagnóstico de cáncer de pulmón comprendidos entre junio 2001 a julio 2022, en la primera década 211 pacientes y 205, en la segunda. Se excluyeron del análisis 65 pacientes con diagnóstico clínico radiológico de cáncer de pulmón.

Del total de pacientes 294 (70,7%) eran varones, con edad media de 60 años.

Se observó que 249 pacientes (80,72%) padecía una o más comorbilidades y las patologías más frecuentes fueron 146 casos de enfermedad pulmonar obstructiva crónica (58,9%, $p = 0,05$), 19 casos de diabetes (7,7%), 11 pacientes con hepatopatía crónica (5%), 23 casos con patología cardíaca (9,32%) y 10 pacientes con enfermedad renal crónica (4,3%).

El tabaquismo se registró en 320 pacientes (81,3%) incluye a los exfumadores (66,7% de las mujeres y 87,1% de los hombres) con una media de 50 paquetes/año (3 a 169 p/a). El tabaquismo en general disminuyó a expensas de los hombres, pero se evidenció un incremento del hábito tabáquico en las mujeres.

La histología más frecuente fue el adenocarcinoma, con 149 casos (35,6%, $p = 0,04$), seguidos del carcinoma escamoso o epidermoide, con 128 casos (30,8%, $p = 0,04$), 44 casos de carcinoma neuroendocrino de pequeñas células u *oat cell* (10,6%, $p = 0,06$), 65 indiferenciados (15,6%, $p = 0,05$), 10 carcinomas de células grandes (2,4% $p = 0,12$), 7 tumores carcinoides (1,7%, $p = 0,15$) y otras histologías registradas fueron 6 casos de mesotelioma (1,44%) y 7 (1,7%) tumores extrapulmonares.

Se observó que en el segundo período el adenocarcinoma aumentó significativamente del 32,7% al 39,02%, mientras que, para epidermoide, los casos descendieron de 40,7% a 32,8%. También se estableció para los casos indiferenciados un incremento del 9,45% al 21,46% y en los tipos histológicos *oat cell* no se percibieron cambios (10,9% al 10,2%).

Los métodos diagnósticos más utilizados fueron la broncofibroscopia y la punción bajo tomografía computarizada. Se realizaron 172 endoscopias (41,7%) que fueron de mayor rendimiento en el cáncer epidermoide y se realizaron 110 punciones guiadas por tomografía computarizada (26,7%), de mayor rendimiento diagnóstico en el adenocarcinoma.

Para la estadificación se utilizó la edición TNM al momento del diagnóstico, ambos sexos se encontraban en estadios avanzados en las principales estirpes de neoplasias no células pequeñas.

Recibieron tratamiento quirúrgico con intención curativa 92 pacientes (22%), tratamiento oncológico a base de quimioterapia o radioterapia 292 pacientes (70%), y 33 pacientes (8%) recibieron tratamiento paliativo único.

INTRODUCTION

Lung cancer (LC) is a malignancy with a poor prognosis. It is the most common cause of cancer-related deaths, with the highest incidence and mortality worldwide, accounting for 24% of deaths in men and 21% in women. LC represents an important public health problem, with a progressive increase in mortality since the beginning of the last century, which led to the first epidemiological studies linking LC to tobacco use.[1-5] In 2018, GLOBOCAN (Global Cancer Observatory) estimated 2.09 million new cases (11.6% of all cancer cases) and 1.76 million deaths (18.4% of total cancer deaths), making it the most common cause of cancer-related deaths in both men and women.[6] Its incidence has significantly increased in women due to the rise in smoking habits among them. If the current trend continues, it is estimated that by 2045, deaths from LC in women will surpass those in men. Identified risk factors include smoking, environmental factors, occupational factors, and biological and genetic factors related to the host. The World Health Organization (WHO) estimates that 48% of men and 10% of women globally are smokers. Up to 80% of current smokers live in low- and middle-income countries, and more than half of lung cancer deaths occur in less developed regions, likely due to limited access to healthcare resources. The highest 5-year survival rate is observed in the United States, reaching 15%, while in Europe it is around 8%, similar to the one in countries with lower economic development. Mean age: 70 years.[1, 3, 4]

In Argentina, in 2018, cancer accounted for 19% of all causes of death, and among malignant tumors, LC represented 16% of all cancer-related deaths, with a peak in the 65-74 age group.

In terms of gender, men were the most affected worldwide, with 68%, and 32% for women. In our country, 73% of deaths from this type of cancer occurred in men. However, LC mortality showed a significant decline in men from 2000 to 2015, with an estimated annual percentage change (EAPC) of -1.7% for the entire country. On the other hand, the trend in women was upward, with a significant increase in EAPC of 2.5%.[2]

The three most common histological subtypes are: adenocarcinoma, squamous cell carcinoma, and small cell carcinoma. The declining trend in men was observed for most subtypes except for adenocarcinoma, whereas in women, there continues to be an increasing incidence in all the histological variants, although adenocarcinoma is the most common. The decrease in tobacco consumption explains the lower incidence of squamous cell carcinoma in men. However, the increasing incidence in women suggests different etiologies for the development of different subtypes of LC. The prognosis, although generally poor, is not the same for all subtypes.[7, 8]

The study of lung cancer has shown that it is a heterogeneous tumor with several types of differentiation recognized by the WHO classification. This heterogeneity has been addressed in many ways: histological, cellular, and molecular/genetic, as it has a significant impact not only on tumor classification but also on prognosis and treatment definition. The progressive development of genetic and molecular studies helps determine treatment strategies and improve prognosis.[9]

Given these figures, it is indisputable that LC is a real public health problem and a challenge for healthcare teams. Prioritizing the importance of preventive public health policies, encouraging early consultation in the presence of symptoms,

screening in smoking patients, and mostly adopting a multidisciplinary approach are crucial, given that early diagnosis offers the possibility of surgical treatment and subsequent follow-up, resulting in improved survival.

OBJECTIVE

To analyze the lung cancer situation in a reference hospital in the city of Santa Fe over a 21-year period of data collection in a multidisciplinary committee. The clinical, histological, and epidemiological characteristics of patients diagnosed with lung cancer are described. The changes in two 10-year periods of different subtypes of lung cancer are compared, along with their relationship with different risk factors and their diagnostic and treatment methods.

MATERIALS AND METHODS

Descriptive, observational and retrospective study. A total of 416 adult patients of both sexes diagnosed with lung cancer were studied encompassing the 21 years of operation of the MCLC (Multidisciplinary Committee on Lung Cancer), from June 2001 to July 2022.

In addition to examining general data, analyses were conducted during two periods: 2001-2011 (P1) and 2012-2022 (P2).

