

FREQUENCY OF LUNG TUMORS IN THE PATHOLOGY DEPARTMENT OF SANATORIO ADVENTISTA DEL PLATA, SMOKING AND TYPES OF ANATOMOPATHOLOGICAL DIAGNOSES.

Gabriel S. Urbelz, Medical Student

Yanina G. Nikolaus, Medical Student

Universidad Adventista del Plata, Health Sciences, Entre Ríos, Argentina

Alicia M. Tiscornia

Sanatorio Adventista del Plata, Pathologist, Entre Ríos, Argentina

Lilia G. Cítera

Universidad Adventista del Plata, Pathologist, Entre Ríos, Argentina

Abstract

OBJECTIVES: To evaluate the frequency of lung cancer in the Pathology department of Sanatorio Adventista del Plata (SAP PD) Libertador San Martin, Entre Rios, Argentina during the years 1966-2010. Determine in both genders the smoking as relating it to different histological types. Verify increased adenocarcinoma. Locate the frequency of lung cancer compared to other cancers in the SAP PD.

METHODS: A descriptive, retrospective study. It included 383 men and 72 women diagnosed with lung cancer, from 35 to 86 years of age, between 1966 and 2010 in the SAP PD. File Data pathology were compared with the medical records of every patient, assessing smoking. It was appealed to techniques used in immunohistochemistry. Data were processed using Excel.

RESULTS: Lung cancer is prevalent in the male sex ratio of 5.3:1. Thirty six percent of male cases were squamous cell carcinoma and 54% of cases involving women were adenocarcinomas. 90% were severe smokers and 93% smoked for over 20 years. Until the decade of the 80's squamous cell carcinoma was the most frequent in the SAP PD, however, adenocarcinoma incidence increased, reaching 40% in the last decade. Of all cancers, lung cancer, does not exceed 5%, with the most frequent being skin cancer.

CONCLUSIONS: Lung cancer is more common in men smokers. Adenocarcinoma rise is observed. The incidence of lung cancer in the SAP PD decreased in the last decade)

Keywords: Lung tumors, smoking, histology, gender

1. Introduction

Major causes of lung cancer and cancer in general, include carcinogens such as cigarette smoke, Ionizing Radiation and viral infections. Exposure to these agents cause cumulative changes over DNA cells, genetic alterations accumulate progressively transforming epithelium that lines the bronchi of the lung. As there is more extensive damage, lung cancer develops.

Lung cancer (LC) mainly the type of non-small cell (NSCLC) is the second most frequent type of cancer, if men and women are considered together. Most cases are diagnosed between 55 and 75 years, with a peak incidence between 65 and 70 years. It is a serious public health problem: it is the leading cause of cancer death for both sexes in the U.S. (160,000 deaths estimated in 1999). The most important factor in the development of these neoplasms is associated with the habit of cigarette smoking. The fact is supported by several observations that proved changes in the death rate from lung cancer that evolve in parallel with the prevalence of smoking, the risk of developing LC is 11 to 17 times higher in women and men, respectively, compared between smokers and non- smokers, there is a dose-response with the number of cigarettes smoked per day relationship; suppression of using tobacco leads to a significant, although slow and gradual decrease in risk. Has also reported that carcinogens are the link between nicotine addiction and lung cancer, requires metabolic activation to exert their effects, and substrate are detoxifying metabolic reactions. The balance between activation and detoxification varies markedly for each individual, and affects the cancer risk in relation to the expression of critical genes such as tumor suppressor gene p53 and K-ras oncogene.

In turn, the incidence of adenocarcinoma has increased significantly in the past two decades, and today is the most common form of lung cancer in women and also in many studies in men. However, the basis of changes in the incidence in women and the predominant histological type, has not been elucidated. One possible factor is the increased consumption of tobacco in women, but this only highlights the lack of knowledge about why women tend to have a higher incidence of adenocarcinoma, as the histologic types associated with smoking are squamous cell carcinoma and small cell carcinoma being the most important risk factor remain to be smoking. Furthermore studies show that adenocarcinoma has increased, equaled and even surpassed the incidence of squamous cell carcinoma that occupied the first place.

