Lung Cancer in Young Adults

GENÇ ERİŞKİNLERDEKİ AKCİĞER KANSERLERİ

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Summary

Lung cancer is an uncommon disease in individuals younger than 45 years old. We reviewed the medical records of Atatürk Chest Disease Hospital from 1992 to 1994, and identified 97 patients with a documented diagnosis of lung cancer younger than 45 years old and have compared them with the elder patients. Eighty-seven (89%) of the 97 patients were men and 10(11%) were women. Male to female ratio was 8.7/1. Most of the patients in both groups were smoker. The majority of the patients admitted that they had begun smoking in their early teen years. Thirty-two (32%>) had squamous cell carcinoma, thirty-one (31%>) had small cell lung carcinoma (SCLC) and twenty-six (26%>) had adenocarcinoma. Forty-six (69%) of the patients with nonsma/l cell carcinoma (NSCLC) had unresectable disease at diagnosis (23 had stage IHB and 23 had stage IV). The number of patients with extensive disease (ED) small-cell carcinoma was greater in the young patient group (p<0.()5). The most common symptoms were sputum, hemoptysis and dyspnea and duration of the symptoms was 1-3 months. There were no differences between the two age groups for symptoms, symptom duration and chest roentgenogram findings. The median survival of patients with NSCLC, limited disease (LD) SCLC and ED SCLC were 7.5 months, 10 months and 8 months, respectively. In this series, no statistically significant differences were found with regard to resectability and median survival duration between the two groups.

Key Words: Lung cancer, Risk factors, Cell type, Survival, Young adults, Prognosis

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Ozet

Akciğer kanseri 45 yaş ve altında nadir görülür. Biz bu çalışmada 1992-1994 yılları arasında Atatürk Göğüs Hastalıkları ve Göğüs Cerrahisi Merkezi 'nde 45 yaş ve altında olan akciğer kanseri tanısı konmuş 97 hastayı inceledik ve yine aynı zamanda akciğer kanseri tanısı alan yaşlı hastalarla karşılaştırdık. Doksanyedi hastanın %89 'u erkek, %>11 'i kadın, erkek/kadın oranı ise 8.7/1 idi. Her iki gruptaki hastaların çoğu sigara içiyordu ve sigaraya çok erken yaşlarda başlamışlardı. Histolojik tipler; epidermoid karsinom %>32, küçük hücreli karsinom (KHAK) %>31 ve adenokarsinom %>26 idi. Küçük hücreli karsinom dışındaki akciğer kanserli (KHDAK) hastaların %>69'u (46 hasta) inoperabl evrede (23 hasta evre IIIB, 23 hasta evre IV) idi. Yaygın hastalık evresinde (YH) KHAK'li hastalar genç grupta daha fazla idi (p<0.05). En sık görülen semptomlar öksürük, balgam, hemoptizi ve nefes darlığı olup semptomların süresi 1-3 ay arasında değişiyordu. Her iki grup arasında semptomlar, semptom süreleri ve akciğer grafisi bulguları açısından fark yoktu. Medyan sağkahm KHDAK 'li.KHAK (SH) 7/ (sınırlı hastalık) ve KHAK (YH) 'li hastalarda sırasıyla 7.5 ay, 10 ay ve 8 ay idi. Bu seride rezektabilite ve medyan sağladım süreleri açısından iki grup arasında istatistiki olarak anlamlı bir fark bulunamadı (p>0.05).

Anahtar Kelimeler: Akciğer kanseri, Risk faktörleri, Hücre tipi, Sağkahm, Genç erişkin, Prognoz

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Lung cancer remains the most preventable fatal disease in man, with 85% of the cases said to be related to cigarette smoking. Lung cancer rarely occurs before the fifth decade of life. Several reports (1-6) have suggested that lung cancer in patients less than 45 years of age is more aggressive and rapidly fatal than in older patients. A few reports (7-13) have discussed the prognosis for young patients with this disease, stating that it is no worse than the prognosis for lung cancer patients greater than 45 years of age.