The studied variables included: patients' gender and age, smoking index, patients' comorbidities, diagnostic procedures performed, and therapeutic approach applied. Regarding the variables related to the neoplasm, the following data were recorded: diagnosis date, histological type, and cancer stage at the time of diagnosis according to the TNM classification.

The histological subtypes were defined based on morphology and immunohistochemistry as adenocarcinoma, squamous cell carcinoma, small cell carcinoma, large cell carcinoma, undifferentiated carcinoma, carcinoid tumor, mesothelioma, and others. Only histological groups with a higher number of patients were included in the statistical analysis: adenocarcinoma, squamous cell carcinoma, undifferentiated carcinoma, and small cell carcinoma.

For the statistical analysis of the data in general, summary measures of distribution, including frequency, measures of central tendency, and measures of data dispersion, were first established. Furthermore, regarding the comparison of frequency of cases by their groups, measures of association and comparison between population subgroups were established. Confidence intervals for means and proportions were also established, along with odds ratios, aiming to determine potential impact measures on the variation between period P1 and P2.

RESULTS

Between June 2001 and July 2022, a total of 416 adult patients of both sexes diagnosed with lung cancer were admitted to Hospital Cullen in the city of Santa Fe. The comparison between the two 10-year periods showed 211 patients in the first period and 205 in the second period (Figure 1).

The mean ± standard deviation of the number of patients diagnosed with lung cancer per year was 18.9 ± 10.38 (range 4 to 54 cases, mean 18.8 cases) (Figure 2).

The annual presentation of cases remained stable over the years, with an increase observed from 2020 when the committee switched to virtual meetings due to the pandemic. The number of participating doctors increased, and the weekly frequency was maintained.

Out of the total patients, 294 were male (70.7%) and 122 were female (29.3%), resulting in a male-to-female ratio of 2.4:1. Mean age was 60 ± 10 (range: 22 - 89) and no significant changes were observed in this variable throughout the study period (p 0.04).

In terms of gender, in the last decade, there was an increase in the diagnosis of lung cancer in
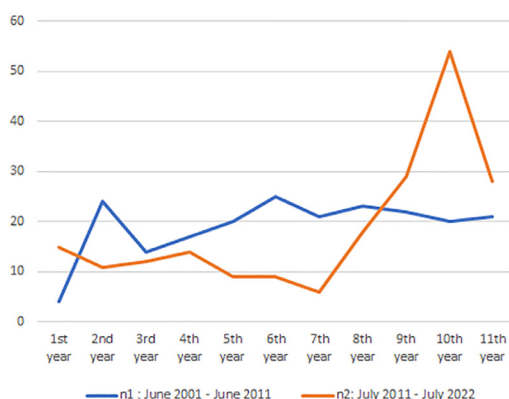

Figure 1. Annual frequency distribution of caseds by period (n1: 211 and n2: 205)

women, from 56 to 66 cases, accounting for a 6% increase (chi-square value of 1.34 and p-value of 0.24; so we can say that this variation is independent between the two periods) (Figure 3). In men, there was a significant decrease in the diagnosis, from 156 cases in P1 to 138 in P2, representing a 6% decline in cases between periods (p 0.06, odds ratio: 0.75, 95% CI between 124 and 151 cases) (Figure 4).

70% percent of the patients fell within the age range of 50 to 70 years. For P1, the mean age was 60 years (range: 32 to 89 years), and 50% of the population was between 54 and 65 years old. In contrast, for P2, the mean age was 62 years (range: 22 to 88 years), with 25% of 55 years and 75% of 70 years. (Figure 2).

In the study of medical history (known comorbidities), 249 patients were registered, with one or more comorbidities observed in 80.72% (95% CI 75.27% - 85.43%). 82.9% of men and 74.2% of women had one or more comorbidities (p 0.132). The most common disease was COPD (159 cases) (58.9% of the registered cases, 95% CI between 53% and 65%); and the other comorbidities accounted for the following percentages: 7.7% (19 cases) of diabetes, 5% (11 cases) of liver disease, 9.32% (23 cases) of heart failure, and 4.3% (10 cases) of renal failure (Figure 5). The cases of women diagnosed
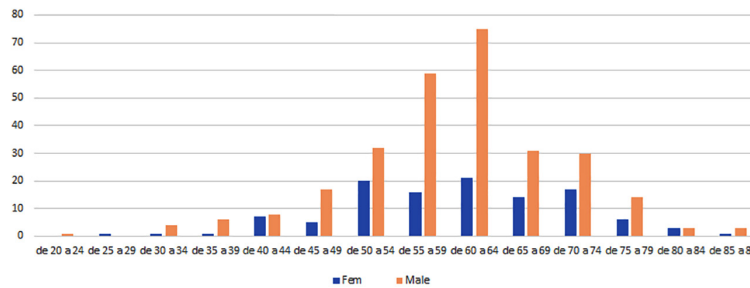

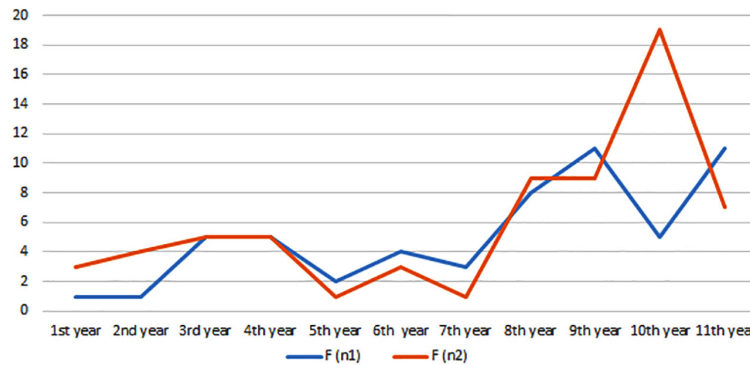**Figure 2.** Frequency distribution by sex according to age group (n: 416)

Figure 3. Annual frequency distribution of female cases Fn (122) by period (Fn1: 56 and Fn2: 66)
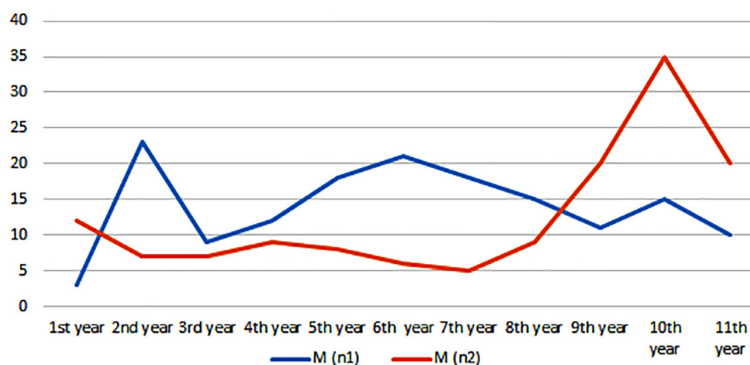

Figure 4. Annual frequency distribution of male caseds (294) by period (Mn1: 156 and Mn2: 138)

with COPD decreased from 71% in P1 to 32.5% in P2 (significant variation according to a chi-square value with one degree of freedom, resulting in p: 0.001). On the other hand, men diagnosed with COPD showed a decrease from 78.2% in P1 to 41.3% in P2 (p greater than 0.5).