Objectives: To assess the frequency of lung cancers in the Pathology department of Sanatorio Adventista del Plata, Libertador San Martin, Entre Rios, Argentina, during the years 1966-2010. Determine the smoking habit in every case of lung cancer as compared to men and women. Establish a relationship between smoking and histological types of tumors detected. Verify the increased frequency of adenocarcinoma versus squamous cell carcinoma. Find the frequency of lung cancer in relation to all registered cancers in the SAP PD cancers.

2. Method

Observational, descriptive and retrospective study. It included 383 men and 72 women diagnosed with lung cancer, ranging in age from 35 to 86, between 1966 and 2010, identified retrospectively in the SAP PD. Those extrapulmonary metastases were also added, with high evidence (smoking, histology and immunohistochemistry identification) corresponding to primary lung cancer. Exclusion criteria were patients with lung metastases, no conclusive evidence of primary lung tumor.

Reports obtained from the files of the SAP PD were compared with the medical records of every patient, assessing the different variables related to smoking (number of cigarettes smoked daily, years of smoking, time elapsed since cessation, family history, etc..) Where that was not possible to reach an accurate diagnosis, immunohistochemical techniques were applied for typing.

Data were processed using Microsoft Excel to statistically assess measures of central tendency and data categorization.

Among the limiting factors include the lack of medical records from the early years of the research, as well as the omission or lack of measurable record of substance abuse in medical records.

3. Results

Table 1

Total number of cases according to gender

# men	383
# women	72
# of cases	455

Given the data seen in table 1, shows that the proportion of lung cancer in men was 84.18% while that for women was the 15.82%, which gives a ratio of 5.3:1. The average age of the patients was 62 years, showing a dispersion of 51 (86 years for senior, 35 minor). Regarding the origin of

patients recorded in medical records, of 131 cases, 89 % were from the province of Entre Ríos, 6% from Santa Fe and 4.5% from other places.

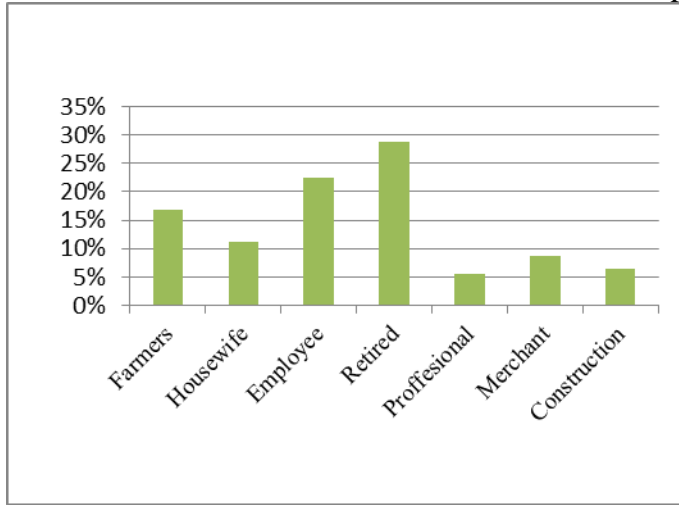


Figure 1. Occupation

As shown in Figure 1, most of observed patients were retired at the time of diagnosis, without mentioning the activity previously carried out in their medical records. Notably, within occupations, 17% of patients who performed agricultural activities, had a diagnosis of squamous cell carcinoma, which translated to 38% of the cases.

Table 2

<i>Farmers</i>	Number of cases
Squamous cell	8
Adenocarcinoma	5
Small cell	5
Large cell	3
Total	21

Shown in table 2 these farmer patients that perform related tasks, have higher prevalence of squamous cell carcinoma, a total of 9 smokers and 12 non-smokers.