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Though lung cancer is mostly seen in males, the ratio is altered in favour of females in the last years, because of increasing incidence of smoking among women. The incidence of lung cancer is lower below the age of 45 and varies between 2.2 and 6% (3,4,14). In our study, clinical and pathologic features of primary lung cancer in young adults (younger than 45 years of age) were evaluated. Survival analysis was made. The characteristics of the young patient group were compared with the characteristics of 100 lung cancer patients older than 45 years old.

Materials and Method

From 1992 to 1994, ninety-seven lung cancer patients under 45 years old, diagnosed and treated in Atatiirk Chest Disease Hospital, were included in the study. During the same period, 100 randomly selected patients older than 45 years old were taken as the control group.

The definitive diagnosis was made by Ultrasonography or computed tomography guided transthorasic biopsies, bronchoscopic biopsies or open lung biopsies. Bronchoscopy, thorax and brain computed tomographies, whole body bone scintigraphy and abdominal ultrasonography were performed and the patients were classified according to TNM classification system. Patients' age, sex, symptoms, duration of symptoms, smoking habits, family history, histopathological type and stage of disease, radiological findings and treatment modalities were documented.

Statistical analysis was performed by chi-square, Mantei-Haenszcl and Kaplan Meier tests (15). A P value less than 0.05 was considered statistically significant.

Results

The characteristics of the patients are shown in Table 1.

As it is shown in Table 1, male/female ratio in young patients was 8.7/1, while it was 13.2/1 in the older patient group. In the older group, the most frequent histopathological type was epidermoid carcinoma, whereas in younger patients, epidermoid, SCLC and adenocarcinoma were seen at the same frequency. In our study, most of the patients

Table 1. The general characteristics of patients with lung cancer

	Age <45 (n:97)	Age >45 (n:100)	p
Male/Female	87/10	93/7	
Ape (median)	41(15-45)	58(47-72)	
Cell tvpc	no.	no.	
Squamous cell	32	44	
Adenocarcinoma	26	31	
Small cell	31	22	p>0.05
Large cell	5	1	
Mixed type	3	1	
Unclassified	0	1	
NSCLC			
Stage			
SCLC			
Limited	9	13	
Extensive	22	9	p<0.05
NSCLC			
I	1	1	
II	9	3	
IIIA	10	9	p>0.05
IIIB	23	40	
rv	23	25	

with NSCLC in both groups have been diagnosed in advanced stages (69% in younger patients, 83% in older patients). There was no significant difference in the stages of presentation between both groups with NSCLC (p>0.05). On the contrary, the number of patients with extensive stage SCLC was greater in the young patient group (p<0.05). In both groups, the predominant histopathological type was adenocarcinoma in females.

Lack of sufficient knowledge in the patient files prevented us to evaluate the occupational and environmental factors. The family history in young patient group was 15%, whereas it was 7% in the old patient group. The difference was not statistically significant (p>0.05).

The symptoms at the time of presentation are listed in Table 2. In both groups, the incidence of cough, sputum and dyspnea was greater than the incidence of other symptoms. The number of asymptomatic patients in the older group was 6 (66%), whereas it was 1 (1%) in the younger group and the difference was statistically significant (p<0.05). The duration of the symptoms in both groups var-

icd between 1 -3 months and the difference was not statistically significant.

The great majority of the younger patients had a history of heavy smoking and had begun smoking prior to the age 20 (41%). The number of patients who were smoking for more than 21 years was naturally higher in the old patients group ($p<0.05$) (Table 3).

Radiological findings are listed in Table 4. The number of masses (hilar and nonhilar) were higher than the other findings in both groups. Pleural effusion was found to be less. When the incidence of radiological findings are concerned, there was no significant difference between the groups ($p>0.05$).