With regard to smoking, 320 patients reported being smokers (80.96%), including former smokers, and 74 (18.78%) had never smoked. When evaluated by sex, 87.1% of men and 66.67% of women were smokers (p: p: 0.047). The mean number of packs per year in smokers was 49.34 +/- 26.1. In the case of men, it was 53.04 +/- 27.37, and in women, it was 37.52 +/- 17.59. (Figure 6).

The most frequent age group was between 54 and 64 years old, with 51.1% of smokers falling within this range. In the comparison of periods, no significant variations in overall tobacco consumption were observed, with approximately 80% of the cases remaining consistent. Smoking in general decreased in men, and there was an increase in the smoking habit in women. In P1, 62.26% of women were smokers (p: (p: 0.067), and in P2, it increased to 70.5% (p: 0.02). (according to the chi-square value of 0.863 calculated for this variation with one degree of freedom, the probability is greater than p: 0.35, indicating a statistically insignificant independent variation). Among men, there was a decrease in smoking habits from P1, with 88.7%, to P2, with 84.5%, which was not statistically significant.

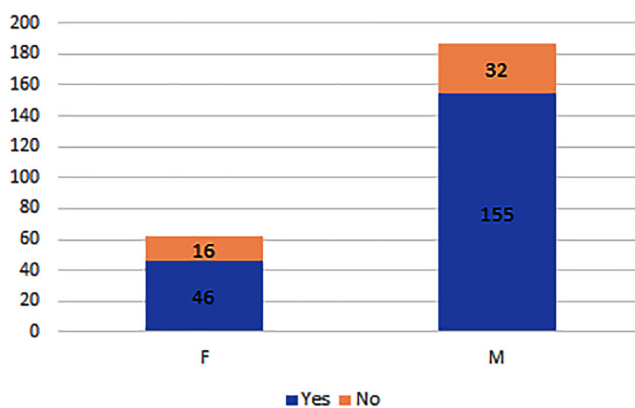The analysis of tumor strains revealed that the most frequent histology was adenocarcinoma with

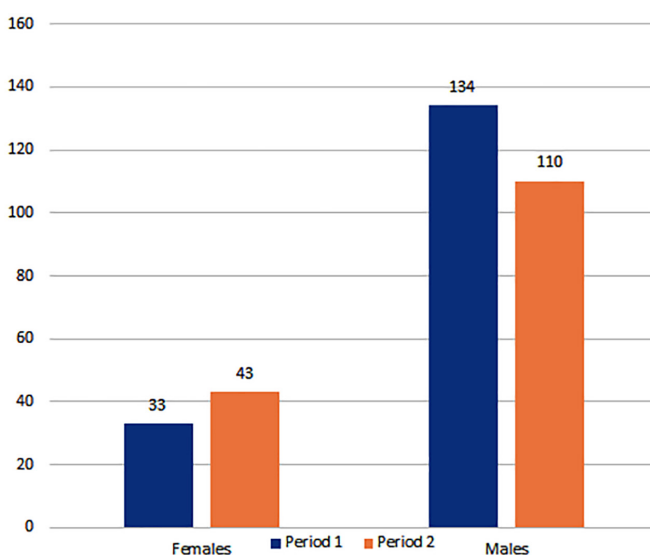**Figure 5.** Frequency distribution of accumulated comorbidities by sex (n: 249)

Figure 6. Distribution of tobacco consumption per period by sex (n: 320)

149 cases (35%, p: 0.04), followed by squamous cell carcinoma with 128 cases (30.8%, p: p: 0.04). The remaining histological variants were distributed as follows: 44 small cell neuroendocrine carcinomas (10.58%, p: 0.06), 65 undifferentiated carcinomas (15.6%, p: 0.05), 10 large cell carcinomas (2.4%, p: 0.12), 7 typical carcinoid tumors (1.7%, p: 0.05); and other recorded histology types included 6 mesotheliomas (1.6%) and 7 isolated cases (1.7%) of extrapulmonary tumors (thymoma, low-grade mucoepidermoid tumor, sarcoma, lymphomas, ovarian granulosa cell tumor) (Figure 7).

The male-to-female ratio varies depending on the tumor strains: males generally predominate except for carcinoid tumors, which had 6 cases in females and 1 case in a male. In adenocarcinoma, 60.8% are men (p: 0.001), while in squamous cell carcinoma, 78.9% are men (p: 0.0139). For large cell tumors, 70% are men, and for small cell tu-

mors, men account for 77.3% (p: 0.3). Among the 6 cases of mesothelioma that have been registered, there is an equal number of men and women (Figure 8). The mean age is 60 years, except for carcinoid tumors that occurred in much younger women. (Table 1)

The behavior exhibited by the adenocarcinoma is very interesting, with a gradual frequency increase starting from 2005 until it surpassed the squamous cell carcinoma in 2008, and remaining as the most commonly diagnosed histology, except in 2018 when only 6 tumors were recorded (4 squamous cell carcinomas, 1 undifferentiated, and 1 small cell carcinoma). It is assumed that no adenocarcinoma was observed due to underreporting of presented patients (Figure 9).

