

Lung Cancer in Non-smokers

Adnan Yılmaz, MD¹; Reba Baran, MD¹; Birol Bayramgürler, MD¹; Ergün Karaballı, MD¹; Sibel Unutmaz, MD¹; T. Bahadır Üskül, MD¹

¹ SSK Süreyyapaşa Center for Chest Diseases and Thoracic Surgery, İstanbul, Turkey.

Abstract

Objective: To evaluate the characteristics of lung cancer in non-smokers.

Design: 3211 primary lung cancer cases diagnosed in our center between January 1992 and December 1995 were determined on the basis of pathology laboratory records. Clinical files of all the patients were analyzed retrospectively.

Patients: The study included 368 non-smoker lung cancer patients. The control group was composed of 736 patients selected by systemic sampling method from 2560 smoker lung cancer patients.

Interventions: Non-smoker and smoker patients were determined. Characteristics of the patients, tumor type, and possible risk factors for lung cancer were analyzed.

Results: Of 3211 cases, 368 (11.4%) were non-smoker and

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2560 (83.1%) were smoker. The proportion of non-smokers was 84.1% (186 of 221) for female patients and 7.9% (182 of 2525) for male patients with a ratio of 1.03:1. The ratio of adenocarcinoma was 50.6% in non-smokers and 19.3% in smokers ($p<0.0001$). The ratio of squamous cell carcinoma and small cell carcinoma was higher in the smoker group. Forty-two percent of the non-smoker patients and 1.2% of the smoker patients were housewives ($p<0.0001$). The most frequently seen occupations among the smoker patients were farming and driving, 15.4% and 12% respectively. In the non-smoker group, mining ($n=20$), textile-related jobs ($n=15$), previous tuberculosis history ($n=13$), and asbestos exposure ($n=12$) were most frequently detected possible risk factors.

Conclusion: There are significant differences between smoker and non-smoker lung cancer patients with respect to tumour type, sex distribution and occupation.

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Introduction

The association of tobacco with lung cancer has been known for more than 50 years. Extensive laboratory and epidemiological evidence has established cigarette smoking as a cause of lung cancer (1-4). In fact, most lung cancer cases in the United States can be attributed to tobacco smoking (5). The relative risk of developing lung cancer for female smokers ranged from 0.2 to 6.8. For male smokers, this risk ranged from 1.2 to 36.0 (3).

Lung cancer does infrequently occur in non-smokers (6-8). Several features distinguish the lung cancer in non-smokers from that occurring in smokers (6). The most prominent of these differences are sex distribution and frequency of tumor types. Most of the non-smoker lung cancer patients are women and adenocarcinoma is the most common type, especially in women (6,9-11). In this study, we aimed to evaluate the characteristics of non-smoker lung cancer cases and the possible risk factors.

Correspondence: Dr. Adnan Yılmaz
Zümrütevler Atatürk Caddesi Abant Apt.
No:30 Daire:1 81530 Maltepe, İstanbul, Türkiye
E-mail: elifim @ rt.net.tr

Methods

3211 primary lung cancer cases diagnosed in our center between January 1992 and December 1995 were determined on the basis of pathology laboratory records. Clinical files of all the patients were analyzed retrospectively. The patients were divided into 3 groups as non-smoker, ex-smoker, and smoker. non-smokers are those who have never smoked as much as one cigarette, one cigar, or one pipeful of tobacco per day for lifetime. This study included 368 non-smoker cases. The control group consisted of 736 cases, selected by systematic sampling method from 2560 smoker lung cancer patients. The clinical files of the patients were examined retrospectively. Characteristics of the patients, tumor type, and possible risk factors for lung cancer were recorded. The tumor classification of the World Health Organization was used (12). Characteristics of the groups were compared by Chi-square test.

Results

We analyzed 3211 primary lung cancer cases. Of these cases, 368 (11.4%) were non-smoker and 2560 cases (83.1%) were smoker. The total number of women having primary lung cancer was 221, 186 of which (84.1%) were non-smoker. This ratio for male patients was only 7.9%. Table 1 indicates sex and age distribution of the groups. The number of female patients is higher in the non-smoker group ($p < 0.0001$).

| | NON-SMOKER | | SMOKER | | P value |
|--------------|-------------|------|------------|------|----------------|
| | n | % | n | % | |
| Female * | 186 | 50.5 | 13 | 1.8 | * $p < 0.0001$ |
| Male * | 182 | 49.5 | 723 | 98.2 | |
| Female: male | 1.03:1 | | 1:55.6 | | |
| Mean age† | 56.9 ± 12.1 | | 57.8 ± 9.7 | | † $p > 0.05$ |
| ≥40 | 41 | 11.2 | 42 | 5.8 | |
| 41-45 | 22 | 6 | 46 | 6.2 | |
| 46-50 | 32 | 8.9 | 69 | 9.3 | |
| 51-55 | 46 | 12.5 | 98 | 13.3 | |
| 56-60 | 63 | 17.1 | 153 | 20.8 | |
| 61-65 | 76 | 20.6 | 173 | 23.5 | |
| ≥66 | 88 | 23.7 | 155 | 21.1 | |

The most frequently seen occupations among the smoker patients were farming and driving, 15.4% and 12% respectively. Forty-two percent of the non-smoker patients were housewives (Table 2).

