
Lung cancer histopathology in the Thrace region of Turkey and comparison with national data

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ÖZET

Trakya bölgesinde akciğer kanseri histopatolojisi ve ulusal verilerle kıyaslanması

Akciğer kanserinin morbidite ve mortalite hızlarının izlenmesi, daha önceki sigara içme trendleri ve bazı coğrafi faktörler hakkında ipuçları verebilir. Trakya bölgesindeki akciğer kanserli hastaların demografik özellikleri ve histopatolojik dağılımları daha önce incelenmemiştir. 1992-2001 yılları arasında, Trakya Üniversitesi Tıp Fakültesi Göğüs Hastalıkları Kliniği'ne başvuran primer akciğer kanserli hastaların dosyaları retrospektif olarak değerlendirildi. Beşyüzaltmışyedi hastanın 521'inin dosyası değerlendirmeye uygundu. Yaş ortalaması 61 ± 10 yıldır (30-86) ve 497 (%95.4) hasta erkekti (erkek/kadın oranı= 20.7). Ulusal ve diğer ülkelerin verileri ile karşılaştırıldığında, Trakya bölgesindeki akciğer kanserli hastalardaki erkek/kadın oranı daha yüksekti. Adenokarsinom 24 kadın hastanın 7 (%29.2)'sinde mevcuttu ve erkeklere göre bu oran 2.5 kat daha fazla idi ($p < 0.05$). Kadınlarda yaşla histolojik tip değişmezken, 45 yaşın altındaki erkeklerde küçük hücreli akciğer kanseri daha sıkı ($\text{yaş} \leq 45$ ise %44.7 iken, > 45 ise %29.1; $p < 0.05$). Bu veriler, bölgemizdeki sigara ile ilişkili akciğer kanseri salgınının halen erken epidemik dönemde olduğunu destekleyebilir. Bölgemizdeki akciğer kanseri trendlerinin izlenmesi, sigara üretim teknolojilerindeki değişiklikler, sigara içme davranışları ve coğrafi etkilerin değerlendirilmesi için yararlı olabilecektir.

Anahtar Kelimeler: Akciğer kanseri, histopatolojik tip, Trakya bölgesi, coğrafi dağılım.

SUMMARY

Lung cancer histopathology in the Thrace region of Turkey and comparison with national data

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Following the trends in lung cancer (LC) morbidity and mortality rates can show past trends of cigarette smoking and can give clues on some geographical factors. The demographics of LC patients and the histopathologic distribution of their disease in the Thrace region of Turkey have yet to be defined. A retrospective chart review of primary LC patients admitted to the pulmonology department of Trakya University Hospital between 1992 and 2001 was performed. Charts were available for review in 521 of 567 patients. The mean age was 61 ± 10 years (30-86 years) and 497 (95.4%) patients were ma-

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le (male/female ratio= 20.7). When compared with national and international data, male/female ratio for the LC patients from Thrace region was higher than the ratio found from Turkey in general and also from other countries. Adenocarcinoma (ADC) was present in seven of the 24 (29.2%) of the females and prevalence of ADC was more than 2.5 times in females than males ($p < 0.05$). Squamous cell types were more common in males. Histopathological type did not vary with age in females, but small cell carcinoma was more prevalent in males under the age of 45 (44.7% if ≤ 45 years old vs. 29.1% if > 45 years old, $p < 0.05$). These data may support that the LC associated with smoking is in the earlier phase of the epidemic in Thrace region. Monitoring the LC trend in our region can give clues on evolving cigarette design and smoking attitudes and geographic factors.

Key Words: Lung cancer, histopathologic type, Thrace region, geographical distribution.