The most common strain in smokers was squamous cell carcinoma (110 cases). According to the statistical analysis, it varied from 43.7% of cases
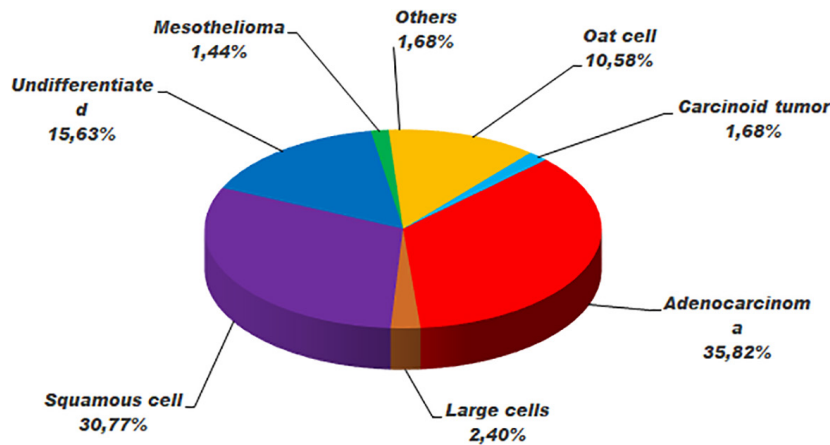

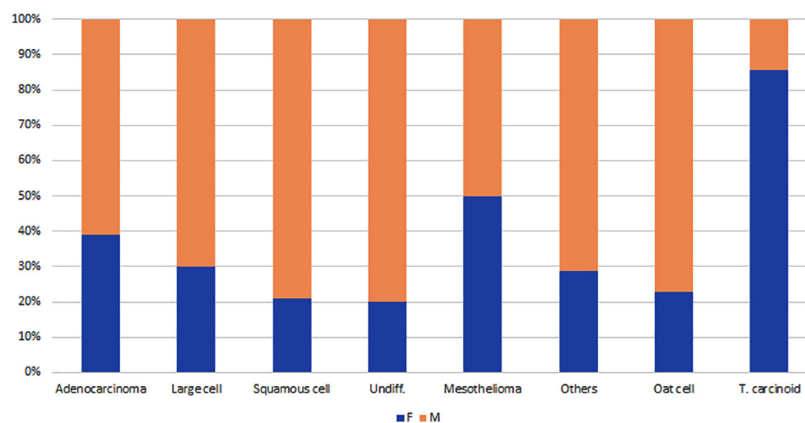**Figure 7.** Percetage distribution of histological findings (n: 416)

Figure 8. Percentage distribution of patients per histological finding by sex (n 416)

at P1 (p: 0.0007) to 32.2% of cases at P2 p: 0.007). The second most common strain, with a very small difference, was adenocarcinoma with 108 cases (p: 0.007). Adenocarcinoma with 31 cases was the most common strain in non-smokers, representing 41.9% of tumors diagnosed in non-smoking patients (p: 0.19). Among non-smokers, 51.6% of adenocarcinoma cases were women, with 16 cases: 9 patients at P1 and 7 at P2 (p: 0.013). Undifferentiated carcinoma in smokers showed a growth from 10% to 21.7% in period 2 (chi-square test with 1 degree of freedom yielded p: 0.0007) (Figure 10).

If we analyze the data by periods, the number of adenocarcinoma cases increased from 69 (32.7%) in P1 to 80 (39%) in P2 (the variation is not significant, with a chi-square value resulting in p: 0.17). The number of cases of squamous cell carcinoma significantly decreased from 86 to 42 (40.7% to 20.4%, respectively). (p: 0.000007). Undifferentiated tumors increased from 9.45% to 21.46% (p: 0.002). No changes were observed in oat cell histological types, (10.9% to 10.2% of cases in each period) (Figure 11).

The observed increase in adenocarcinoma cases appears to be related to a higher number of diagnoses in women: in P1, there were 24 cases, which increased to 34 cases in P2 (from 42% to 51%). However, no statistical relationship was found (p: 0.33), always considering the small number of patients. (Figure 12). In the case of men, a clear negative variation is observed in the squamous cell carcinoma strain, with cases decreasing from 69 to 32 in both periods (representing a percentage

TABLE 1. Age per histological group

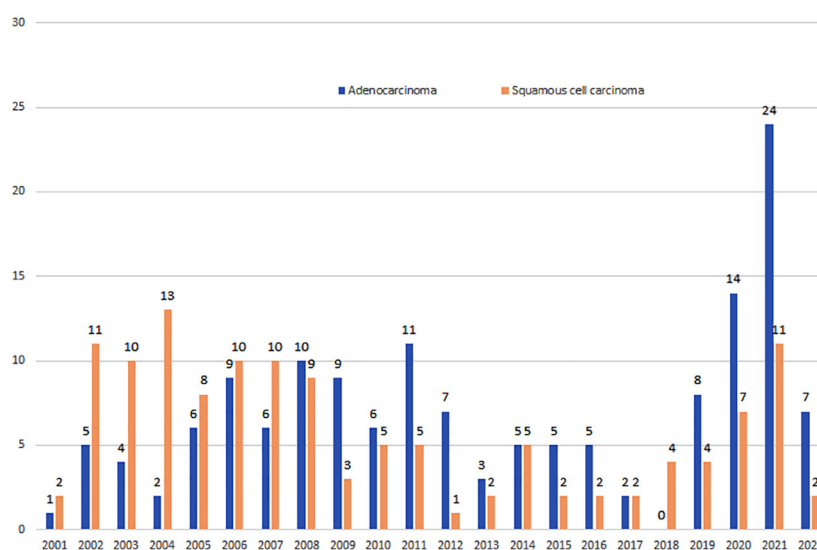|	Obs.	Minimum	25%	Medium	75%	Maximum
Adenocar.	140	37	54	60	67	88
Large cells	10	47	61	64	70	74
Squamous cell carcinoma	123	39	56	61	66	89
Undifferentiated	70	22	56	61	68	75
Mesothelioma	5	36	54	54	59	64
Oat cell	40	45	54	61	66	83
Less common	7	33	55	45	60	77
Carcinoid tumor	7	28	32	45	52	67

Figure 9. Annual frequency distribution of squamous cell carcinoma (n: 128) and adeno-carcinoma (n: 149)

change from 44.5% to 23%, respectively, with a p-value of 0.0001) (Figure 13).

Regarding the undifferentiated strain, there appears to be an apparent relationship with an increase in men. The number of cases went from 16 in P1 to 36 in P2 (from 10.3% to 25.9% of the cases). (p: 0.50). In the second period, a total of 79 patients with undifferentiated carcinoma underwent immunohistochemistry methods for further characterization. As a result, it was determined that 38% of these tumors (30 cases) were adenocarcinoma, while 34.18% (27 cases) remained undifferentiated. If we focus on the last 3 years, 28 undifferentiated tumors were diagnosed, out

of which 26 underwent immunohistochemistry techniques. This allowed for the differentiation of the morphology in 10 cases as squamous cell carcinoma, 7 cases as adenocarcinoma, and 2 cases as undifferentiated carcinoma. 2 patients were diagnosed with extrapulmonary tumors, 4 cases lacked documentation, and in 2 cases, the techniques were not performed due to patient death.