Table 2. Symptoms

	Age <45 (n:97)	Age >45 (n: 100)	p
Asymptomatic	1	6	p<0.()5
Symptoms			
Cough	53	49	
Sputum	23	31	
Hemoptysis	22	17	
Dyspnea	34	34	p>0.05
Weight loss	24	20	
Hoarseness	g	12	

Table 3. The distribution of the patients according to the duration of smoking cigarettes

Years	Age <45(n:97)	Age >45(n:100)	
never smokers	18	24	
<10	4	1	
11-20	34	9	
			p<0.001
21 +	41	66	

Table 4. Roentgenographs findings*

	Age <45	Age >45
Hilar-Parahilar masses	29	43
Atelectasis	5	14
Peripheral masses	49	52
Pleural effusion	10	11
Reticulonodulary or miliary appearance	5	2

**One patient has more than one roentgenographicfindings*

Table 5. The modalities of treatment

	Age <45 (n:97)	Age >45 (n:100)
No treatment	14	0
Chemotherapy alone	50	68
Chemotherapy+Radiotherapy	11	20
Radiotherapy alone	9	1
Surgery alone	6	1
Surgcry+Chemothcrapy	6	8
Surgcry+Chemotherapy+ Radiotherapy	1	2

Treatment modalities used in the study are shown in Table 5. In the young group, because of the social problems, 14 patients did not receive treatment. Among these patients 10 were NSCLC (two with stage IIIB and 8 with stage IV disease), four were SCLC (three patients with ED and one patient with LD). These patients received only symptomatic care. Chemotherapy was given to more than 50% of the patients in both groups. Surgery, combined with other modalities of treatment, was applied to 19.6% of the younger group and 14% of the older group.

The median survival of young patients with NSCLC was 7.5 months and the old patients with NSCLC was 10 months. In the younger and older groups with limited SCLC the median survival were respectively; 10 months and 9 months. In advanced stage SCLC, it was 8 months in younger patients and 9 months in older patients. There was no statistically significant difference between the groups in the survival rates for 1 year (55% vs 46%). However, 2 or more year survival rates were significantly higher in the young group (41% vs 28%) ($p<0.05$).

Discussion

Age is an important risk factor in most cancer types. Lung cancer is a predominant disease for males in middle and old ages. Lung cancer cases below the age of 40 represent 6% of all lung cancer cases. The incidence rises to 7-12% at the 5th decade, and makes a peak at the age of 70 (7,14,16).

The ratio of men to women (M/F) among lung cancer patients below the age of 45 varies in different countries. The adenocarcinoma was not thought to be in relation with the smoking habit as strongly as squamous cell carcinoma, but now, especially after the increase in the number of women smokers, this lung cancer type is becoming to be the main type reported for men and women (17). While the ratio in England and North European countries is 2-3/1, it is 10/1 in France, Italy and Spain (18). The common characteristics in this sense is that this ratio is lower in the younger age group. In this report, the male to female ratio was 8.7/1, whereas the ratio in the older group was 13.2/1. The prevalance of the various histopathological cell types of lung cancer varies considerably from series to series and country to country and may depend not only on the nature of the study populations (e.g., surgical vs autopsy series) (1,19), but also upon the chosen design and location of the various studies. Histopathological types of lung cancer in young adults show variation between different countries. Adenocarcinoma in USA, SCLC in England and epidermoid carcinoma in Italy are the predominant types (1,17). From Turkey, Misirhgil et al (20) also showed that, among young patients, 29.3% had squamous cell carcinoma, 25.9% had adenocarcinoma, 20.7%o had small-cell carcinoma. In our series, 32.5% had squamous cell carcinoma, 31% had small cell carcinoma and 26% had adenocarcinoma.

Several studies have reported that smoking is an important factor in the occurrence of lung cancer in young people, and the reason for the relative increase in the number of women among the young patients is the increase of number of women smokers. Risk factors other than smoking that have been cited in these patients include genetic predisposition, occupational exposure to respiratory irritants, and perhaps enviromental factors, particularly in geographical areas with a high concentration of petrochemical industries (1). In our study, history of cigarette smoking which is one of the major risk factors was similar in both groups (81% vs 76%). The duration of cigarette smoking was naturally longer in the older age group. Most of the patients in both groups were smoking 11-20 cigarettes/day. There arc various reports stressing the importance of familial factors (3,8,12). In our study, 15 patients from the younger group and 7 from the older group had a family history, but the difference between the groups was not statistically significant ($p>0.05$).