Despite anti-tobacco campaigns, new diagnostic and therapeutic modalities, lung cancer (LC) causes one million deaths per year worldwide (1). Reliable epidemiologic data about the prevalence, characteristics, and natural history of disease is the foundation for primary and secondary disease prevention. Following the trends in LC incidence and mortality rates can readily show past trends of cigarette smoking. And following the patterns of LC histologic types can give additional information on evolving cigarette design and the effects of geographical factors (2,3). The true incidence of LC in Turkey is unknown. An official nationwide “passive cancer registry” has been in place since 1983, but up to 75% of patients are not documented in this sys-

tem (4). Studies from reference centers give relatively suitable data on the histologic types of LC in a region.

This study was designed to evaluate the clinical files retrospectively and to compare the data with others from Turkey. This tertiary care unit in the university hospital serves a population of about 1.000.000 in the Thrace region of Turkey except west part of Istanbul city and Gallipoli part of Canakkale city (Figure 1). Thrace region has three city named Edirne, Kırklareli and Tekirdag. Thrace region and the city Edirne is the gateway of Turkey to Greece and Bulgaria and so to the Europe.



Figure 1. The Thrace region of Turkey with its three largest cities: Edirne, Tekirdag, and Kırklareli.

MATERIALS and METHODS

Medical records of all patients hospitalized in the department of pulmonology of university hospital between 1992 and 2001 were reviewed: manually for the period of 1992-1995, and through a computer database which contain names and diagnosis of the patients, for the period of 1995-2001. Of the total of 3471 patients, 567 patients had positive pathology reports for cancer. Data was collected on these patients from X-ray reports, pathology reports and discharge summaries. Minitab (S0064 Minitab Release 13, License: WCP 1331.00197) was used for statistical analysis. Descriptive statistics, t-test for age, and chi-squared testing was used for the nominal data.

RESULTS

Of the 567 consecutive patients with LC, 521 (92%) had complete medical records available for analyses. Most of the patients were male (92%), and the mean age was 61 ± 10 years (30-86). All patients' demographics data are

shown in Table 1. Of these 69.4% and 29.8% were histologically classified as non-small and small cell cancer. Among the non-small cell cancer patients, there were squamous cell carcinoma (SCC) in 49.5%, adenocarcinoma (ADC) in 12.3%, undifferentiated carcinoma in 7.7% and large cell carcinoma (LCC) in 0.4% (Table 2). ADC was more prevalent in females ($p=0.04$) that 29.2% of LC in females was ADC while 11.5% in males. In other words, proportion of ADC in all LC for females was more than 2.5 times for males (Figure 2).

It was determined that 9.2% of cases were in early age (≤ 45 years) and 90.2% of them were in older age (age > 45). When the early and older age cases has been investigated for histological distribution related with gender, there was no statistically significant effect in females, but small cell carcinoma was seen 44.7% in younger males and 29.1% in older males (Table 3).

It was determined that 19.8% of cases were in early stages (Stage I-IIIa) and 80.2% of cases

Table 1. Demographic data of the lung cancer cases.

	Age on admission, years		Total	Statistic
	≤ 45	> 45		
n	48 (9.2%)	473 (90.8%)	521 (100%)	
Mean age (year)	40.5 ± 3.5	62.8 ± 8.1	60.8 ± 10.1 (30-86)	0.000
Sex				
Male	47 (97.9%)	450 (95.1%)	497 (95.4%)	NS
Female	1 (2.1%)	23 (4.9%)	24 (4.6%)	NS
M/F ratio	47	19.6	20.7	NS
Total	48 (100%)	473 (100%)	521 (100%)	

NS: Not significant.

Table 2. Histological distribution according to sex.

	ADC*		SCC		LCC		NSCLC, Undif.		SCLC		LC, Undif.		Total	
	n	%	n	%	n	%	n	%	n	%	n	%	n	%
Gender														
F	7	29.2	10	41.7			4	16.7	3	12.5			24	100
M	57	11.5	248	49.9	2	0.4	36	7.2	152	30.6	2	0.4	497	100
Total	64	12.3	258	49.5	2	0.4	40	7.7	155	29.8	2	0.4	521	100

ADC: Adenocarcinoma, SCC: Squamous cell carcinoma, LCC: Large cell carcinoma, NSCLC: Non-small cell lung cancer, SCLC: Small cell lung cancer, LC: Lung cancer.