For the staging distribution, the TNM edition was used at the time of patient diagnosis. The patients for whom TNM was determined totaled 330 (234 male and 96 female) and were distributed in stages (S). SI: 12.4%, SII: 7.58%, SIIIA: 17.88%, SIIIB: 23.33% and SIV: 38.8%. (Figure 14, table 2).
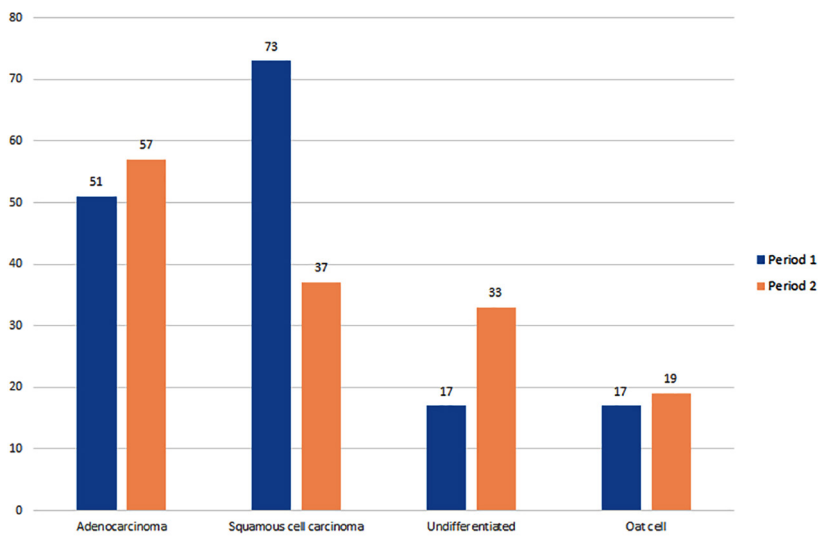

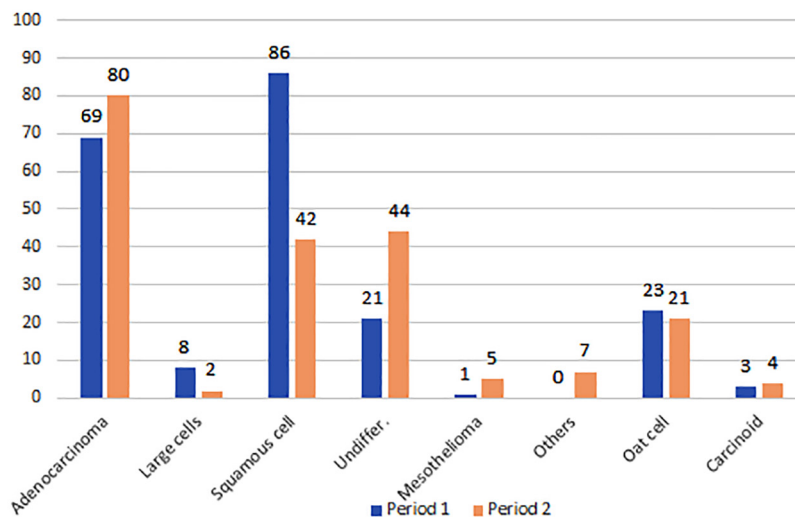**Figure 10.** Frequency distribution of smoking patients per preriod by histological strain

Figure 11. Frequency distribution of histological results by period (np1: 211 and nop2: 205)

The majority of patients of both sexes were in advanced non-surgical stages at the time of diagnosis.

One of the significant findings we were able to provide was the fact that patients diagnosed in stage IV increased from 30.8% in P1 to 47.7% in P2. (p: 0.001). On the other hand, cases in stage IIIA decreased from 44 to 15 in the respective periods (from 25.1% to 9.6%, p: 0.002). (Figure 15)

There were 16 cases of patients in stage I who underwent curative surgery, and the histological type in most of them was adenocarcinoma.

Regarding the three analyzed histological types, it was also observed that they were in advanced non-surgical stages (Figures 16 to 18).

Half of the 65 patients with clinical and radiological diagnosis were in advanced stage IV with poor performance status and did not undergo diagnostic methods or treatment. For the remaining patients, histology data could not be retrieved, so it was decided to exclude them from the patient group.

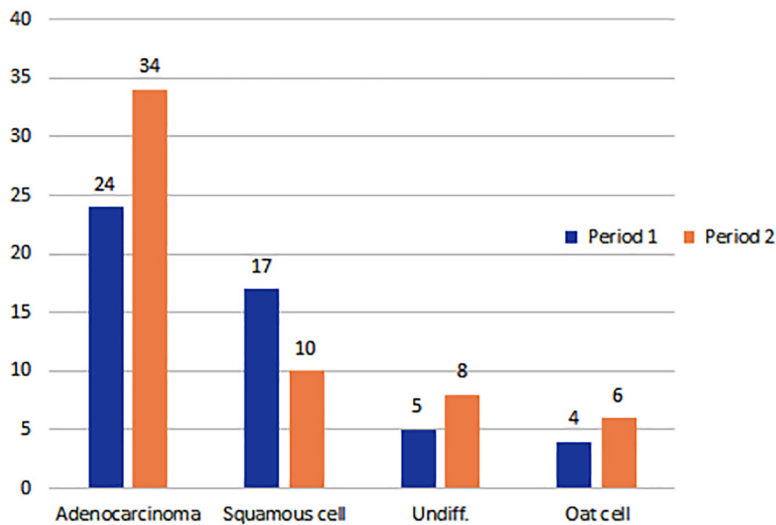The most commonly used diagnostic methods in our practice to determine the histological strain

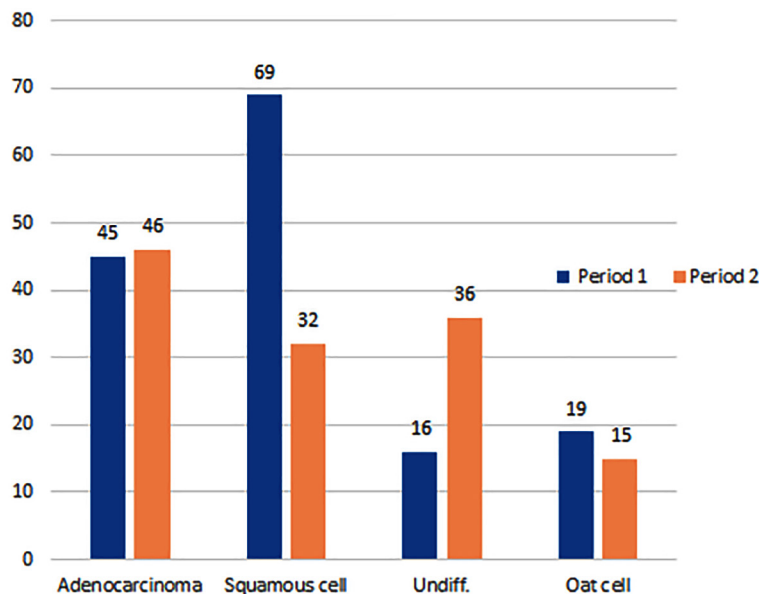**Figure 12.** Frequency distribution of main histological strains in females (Fn: 122)

