Original Article

Location of lung carcinoma in relation to the smoking habit and gender*

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ABSTRACT

Objective: To analyze the locations of lung carcinomas in relation to patient gender and smoking status. **Methods:** In order to test the hypothesis that lung carcinoma location (upper or lower lobe; left or right side) is correlated with smoking status and gender, we conducted a retrospective study of 697 patients with bronchogenic carcinoma treated at the Pulmonology-Oncology Outpatient Clinic of the Federal University of São Paulo. **Results:** We found that the bronchogenic carcinomas occurring in smokers were more frequently located in the upper lobes, whereas those occurring in nonsmokers were more frequently located in the lower lobes. In women, the neoplasms were more often seen in the lower lobes, especially in nonsmokers. Based on the available data, there were no differences in terms of the side affected (left or right). **Conclusion:** Overall, bronchogenic carcinomas are predominantly found in the upper lobes. However, in nonsmokers, they occur more frequently in the lower lobes. In females, bronchogenic carcinomas present a tendency to occur more often in the lower lobes.

Keywords: Lung neoplasms; Sex factors; Smoking

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INTRODUCTION

Lung cancer is the leading cause of death from cancer worldwide. In the USA, where adequate statistics are compiled, the number of deaths from lung cancer is higher than the total number of deaths from the three most common types of cancer: colon (48,000); prostate (30,200); and breast (40,000). Among men and women, respectively, lung cancer accounts for 32% and 25% of the total number of deaths from cancer. In Brazil, the incidence of lung cancer is 22,085 cases per year, and the death rate is 16,230 cases per year.[1] In the USA, these data are 172,570 cases per year and 167,510 deaths per year.[2-3] In Europe, in 1995, lung cancer caused the death of 266,000 men and 64,000 women. Unfortunately, two-thirds of all cases are only discovered after the disease has reached an advanced stage and therefore cannot be operated. The great majority of patients undergo palliative treatments, such as chemotherapy and radiotherapy. Despite of the development of new drugs, five-year survival remains low, between 10% and 15%.[4-5]

The main etiological factor of the disease is the smoking habit. Approximately 80% of those presenting the disease report beings smokers, a well-established cause-and-effect relationship. Other occupational factors, such as exposure to asbestos, beryllium, pollution and ionizing radiation, have also been mentioned.[4-6]The literature shows that lung cancer, as a whole, tends to be located in the upper portion of the lung. It presents a ratio of 2.5:1 between upper and lower locations. In the literature, we found no reports that lung cancer location is related to smoking status or gender. In this study, we studied the location of lung tumors, comparing nonsmokers and smokers, as well as looking for gender-related differences.[6-9]

METHODS

We evaluated 697 patients presenting lung tumors, all of which were submitted to chest X-rays and computed tomography scans of the chest. The diagnoses were confirmed through anatomopathological examination of material obtained from bronchoscopy or open lung biopsy. These patients were admitted to the Pulmonology-Oncology Outpatient Clinic of the University of São Paulo, between 1986 and 2004. The tumor sites were evaluated through imaging, and were classified as follows: right and left sides; upper and lower lobes; in smokers and in nonsmokers; in males and in females. Upper lobe tumor sites were defined as those located in the upper or middle lobes of the right lung or in the upper lobe of the left lung, whereas those located in the lower lobes were considered lower lobe tumor sites. Patients in which tumors were seen on both sides (right and left) or in both lobes (upper and lower) were excluded from the analysis, since it was not possible to determine the initial site of the tumor. In relation to the sides, 49 patients were excluded (40 males and 9 females), and in relation to the lobes, 168 patients were excluded (117 males and 51 females).

Upon admission to the outpatient clinic, the patients authorized the use of the data for research. The location of the tumor was evaluated by the radiologist of the clinic and compared with the smoking habit and in relation to gender.

For the statistical analysis, the chi-square test or Fisher's exact test were used whenever indicated.

RESULTS

The characteristics of the patients evaluated in the study are summarized in Table 1.

Most of the patients presented defined sides and lobes and were included in the study. Most were smokers (N = 598, 85.7%).

The distribution of the lung tumor mass according to the smoking habit is shown in Table 2.

Among the smokers, the lung masses developed mainly in the upper lung lobe. This difference was significant (p = 0.0143) in relation to nonsmokers. Among smokers, the ratio between the upper and lower lobes was 2.29, compared with 1.18 among nonsmokers. Upper lobe lung masses were seen

TABLE 1

Patient characteristics

	Smoker	Nonsmoker
Male	471	27
Female	127	72
Defined sides	558	90
Defined lobes	457	72
Both sides (excluded)	40	9
Both lobes (excluded)	141	27

TABLE 2

Distribution of the smoking habit and pulmonary lobes among patients with lung cancer

Smoking habit	Upper	Lower
Smoker	318 (69,6%)	139 (30,4%)
Nonsmoker	39 (54,2%)	33 (45,8%)
Total	357	172

p = 0.0143; odds ratio = 1.936

predominantly in males. The ratio between the upper and lower lobes was 2.46 for men and 1.11 for women (Table 3). This difference was quite significant (p = 0.0052).

When the patients were separated by gender, lung lobes and smoking habit, we observed that, in smokers, regardless of their gender, the masses were predominantly found in the upper lobes. Among nonsmokers, the upper lobe tumors were predominant among men, and lower lobe tumors were predominant among women (Table 4).