* Adenocarcinoma is more frequent among women: Pearson chi-squared test= 11.51, $p=0.04$.

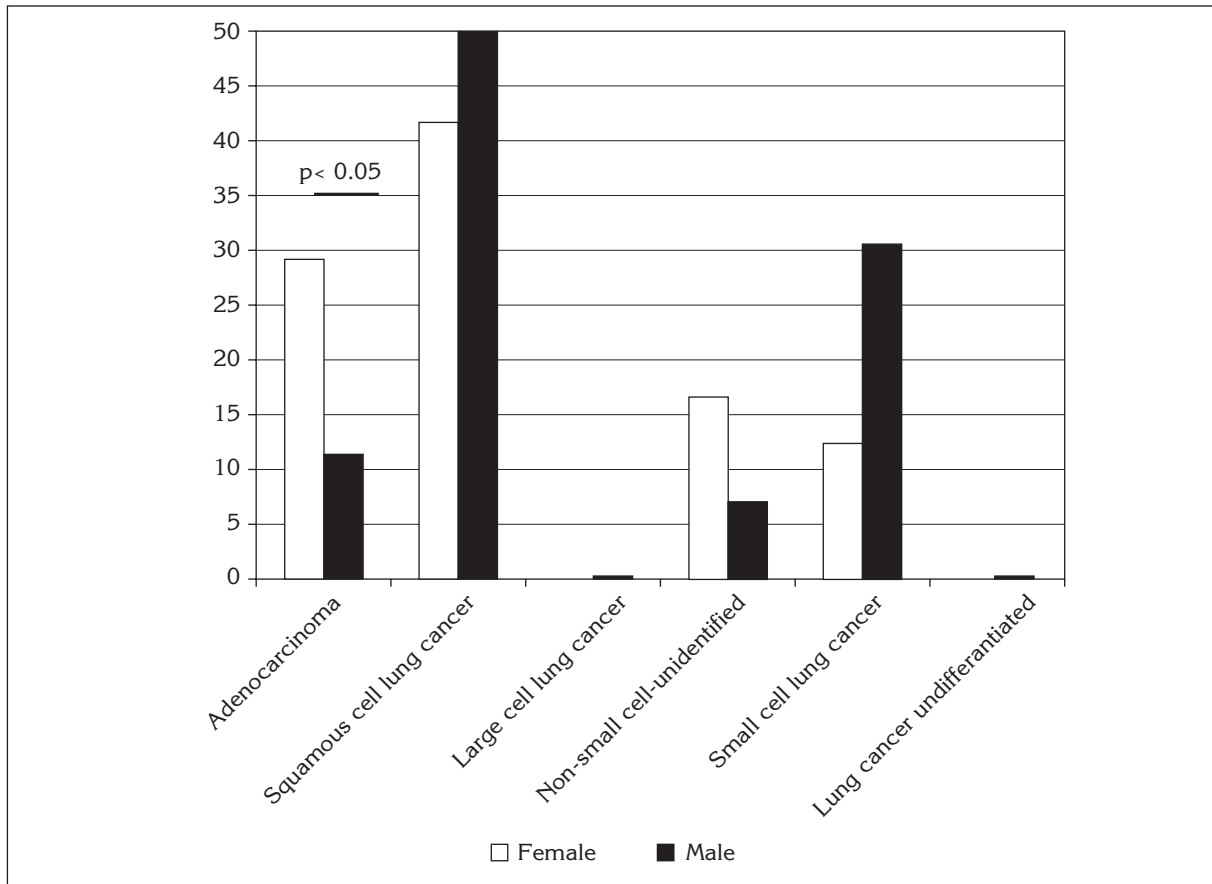


Figure 2. Distribution of cancer types by histologic pattern and gender.

Table 3. Histologic distribution of lung cancers according to gender and age.