Figure 13. Frequency distribution of histological strains in males by period (Mn: 294)
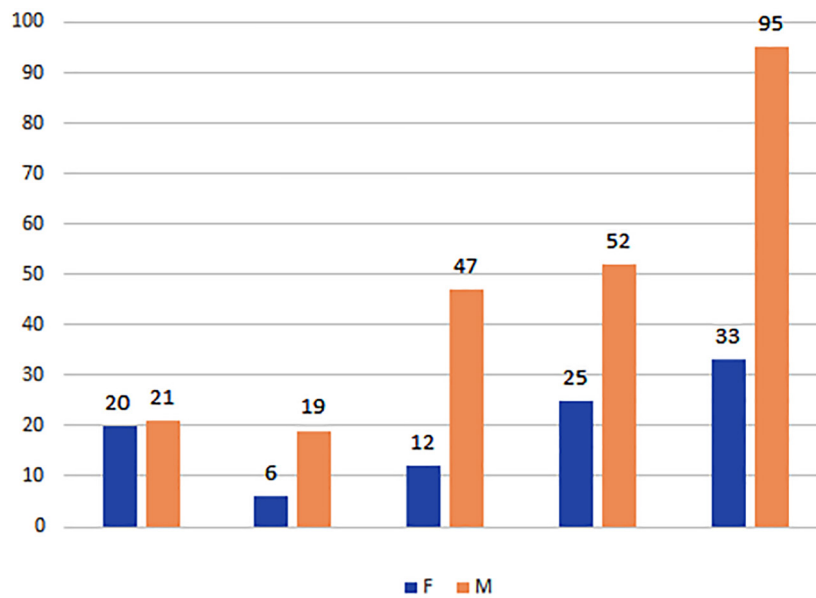
Figure 14. Frequency distribution per stage by sex (n: 330)

TABLE 2. Sex-related stages

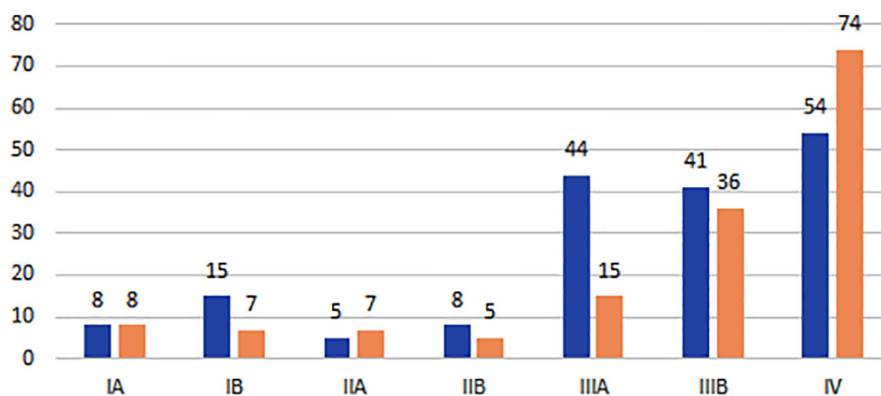| STAGES	F	M	Total	%
IA	11	6	17	5,15 %
IB	9	15	24	7,27 %
Total stage I	20	21	41	12,42 %
IIA	4	8	12	3,64 %
IIB	2	11	13	3,94 %
Total stage II	6	19	25	7,58 %
IIIA	12	47	59	17,88 %
IIIB	25	52	77	23,33 %
Total stage III	37	99	136	41,21 %
Total stage IV	33	95	128	38,79 %
Overall total	96	234	330	100,00 %

Figure 15. Frequency distribution of cases per histological stage by period (nS1: 175 and nS2: 155)

were fiberoptic bronchoscopy and CT-guided biopsy, followed by surgical methods (Figure 19). Other methods that haven't been that common over the years included 9 radioscopy-guided biopsies and 11 sputum cytologies, which are now obsolete. A total of 172 fiberoptic bronchoscopies and 110 CT-guided biopsies were performed. When considering the various surgical methods used to reach a histological diagnosis, the most frequent were: 39 lung resection surgeries (for diagnosis/treatment in early stages), 21 pleural studies, and 3 pericardial studies (without specifying the method), as well as 17 mediastinoscopies.

With regard to the location of the different strains, CT-guided biopsy was more frequently used for adenocarcinoma, while fiberoptic bron-
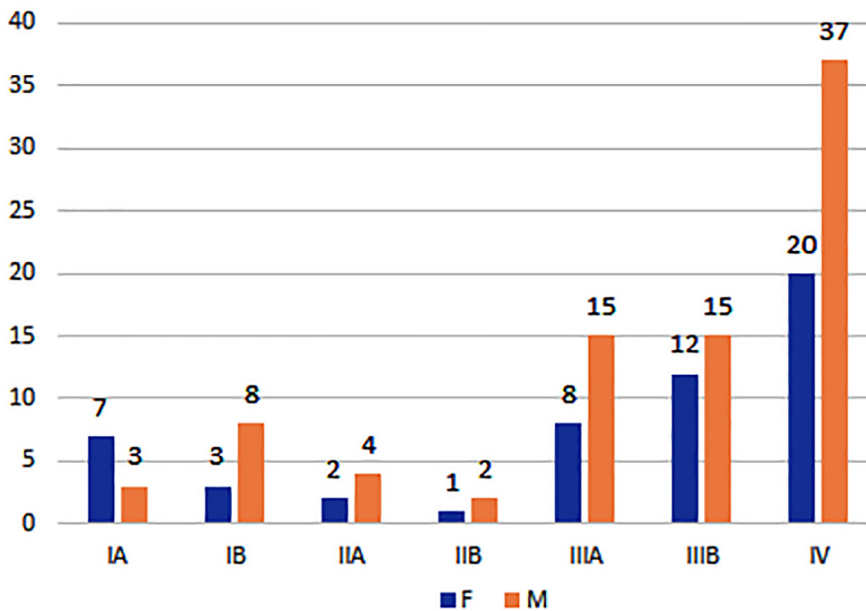