Table 3

Frequency according to WHO classification of lung cancer

	N ° cases	Percentage
Non small cell		
Squamous cell	140	30.7%
Adenocarcinoma	128	28.1%
Large cell	69	15.1%

Small cell		
Small cell	88	19.3%
Other		
Undifferentiated	18	4.1%
Adenosquamous	7	1.5%
Carcinoid	4	0.9%
Sarcoma	1	0.2%
Total	455	1

When viewed, the total number of cases, in table 3, obtained between the years 1966 to 2010, one could say that squamous cell carcinoma has been most frequent in the sum of the period studied. However it is the object of this research to evaluate the tendency in the evolution of the time.

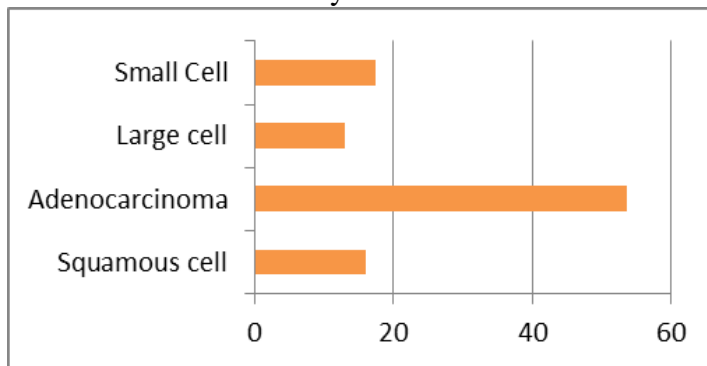


Figure 2. Lineage more prevalent in women since 1966 to 2010
 Note: values expressed in percentages

The prevalence of tumors of the lung depending on its lineage, distributed according to gender can be seen in figures 2 and 3. In the case of women it is observed that adenocarcinoma is the most frequent and the squamous cells to the male gender.

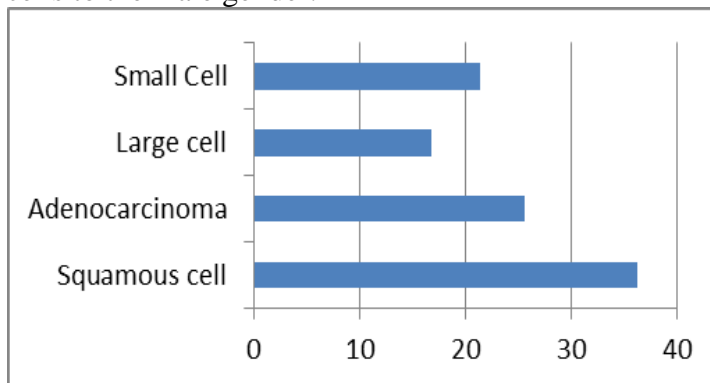


Figure 3. Lineage more prevalent in men from 1966 to 2010
 Note : values expressed in percentages

Table 4

Smoking

Daily amount	N ° cases
Smoker severe (> 16 cig.)	56
Smoker moderately (5-15)	5
Smoker mild (< 5 cig.)	1
Years of smoking	
Smoke less than 20 years	3
Smoke for over 20 years	40
Years of smoking cessation	
Ex. smoker less than 5 years ago	10
Ex. smoker between 5 - 10 years	4
Ex. smoker more than 10 years	10
Other	
Not smoker	13
Unreported	43
Records not found	322

In table 4, there are variables to consider in the patient that smokes. These are; daily amount smoked, years of smoking and time of quitting smoking. The majority of patients, is cataloged within the range of active smoker and severe, smoking 16 cigarettes a day for more than 20 years.