| | NON-SMOKER | | SMOKER | | P value |
|----------------------|------------|------|--------|------|----------------|
| | n | % | n | % | |
| Farmer | 30† | 8.3 | 115† | 15.4 | † $p < 0.005$ |
| Driver | 12‡ | 3.3 | 88‡ | 12 | ‡ $p < 0.005$ |
| Independent business | 10 | 2.8 | 49 | 6.5 | |
| Textile-related jobs | 15 | 4.2 | 23 | 3.1 | |
| Miner | 20 | 5.7 | 42 | 5.8 | |
| Building worker | 13 | 3.5 | 46 | 6.3 | |
| Housewife | 154 * | 41.9 | 9 * | 1.2 | * $p < 0.0001$ |
| Metal worker? | 4 | 1.1 | 33 | 4.5 | |
| Officer | 2 | 0.6 | 40 | 5.4 | |
| Other | 84 | 24 | 254 | 34.8 | |
| Unknown | 24 | 6.6 | 37 | 5 | |

Table 3 shows the distribution of tumor type in the groups. The distribution of cell types was significantly different between non-smokers and smokers. While the ratio of adenocarcinoma was higher in the non-smoker group ($p < 0.0001$), the ratio of squamous cell carcinoma and small cell carcinoma was higher in the smoker group ($p < 0.0001$).

| | NON-SMOKER | | SMOKER | | P value |
|-------------------------|------------|------|--------|------|----------------|
| | n | % | n | % | |
| Squamous cell carcinoma | 140 * | 38.1 | 442 * | 60.1 | * $p < 0.0001$ |
| Adenocarcinoma | 186† | 50.6 | 142 † | 19.3 | † $p < 0.0001$ |
| Small cell carcinoma | 38 ‡ | 10.3 | 143 ‡ | 19.4 | ‡ $p < 0.0001$ |
| Large cell carcinoma | 2 ** | 0.5 | 5 ** | 0.6 | ** $p > 0.05$ |
| Adenosquamous carcinoma | 2§ | 0.5 | 4 § | 0.4 | § $p > 0.05$ |

Among the non-smoker lung cancer patients, mining, textile related jobs, previous tuberculosis history, and asbestos exposure were most frequently detected possible risk factors (Table 4).

| POSSIBLE RISK FACTORS | NUMBER |
|----------------------------------|--------|
| Mining | 20 |
| Textile-related jobs | 15 |
| Tuberculosis | 13 |
| Asbestos exposure | 12 |
| Alcohol use | 10 |
| Other organ malignancies | 5 |
| Malignancy in family memberships | 4 |
| COPD/Asthma | 4 |
| Radiation | 3 |
| Petrochemistry | 3 |
| Sarcoidosis | 1 |

Discussion

The etiological relationship between cigarette smoking and the development of primary lung cancer is firmly established (1,2,8,10). It is estimated for the United States that 85 to 90% of the lung cancer cases among men and around 70% or more in women are presently attributable to cigarette smoking (1). Lung cancer also occurs in non-smokers. Most of the non-smoker lung cancer patients are women and adenocarcinoma is more common in women (6,9,11,13). The percentage of non-smokers among male patients having lung cancer has ranged from 0.5% to as high as 15.3% (6, 11,13,14). The percentage of non-smokers among female patients having lung cancer was reported as 13% and 41% in two series (6,9,13). The ratio of the female patients having primary lung cancer was reported as higher than 20% in several studies (8,10,15,16). In a previous study, while one-third of the female cases who smoked had adenocarcinoma, two-thirds of the non-smoker female cases had adenocarcinoma. There were only 7 non-smoker cases among 117 women with squamous cell, small cell, or large cell carcinoma (17). In our study the ratio of non-smoker lung cancer cases was 7.9% in male patients and 84.1% in female patients. The number of the female smoker lung cancer cases was too low in our series. Squamous cell carcinoma was the predominant type in the smokers, whereas adenocarcinoma was more common in the non-smokers, especially in women. Smoking is highly prevalent in our country. There are more male smokers than female smokers. While 5% of the male patients with lung cancer were non-smoker, 77% of the female patients were non-smoker. Adenocarcinoma was most frequently found in the non-smokers (11).

When our patients were evaluated with respect to occupation, the most frequently seen occupation groups were housewife, farmer and miner in the non-smoker group, and farmer, driver and building worker in the smoker group. The results of two previous studies suggested that the ratio of housewives among the non-smoker lung cancer cases was high (3,13). The other study reported that forty-four percent of the female patients with lung cancer were housewives and 14.2% were farmer housewives. In the latter study, 47% of the male patients with lung cancer were farmer (10). Among the patients with lung cancer, miners were infrequent (6,10)

When the non-smoker lung cancer cases were evaluated with respect to possible risk factors, most frequently detected risk factors were mining, textile-related jobs, previous tuberculosis history and asbestos exposure. Hinds et al (18) reported that among non-smoker women, those with a history of pulmonary tuberculosis infection may be at approximately 8 times greater risk of lung cancer than similar women without a history of

tuberculosis. Kabat et al. (6) found that the risk of lung cancer among non-smoker women who reported having worked in the textile-related jobs was high. But, many reports indicated that among the non-smoker patients with lung cancer, asbestos exposure was low (6,10,13).

In conclusion, the high ratio of smokers among lung cancer patients indicates the importance of smoking in lung cancer etiology. There are significant differences between smoker and non-smoker lung cancer patients with respect to tumor type and sex distribution. Mining, textile-related jobs, previous tuberculosis history and asbestos exposure was significant risk factors for our patients. The number of female patients with lung cancer was low in our series. We conclude that with changes in smoking patterns of females, there will be changes in the frequency of tumor types and an increase in the number of female patients over years in our country.

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