Figure 16. Distribution of adenocarcinoma cases per stage by sex (n: 140)
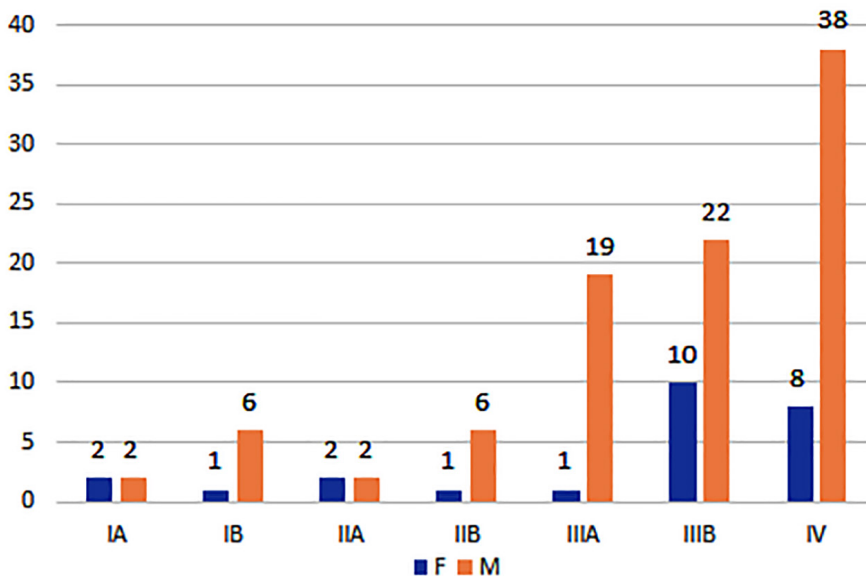

Figure 17. Distribution of squamous cell carcinoma cases per stage by sex (n: 120)

choscopy was more commonly used for squamous cell carcinoma. (Table 3)

In terms of treatment, 92 patients (22%) received surgical treatment with curative intent, 292 patients (70%) received oncological treat- ment based on chemotherapy and/or radiation therapy, and 33 patients (8%) received only palliative treatment due to their advanced condition and poor performance status (PS) (Figures 20 and 21).
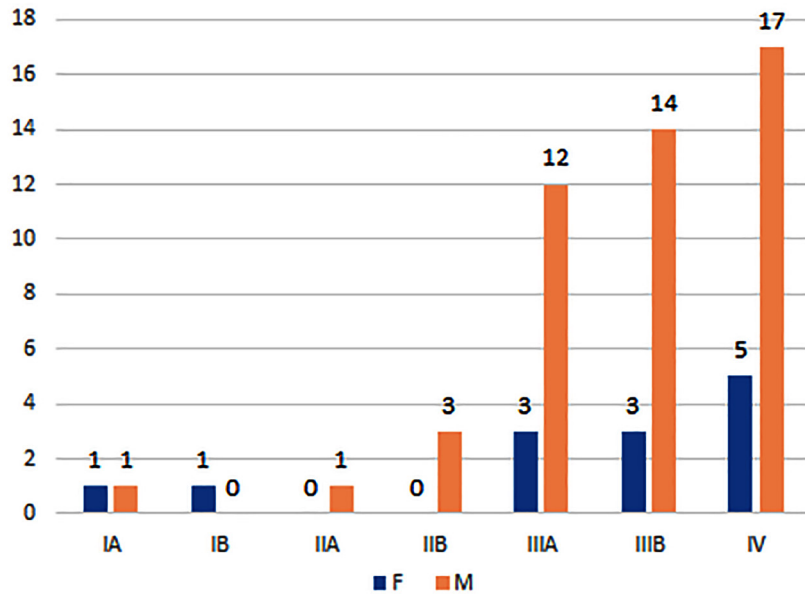

Figure 18. Distribution of undifferentiated carcinoma cases per stage by sex (n: 61)
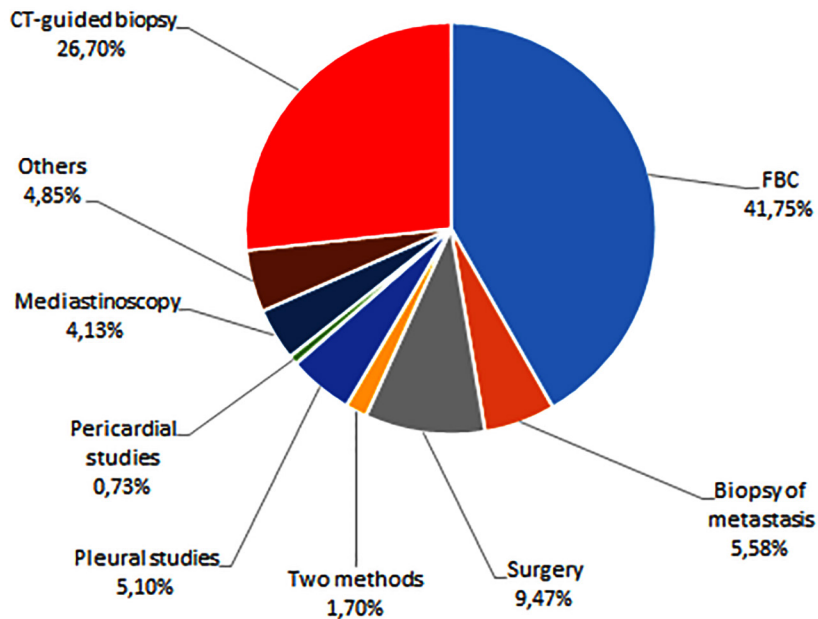

Figure 19. Percentage distribution of the diagnostic methods that were used (N: 412)