Gender	Age				Total		p
	≤ 45		> 45		n	%	
Male							
Histologic category							
ADC	5	10.6	52	11.6	57	11.5	NS
SCC	18	38.3	230	51.1	248	49.9	NS
LCC	1	2.1	1	0.2	2	0.4	NS
NSCLC, undif.	1	2.1	35	7.8	36	7.2	0.022
SCLC	21	44.7	131	29.1	152	30.6	0.013
LC, undif.	1	2.1	1	0.2	2	0.4	NS
Total	47	100	450	100	497	100	
Female							
Histologic category							
ADC			7	30.4	7	29.2	NS
SCC	1	100	9	39.1	10	41.7	NS
NSCLC, undif.			4	17.4	4	16.7	NS
SCLC			3	13	3	12.5	NS
Total	1	100	23	100	24	100	

ADC: Adenocarcinoma, SCC: Squamous cell carcinoma, LCC: Large cell carcinoma, NSCLC: Non-small cell lung cancer, SCLC: Small cell lung cancer, LC: Lung cancer, NS: Not significant.

were in late stages (IIIB-IV). Early stages were more frequently presented in older patients (20.3%) when comparing to younger ones (14.6%) ($p= 0.033$). A statistically significant relationship between histological type and stage of tumor was not found (Table 4).

DISCUSSION

In Turkey, LC with 17.6% ratio is the number one killer among all cancer types. In males, it is the number one among all cancer types with 26.3% and it is the fourth one with 4.5% in females (5).

Peak incidence of LC is between 60-69 years although tendency toward occurrence at younger ages has been observed (6). Evaluations of LC ca-

ses at 16 centers in Turkey, in 1985-1990, showed that mean age was over 65 years in males and between 50-70 years in females (Table 5). Yurdakul et al studied 2216 patients with LC between January 1997 and December 2000 and found that mean age was 57.3 years (56.8 in females and 57.3 in males) (7). In Turkey, in 8533 cases studied by different investigators including our cases, mean age differed between 56.2 to 60.9 years and average of the total was 59.3 years. In this study, mean age was 61 years. When ≤ 45 years was taken as criterion, 9.2% of cases were in younger age which was compatible with literature (8).

In Turkey, male to female ratio was 10/1 in 1985-1990 and this ratio was same in 1998 (7,9). Ac-

Table 4. Stage of disease upon presentation according to age.

Stage of disease	Age (years)				Total		p
	≤ 45		> 45		n	%	
	n	%	n	%			
Early stages (I-III A)	7	14.6	96	20.3	103	19.8	0.033
Later stages (IIIB-IV)	41	85.4	377	79.7	418	80.2	NS
Total	48	100	473	100	521	100	NS

NS: Not significant.

Table 5. Mean patient age and lung cancer histologic type in past surveys in Turkey.*

Author (s)	Year	Number (n)	Mean age (years)	SCC (%)	SCLC (%)	ADC (%)	LCC (%)
Özdemir N, et al. (21)	1991	50	59.6	48.0	22.0	16.0	4.0
Kayık A, et al. (22)	1991	350	-	64.2	22.9	10.5	1.7
Erkan L, et al. (23)	1991	72	60.9	63.8	27.7	1.3	2.7
Çıkrıkçıoğlu S, et al. (24)	1992	650	58.0	52.8	18.0	23.5	2.0
Sözer K, et al. (25)	1992	202	-	59.4	16.5	17.6	2.9
Yaman M, et al. (26)	1993	1316	-	57.8	22.9	15.7	2.6
Özbek Ü, et al. (27)	1994	116	59.5	48.0	20.0	16.0	9.0
Erginel S, et al. (28)	1994	131	60.7	38.9	20.6	7.6	3.8
Hazar A, et al. (29)	1994	391	-	62.1	15.6	17.3	2.3
Kıyan E, et al. (30)	1995	209	59.3	41.0	18.0	33.0	1.9
İlgazlı A, et al. (31)	1995	96	-	54.0	15.0	11.0	3.0
Tanlak MG (32)	1995	1017	57.4	56.8	13.0	10.7	2.3
Muz MH, et al. (33)	1995	49	59.3	40.8	10.2	8.2	4.1
Dikmen E, et al. (34)	1995	627	56.2	68.7	13.3	11.4	2.5
Yorgancıoğlu A (35)	1995	1962	60.1	68.3	17.6	8.2	4.9
Sevinç C, et al. (36)	1998	774	59.3	43.7	18.7	17.8	1.8
This study	2003	521	60.8	49.5	29.8	12.3	0.4
Total		8533	59.3	54.0	18.9	14	3.1