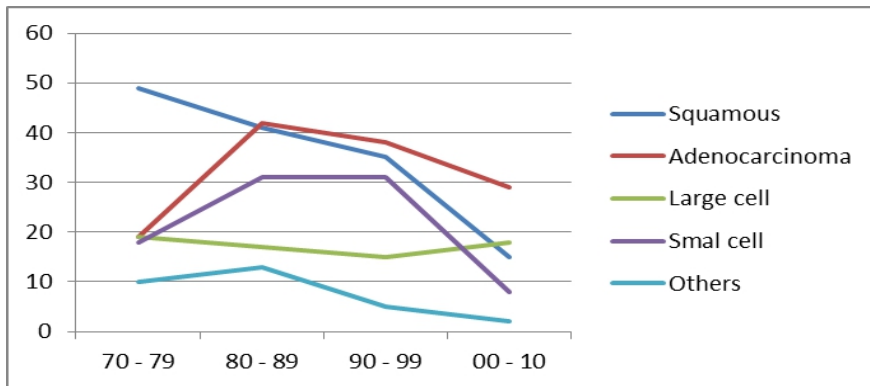


Figure 4. Evolution over time of the lung cancer in the SAP PD

Figure 4 shows the evolution in time of the different lineage of Lung Tumors, noting a marked rise of adenocarcinoma in the 80's, and a marked drop in the squamous carcinoma throughout the decades especially in the 90's. Large-cell is the most steady remaining in time, while small cell tumor presents a marked decline accompanying Squamous. Also a clear descent of all Lung Tumors, can be seen, by the end of 2010.

Table 5

Location of carcinoma of lung in relation to the rest of carcinomas.

Type of Cancer of the 90'	N ° cases	Percentage
Skin	1250	22
Mama	612	11
Colon	581	10
Prostate	551	10
Bladder	537	10
Cervix	289	5
Straight	226	4
Stomach	203	4
Kidney	168	3
Ovary	142	3
Thyroid	137	2
Lung	124	2
Endometrium	105	2
Lymphoma	103	2
Other	552	10

As shown in table 5, skin carcinoma is with a wide difference, the most frequent in the SAP PD, followed by carcinoma of breast and colon, placing the carcinoma of lung in twelfth place.

Table 6

Location of carcinoma of lung in relation to the rest of the carcinomas

Type of Cancer of the 70'	N ° cases	Percentage
Skin	451	21
Prostate	259	12
Bladder	208	10
Mama	199	9
Colon	130	6
Stomach	115	5
Lung	105	5
Other	721	33

In table 6 lung cancer ranks seventh in frequency in relation to the rest of carcinomas.

Conclusion

As can be seen in the results, lung cancer is much more common in men than in women and its main risk factor is the use of tobacco. The majority of patients who enter the smoking habit, do so in severe range (more than 16 cigarettes per day) and for more than 20 years, significantly increasing the risk of contracting lung cancer. According to Jean Charles Soria, "The use of tobacco in women has risen sharply. This is a worldwide phenomenon, searched through the strategies of the tobacco industry, since

women, as usual, when they do something, they do it big. Unfortunately, they become prey of cigarette smoking. The second problem that we have is that tobacco use begins increasingly at a younger age. Men used to begin to smoke at the age of military service and now women begin smoking in adolescence, even at a school age. This is something very serious, because the risk of lung cancer from smoking doesn't relate to the amount smoked as much as the length of time being a smoker. People are not aware of this fact, it is more dangerous to smoke five cigarettes a day for five years, than smoking five packs of cigarettes for one year. Cancer risk is much higher when a duration of consumption is more than 20 years, and this now makes women less than 40 years of age, younger, with children, with a diagnosis of lung cancer”.

In the present study, histological changes are seen in recent decades. It follows the abrupt descent of squamous cell carcinoma, and the marked rise of adenocarcinoma, confirming other studies. However the incidence of the lung cancer in general at the SAP PD has dropped significantly in the last decade.

Add Jean Charles Soria *There is a new phenomenon that is increasing and that increase is seen around the world although it is stronger in Asian countries, which is a gene mutation: EGFR (Epidermal Growth Factor Receptor). This is one of the main reasons for cancer in non-smokers, what Americans call "undeserved cancer" (cancer not deserved), because the person never smoked, but has cancer. It is a cancer whose precise origin is unknown, but is linked to a mutation in a gene, which currently represents 10% of all lung cancers. In Asian countries, gets to represent 30% of the cases. In Argentina, where there is a European genetic background, we are at 10%.*”

Currently in the world they are reviewing classical lung cancer classifications, inserting the molecular aspects of each tumor in particular. In this way, you can identify specific mutations in each case, and guide the therapeutic targets.