TABLE 3. diagnostic methods related to histological types

| Diagnostic methods	Adeno	Large cells	Squam. cells car.	Undiff.	Mesot.	Other	Oat cell	C. tumor	Total
				Histological type					
FBC	41	4	61	33	0	2	27	4	172
Biopsy of metastasis	5	1	11	2	0	0	4	0	23
Surgery	22	0	4	3	4	2	1	3	39
Two methods	3	0	1	1	0	0	2	0	7
Pleural studies	15	0	3	0	2	0	1	0	21
Pericardial studies	3	0	0	0	0	0	0	0	3
Mediastin.	7	0	2	4	0	2	2	0	17
Other	4	0	12	3	0	0	1	0	20
CT-guided biopsy	47	5	33	18	0	1	6	0	110
TOTAL	147	10	127	64	6	7	44	7	412
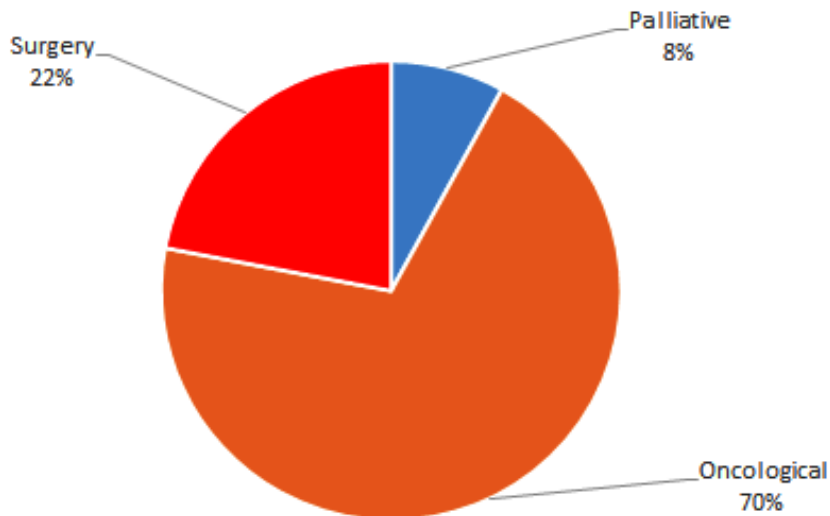
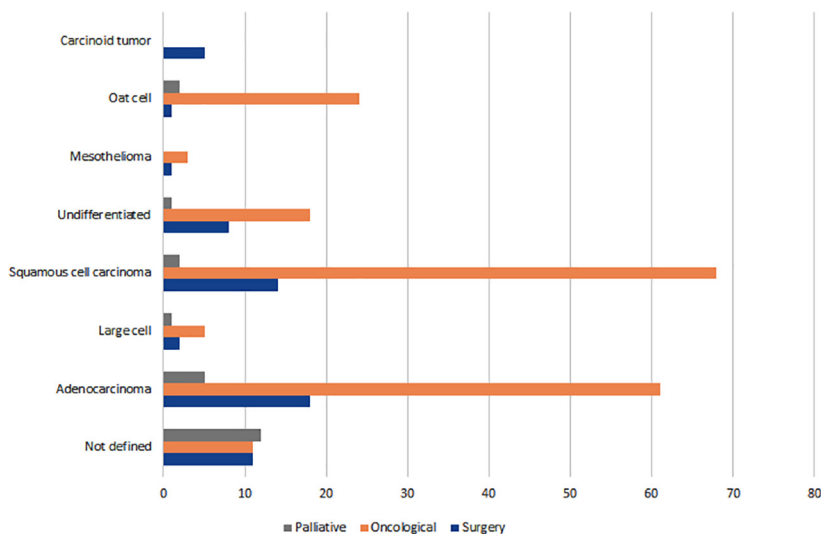**Figure 20.** Percentage distribution per treatment type

Figure 21. Frequency of treatment types used in diferent histologies

DISCUSSION

In our study, we observed that out of the 416 patients diagnosed with lung cancer over these 21 years at MCLC, 71% were male and 29% were female. When comparing the two

decades, we noted a decrease in the number of cases in men and an increase in women, but without statistical significance.

The mean age of 60 years is lower than the one reported in the literature, and it did not vary over the years.[1,3]

Both men and women showed comorbidities in 80% of the cases. COPD is the most prevalent condition, but we did not prioritize its staging.

Smoking is the leading cause related to lung cancer, with 81% of our patients being smokers. It is predominant in both sexes, although more prevalent in men, in accordance with the literature[10]. The mean pack-years reached 51. Smoking itself has decreased over the years, primarily among men, while in women, the rate has increased significantly.

We did not prioritize the registration of occupational exposure, which is considered potentially risky for the development of lung cancer, so we cannot describe any relationship.

The comparative analysis between the two decades confirms a shift in the distribution of histological strains of lung cancer, with an increased percentage of adenocarcinoma and a decrease in squamous cell carcinoma. In our series, the increase in adenocarcinoma is associated with the female gender, as it remained stable in men. Unlike the undifferentiated types that increased in both sexes but more significantly in men, we were unable to conduct a complete analysis of these subtypes with post-immunohistochemistry diagnosis since we have records starting from the second decade, and most of this group would possibly be cases of adenocarcinoma. Squamous cell carcinoma decreased in both sexes, but more significantly in men. Oat cell carcinoma showed no changes.

The incidence of lung cancer is decreasing for all subtypes in men, except for adenocarcinoma. The incidence rates in women continue to increase, particularly for adenocarcinoma. This trend has been observed in the literature since the current century.[11-13] This histological variant is the most common worldwide, especially in women. This fact could be explained by several reasons: the increase

in the number of female smokers, the decrease in the overall male smoking population, and changes in smoking habits, that is to say, the consumption of filtered and low-nicotine cigarettes, with consequent changes in the way tobacco smoke is inhaled. On the other hand, the high percentage of adenocarcinoma among non-smoking women requires further investigation into the role of other carcinogens apart from those found in tobacco smoke. Several factors are proposed for the development of this subtype, such as exposure to cooking fumes, environmental pollution, radiation, as well as genetic susceptibility, nutritional status, immune dysfunction, tuberculosis, asthma, and HPV. However, further research is needed to clarify the main etiology.[9]

The diagnostic method that yielded the highest results in adenocarcinoma was the CT-guided biopsy, while for squamous cell carcinoma, the fiberoptic bronchoscopy; this is associated with the anatomical location of each strain. The evolution of Diagnostic methods throughout these years, from the sputum cytology until the use of the PET-CAT, EBUS and the availability of mediastinoscopies have allowed for a more precise diagnosis and the indication of targeted treatments.[14]

At the time of diagnosis, 62% of patients were in advanced non-surgical stages (IIIB and IV), both men and women, as observed in the three most common histological types analyzed. Even in the second decade, the increase in stage IV cases was evaluated. This defined the fact that the primary treatment established was oncological, and contributes to explain the limited number of potentially curable patients.

Regarding the diagnostic certainty, the percentage of patients who have lung cancer but do not have histological confirmation ranges from 4 to 26% according to different series (11). In our study, there were 65 patients (13%) with a clinical and radiological diagnosis. Half of these patients were in stage IV and only received palliative treatment.

As for stage I cases, they represented 12%; and out of the 41 cases, only 16 patients underwent surgery with curative intent. We do not have data on the follow-up of patients with stages I and II who were operated on in the first two years to assess recurrence.[11, 12]

We can't provide information on the improvement in adenocarcinoma survival rates with the new targeted molecular therapies described in

the literature due to the lack of continuity in the follow-up of our patients.

Among the rare tumors, the carcinoid tumors had the best survival, and all of the cases underwent surgery.

This study has several limitations, such as data underreporting and lack of patient follow-up, which prevent us from drawing conclusions.

In the last decades, we have witnessed a progressive improvement in healthcare in our country, particularly in the advancements of diagnostic and staging procedures. Advancements in the staging methods may have shifted the percentage of patients previously classified as localized stage to non-localized stages.[7] However, in our series, we did not observe an increase in patients diagnosed at regional stages. Emphasizing the importance of early diagnosis to improve prognosis remains one of the unresolved challenges in the management of lung cancer patients.

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