A major issue debated in the literature is whether lung cancer in the young are biologically more aggressive. Studies by Dc Caro, Benficld and Neuman et al have postulated that malignant neoplasm in the young are indeed more aggressive neoplasms (4,6). Icard (13) and colleagues also reported, the prognosis for patients less than 45 years of age with primary lung cancer seems to be related more to the extent of the disease than to a particularly aggressive behavior pattern of the cancer. On the other hand, in three large series, no difference was found in survival between the young patients and an older group with carcinoma of the lung (8,12,16). We also, could not find a significant difference between the median survivals of the two groups.

Advanced stage at diagnosis has been previously observed in young patients. Onuigbo noted that in advanced stage, lung cancer tends to be more localized and to metastasize to fewer organs. Strauss and Weber analysed 296 cases of bronchogenic carcinoma and observed that adenocarcinoma and undifferentiated carcinoma of the lung, in general, had greater tendency to metastasize than squamous cell carcinoma (18). Some authors have previously identified a trend toward early stage lung cancer as age increases (21). This inverse relationship between age and stage of disease is mostly marked for squamous cell carcinoma and adenocarcinoma, but has also been shown in SCLC. In addition, Huang et al (5) suggested that younger patients have a high nuclear protein content (nuclear protein/DNA ratio) which may cause a higher tumor proliferation rate and consequently high metastasis rate. Some authors feel that the disease is in a more advanced stage when diagnosed since it was not suspected (3,4). Green and et al (22) found 71-87% of patients presenting with stage III and IV. Ganz (7) reported 20% of patients has resectable, whereas 40% had "locally unresectable" disease and 40% had metastatic disease at presentation. Whereas most studies report the rate of resectability approximately 20-25% (20-22), only a study by Kyriakos (8) reported a high rate of curative resection (57%). In our study, most of the

patients with NSCLC in both groups have been diagnosed in advanced stages (69% in younger patients, 83% in older patients). The rate of the patients operated in the younger and older age groups in our study was respectively 19.6% versus 14%. While most of the younger patients with SCLC are diagno-sed in advanced stage of disease, most of the older patients had limited SCLC when diagnosed. These findings support the hypothesis that lung cancer is usually diagnosed in advanced stages in young patients. In these series, no statistically significant differences were found with regard to resectability and median survival length, between those younger than age 45 and those older. Similar findings have been reported by other authors (7-11,23).

However, most of the recent reports declare that there is no significant difference in median and 5 year survival rates between the younger and older patients (4,9,12,14). There was no significant difference in 1 year survivors of both groups. However, 2 or more year survival rates were significantly higher in the younger group ($p<0.01$). Younger patients often can receive more aggressive therapy because of their prior good health and the absence of other significant major medical illness and this may be the reason why the survival rate for the younger patients with advanced disease is better than that of the older patients in our scries.

In summary, we can state that 79% of the young lung carcinoma patients are heavy smoker, 99%) have nonspecific symptoms and advanced stage at diagnosis. This study strongly suggests that smoking is an important risk factor for lung cancer in the young. However, the role of other unidentified cnviromcntal or genetic factors remains unknown. Clearly, prevention of lung cancer in these young individual should be primary objective. It is obvious that the main target should be to organize effective campaigns against smoking and thus to prevent the disease. Differences in the behavioral pattern in lung cancer should modify the thinking of the general practitioner who is the first to see these patients. Also, if lung cancer in young patients is diagnosed in early stages, the chance for treatment will increase as will expectancies for survival. This study and others suggest that patients who have persistent signs of pulmonary disease and history of heavy smoking, regardless of age or sex, must be considered at risk for lung cancer. Diagnostic tests should be performed early to exclude the possibility of lung cancer.

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