Statistical increase from other types of cancer, may be due to a true increase in incidence, as well as better diagnostic methods incorporated into the SAP.

Although indirectly, since it was not part of the objectives of this research, can be seen to skin cancer in all the decades it has been the most frequent in SAP PD, which can be explained by the ethnicity of the majority of the patients coming to the service, as well as by exposure to the Sun to which they experience on a daily basis through rural work. Such data may be relevant, to implement plans for the prevention and early diagnosis of skin cancer.

It would be very useful having a digitized database in SAP, which systematically would record the risk factors and family history of each patient, as a starting point for new statistical research. In this way, although for reasons of physical space, old medical records should be discarded, data essential for medical institutions that values its own statistics, should be preserved. Of course, more important will be the necessary awareness in each doctor, to collaborate in the accurate and comprehensive record of such data of their patients.

Acknowledgment:

Thanks especially to the pathology and medical records departments of the Sanatorio Adventista del Plata, whom have invested their time and their willingness to make this work be carried out, as well as the Department of science and technology of the Universidad Adventista del Plata, which has contributed to the financing of the project. Thanks to Dr. Ronaldo Gnass for his contribution at the beginning of this research.

References:

- Shaw GL. (1999). Additional clues to lung cancer risk. *Cancer Investigation*, 17, 661-662.
- Huber MH, Lippman SM. (1993). Non-small cell lung cancer. *Medical Oncology. A comprehensive review*. PRR.,(pp.127-146). Huntington, New York.
- Hecht S. Tobacco (1999). Smoke carcinogens and lung cancer. *J. Natl. Cancer Inst.*; 91, 194-1210.
- Taioli E, Wynder the. (1994). Re: endocrine factors and adenocarcinoma of the lung in women. *J Natl Cancer Inst.*;86, 869-70.
- Zang EA, Wynder the. (1996). Differences in lung cancer risk between men and women: examination of the evidence. *J. Natl. Cancer Inst.* 88, 183-192.
- El-Torky M., et to the. (1990). Significant Changes in the Distribution of Histologic Types of Lung Cancer. *Cancer. American Cancer Society.* (Vol. 65, pp. 2361).
- Medina-Morales, f. et al. (2002). Characteristics of lung cancer in a tertiary hospital. *Pneumology and thorax surgery.* (Vol. 6, 2:27-30).
- Ellis L, Fox J, Peake MD, Coleman MP. (2010). Lung cancer in young women remains rare. *Lung Cancer.* 67 (1): 124-5.
- Paris C, Clement-Duchêne C, Vignaud JM, Gislard A, Stoufflet a., Bertrand O, Thiberville L, Grosdidier G, Martinet and Bénichou J, Hainaut P. (2010) Relationships between lung adenocarcinoma and gender, age, smoking and occupational risk factors: A case - study case. *Lung Cancer.* May; 68 (2): 146-53. EPUB 2009 Jul 7.

- Cotran, Ramzi, Vinay Kumar and Tucker Collins. (2010). *Structural and functional pathology*. Mexico. (8th ed.). Mc Graw Hill-American.
- Sternberg, Stephen S. Diagnostic Surgical Pathology (1999). China. 3rd ed. Vol. I. Lippincott Williams & Wilkins.
- Colby, Thomas v, Michael N. Koss and William D. Travis. (1994). Atlas of Tumor Pathology. *Of the Lower Respiratory Tumors*. Fascicle 13. Third Series. Advisory Board. Washington.
- Rosai, Juan. Ackerman's. (2011). *Surgical Pathology* (10th ed. Vol. I). St. Louis Missouri: Mosby.
- Kato, Ikuko, Richard K. Severson, and Ann G. Schwartz. (2001). Conditional Median Survival of patients with Advanced Carcinoma: Surveillance, Epidemiology, And End Results Data. *Cancer American Cancer Society*. (Vol. 92. pp. 2211).