There were no significant differences related to smoking or gender in terms of the sidedness of the lung tumor (Table 5).

TABLE 3

Distribution of gender and pulmonary lobes among patients with lung cancer

Gender	Upper	Lower
Male	271 (71.1%)	110 (28.9%)
Female	86 (58.1%)	62 (41.9%)
Total	357	172

p = 0.0052; odds ratio = 1.776

TABLE 4

Distribution of gender, pulmonary lobes and smoking habit among patients with lung cancer

	Smoker		Nonsmoker	
	Male	Female	Male	Female
Upper	258 (70.9%)	60 (64.5%)	13 (76.4%)	26 (47.3%)
Lower	106 (29.1%)	33 (35.4%)	4 (23.5%)	29 (52.7%)

male: p = 0.7870; female: p = 0.0574

TABLE 5

Distribution of gender, side of pulmonary involvement and smoking habit among patients with lung cancer

	Male	Female	Smoker	Nonsmoker
Right	277	125	344	58
Left	184	62	214	32

p = 0.1287; p = 0.64; odds ratio = 0.74; odds ratio = 0.8863

DISCUSSION

In the literature, there have been only a few studies associating the location of lung tumors with the smoking habit and gender. These studies mention tumor preference for the upper lobe but, despite the fact that the majority of the patients studied were smokers, do not clearly associate it with the smoking habit, giving more weight to correlations with asbestos exposure and diet.[6-7,10]

In Brazil, ours was the first group to make this correlation with a large number of patients. One limitation of this study is that the data were retrospective, and the population of nonsmokers was small.

The location was determined through the examination of images (chest X-rays and computed tomography scans of the chest), and patients whose images did not exactly confirm its original location were excluded. In this group, there were images to be evaluated for all of the patients, and the diagnoses were confirmed in all cases. During the period in which the data were collected, technological advances did not alter their interpretation. The upper and middle lobes of the lung were considered the upper lobe, since these were equivalent to the upper left lobe (upper division plus lingula).

In relation to the sides (right or left), there was no significant difference between them, even when the smoking habit was analyzed.

In relation to the lobe, there was a clear predominance of upper lobe tumors among smokers, where the majority of tumors found among nonsmokers were lower lobe tumors. These differences were significant. The number of lower lobe tumors was greater among women than among men.

This higher number of lower lobe tumors is due to the predominance of tumors in this region among female nonsmokers. We observed that the ratio between the upper and lower lobes among female smokers was similar to that of males, while among female nonsmokers, tumors tended to be more often located in the lower lobe. This difference in behavior was significant (Table 4).

We observed that, among smokers, the tumor tended to be located in the upper lobe, with an increased ratio between the upper and lower lobes, as shown in another study,[8] in which upper lobe tumors were predominant.

This predominance is not well understood, though there are some suppositions. It is possible that toxins and carcinogens persist in the upper lobes for a longer period, due to the relative lower ventilation or lower efficiency of lymphatic depuration. It can be hypothesized that there is less efficient delivery of food derivatives or protective substances via circulation to the upper lobes, when compared with the lower lobes.[7,10] All of this takes place because the ventilation/perfusion ratio is greater in the upper lobe than in the lower lobe, creating favorable conditions for this predominance in smokers.[7,10]

The decreased forced expiratory volume in one second increases the risk of lung cancer, and risk increases in parallel with decreasing function. However, this relationship is not linear: with a small decrease in the forced expiratory volume in one second, for instance, from 100% to 95%, the risk would increase from 30% to 60%. This risk is amplified in women.

Inflammation of the airways and of the lung is associated with a decline in pulmonary function among smokers. The annual decrease in forced expiratory volume in one second is correlated with the amount of cigarettes smoked. Among nonsmokers without any respiratory disease, the forced expiratory volume in one second decreases, from 35 years of age, by 25 to 30 ml/year, and this rate increases with age. Among smokers, it decreases by 60 ml/year and can reach 100 ml/year in 5.8% to 8.2% of smokers.

Inflammation is an important mechanism in the proteolytic destruction of the lung, as well as in the remodeling and narrowing of the small airways, such factors leading to the reduction of pulmonary function in smokers, to chronic obstructive pulmonary disease, to asthma and to pulmonary fibrosis. Cigarette smoke and other irritants stimulate the inflammatory response in the airways, leading to the recruitment and activation of pro-inflammatory cells, such as leucocytes, which propagate the inflammatory cascade, releasing several cytokines and oxidants. As a consequence, there can be oxidative damage and DNA mutation.

In individuals with diminished forced expiratory volume in one second, the clearance of inhaled carcinogens is impaired. This leads to greater contact time between carcinogens and epithelial cells.

These considerations explain the greater incidence of tumors in the upper lobes of smokers but not the greater number of tumors in nonsmokers.

We believe that, in addition to the above considerations, smokers achieve a deeper inspiratory capacity, which carries the carcinogens preferentially to the upper lobes. Nonsmokers, however, inhale the carcinogens at a lower inspiratory capacity, which carries the carcinogens preferentially to the lower lobes.

In women, lower lobe tumors predominated, since the percentage of female nonsmokers is greater than that of male nonsmokers.

Lung neoplasms are predominantly seen in the upper lobes due to the great number of smokers. However, among female nonsmokers, lower lobe tumors were more prevalent.

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