* The Table except the last two lines is from C. Sevinç (36) and we thank him for kindly permission.

ording to the largest series in Turkey, Goksel et al found as 90.4% of cases were male and 9.6% female and 79.5% of cases non-small cell lung carcinoma (NSCLC) and 20.5% small cell lung carcinoma (SCLC) (10). In this study, male to female ratio was found as 20.7 and this was higher than the Turkey's average and other countries' ratios (6,11). It might be explained that increase in frequency of smoking in woman has not been seen as LC in Thrace region, yet. It is known that male to female ratio has decreased in time especially in North American countries. In North American countries, the ratio was 5 in 1950, but decreased to 2.6 in 1980s (12). However in European countries this ratio is higher up to 12/1, except United Kingdom and Denmark (13). This study showed the highest male to female ratio of Turkey and many other countries.

There are four main histologic types making up 90-95% of all LC cases: SCC, ADC, LCC and small cell carcinoma (2). Squamous cell type of NSCLC has the highest incidence with 35-71%. Mc Duffie et al reported 49% of 1939 patients were squamous cell type consistent with our result 49.5% (14). An increase in ADC incidence and a decrease in SCC over time since 1970's has been noted and mostly attributed to changes in the characteristics of cigarettes and the consequent changes in the doses of carcinogens inhaled (2). ADC is more common than SCC in USA and Japan, but as this study SCC is still high in Europe (15,16). When the results of all other studies performed in Turkey were evaluated, it was observed that ADC was seen as 14% (Table 5). This ratio can be the mean of the country for Turkey till 2000 and this was European mean between 1970-1980 (13). The reason of low ADC incidence in Turkey might be the low number of female patients with LC which is similar to France. ADC rate in France is 4.65/100.000 and 27/100.000 in USA (13). ADC is seen more frequently in females; in this study the ratio of ADC is 2.5 times higher in females compared to males and it is compatible with the literature (6,17).

In a study reported from Poland, when the age of 50 was taken as limit, small cell and ADC were more prevalent in early ages in both male and female genders and it was reported that LC occur-

red in younger ages in females (6). Cornere et al reported that young LC patients were predominantly female and ADC accounted for a disproportionate number of the histological types (18).

Patients with LC usually present in inoperable stage. Only 15-25% of cases at presentation are in operable stage (19). The result of this study is compatible with this finding and only 19.8% of our cases were in early stages. Early stages of tumor were less frequent in younger cases. This is compatible with the cases of Gadgeel et al; the rate of stage I or stage II diseases in young patient (< 50) are only 4.8% while in older ones are 19.7% (8). It has been tried to explain that suspicion of LC in young patients may be made at later phase or progression of disease may be faster (8,20). It is not easy to compare young cases in literature because lower age limit differs between ages of 45 to 50 years. In this study, the age limit was selected as 45 because it gives more statistically significant results. In addition, because expected life period in Turkey is less than developed countries, the limit of age 45 is thought as appropriate for our country.

In conclusion, important epidemiologic features in the clinical LC data for 1992 to 2001 were observed. Male and female ratio is prominently higher than reported ones in Turkey. ADC is more prevalent in females and small cell carcinoma in young males. In Turkey, SCC has high incidence and incidence of ADC is low unlike developed countries. Diagnosis in early stages was low in younger cases.

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