Smoking Habits in Lung Cancer Patients: A Hospital Based Case-Control Study in İzmir, Turkey

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Abstract

This retrospective, hospital based case-control study was designed to investigate the cigarette smoking history, the relationship between cigarette smoking and the risk of lung cancer in Izmir, Turkey. Six hundred cases with lung cancer (576 males, 24 females) and 600 controls were included in the study. The majority of lung cancer patients (71%) were between 50-69 years old. Seventy three percent of the patients were current smokers, 23% were ex-smokers and 4% were non-smokers. Among the male patients, NSCLC was the most commonly diagnosed tumor type. The crude odds ratio (cOR) was 15.7 for current smokers, 7.4 for ex-smokers. The risk decreased with increase in number of years since quitting and a higher age of starting to smoke. The cOR for current smokers was 21.0 in squamous cell carcinoma, 3.7 in adenocarcinoma, 37.5 in SCLC. Adenocarcinoma was the least related histological type to cigarette smoking. The number of cigarettes smoked per day, duration of smoking and the number of pack-years were found to be important risk factors for lung cancer.

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Introduction

Lung cancer is one of the major causes of cancer deaths in both sexes. It constitutes 12.8% of cancer cases and is responsible for 17.8% of cancer deaths worldwide (1). Cigarette smoking is the predominant cause of lung cancer in both men and women (2). Cigarette smoking in Turkey increased by 10% from 1970 to 1985 and its prevalence went up to 44% in 1988 with a 63% male smoking population and a 24% female smoking population (3).

In a national retrospective hospital based study to determine the pattern of lung cancer in Turkey, conducted by the Lung and Pleural Malignancies Study Group (TTS, LPMSG) of the Turkish Thoracic Society, it was found that the majority of lung cancer patients were current smokers (77.5%) or ex-smokers (10.8%) (4). Moreover, lung cancer is the most common cancer (42.3% of all cancers) in males according to the data of Izmir Cancer Registry. The annual age standardized incidence rate was reported as 61.6 per 100 000 in males and 5.1 per 100 000 in females in 1993-94 (5).

This present study was undertaken to evaluate the risk of lung cancer with the smoking history of the patients and with type of cigarette use.

Table 1. Distribution of the lung cancer patients and control cases by sex, age, education, residence and smoking status				
	Patients		Controls	
	No	%	No	%
Total	600	100	600	100
Sex				
Male	576	96	567	95
Female	24	4	33	5
Age (years)				
30-39	6	1	1	0.0
40-49	89	15	177	30
50-59	186	31	157	26
60-69	239	40	153	26
70-79	76	13	104	17
≥80	4	0.0	8	1
Education (years)				
None	178	30	166	28
1-5	363	61	327	55
6-8	3	5	48	7
9-12	18	3	45	8
≥13	8	1	14	2
Residence				
Urban (> 10.000)	391	65	438	73
Rural (£ 10.000)	209	35	162	27
Smoking status				
Current smoker	437	73	263	44
Ex-smoker	140	24	144	24
Non-smoker	23	3	193	32
Type of cigarette				
Filtered only	164	29	189	46
Nonfiltered only	42	7	72	18
Manufactured	281	49	123	30
Hand-rolled only	13	2	6	1
Hand-rolled and manufactured	77	13	17	5
Urban: Defined as towns with >10 000 inhabitants, Rural: ≤10 000 inhabitants, † P>0.05, * P<0.001.				

Study design

A hospital-based case-control study of patients with lung cancer was conducted in the Izmir Chest Disease and Surgery Training Hospital. The controls were recruited from among the patients of two general training hospitals in the city of Izmir. The lung cancer patients were histologically or cytologically proven lung cancer inpatients. Histological types were classified according to the World Health Organization histological classification (6). Control subjects were inpatients or outpatients with conditions not related with tobacco smoking. This study was conducted between 1999 and 2001. Of the 615 eligible cases, 600 cases (97%) completed the interview. The main reason for non-participation was the pati-

ent's inability to cooperate during the interview as a result of severe physical or mental disability. We did not conduct proxy interviews. Six hundred control subjects were recruited to participate in the study and interviews were completed in all 600. Among the controls, there were 155 (26%) patients with musculoskeletal system disorders (bone fractures and dislocations, injury), 45 (7.5%) patients with ear disease, 72 (%12) patients with eye disease, 60 (10%) patients with parasitic infections, 113 (19%) patients with skin disease, 67(11%) patients with infections in sites other than the respiratory tract, and 88 (14.5%) patients with urinary system disease. The study protocol was reviewed and approved by the institutional review board.

Materials and Methods

Personal interviews were done with all study and control patients using a structured standard questionnaire. The two interviewers were trained extensively to standardize the data collection and coding techniques and to minimize inter-interviewer variation. The smoking history was obtained prospectively.

The questionnaire included questions on:
1) Demographic characteristics (age, gender, education status, place of residence)
2) The smoking status including age of onset of smoking, age of cessation of smoking (for ex-smokers), number of cigarettes smoked per day, and type of cigarettes used.
The duration of cigarette smoking was defined as the period of time between the year of onset and the date of the interview for current smokers, and as the period of time between year of onset and date of quitting smoking for ex-smokers. The number of cigarettes smoked per day was calculated as the mean daily intake of cigarettes over the total number of years. The types of cigarettes smoked were classified as filtered, non-filtered, hand rolled and mixed filtered and nonfiltered cigarettes. Information about depth of inhalation of tobacco smoke was not obtained.
Patients and controls were classified as current smokers, ex-smokers, or non-smokers (13).
1) A current smokers was defined as someone who, at the time of the survey, smokes at least one cigarette daily or an equivalent amount of tobacco per day for at least 12 months.
2) An ex-smoker is someone who was formerly a smoker but who has not smoked for at least 12 months.
3) A non-smoker is someone who has either never smoked or who has smoked less than 100 cigarettes in his lifetime.
Pack-years (PY) of cigarette smoking was calculated as the product of the duration of smoking (in years) and the average number of cigarettes smoked per day, which was divided by 20 to convert to PY.

Statistical analysis

The following variables were calculated for data analysis; the duration of cigarette smoking, the number of cigarette smoking per day, age at start, years since quitting smoking. Chi-

Table 2. Distribution of male cases by cell types/subtypes and smoking status

Cell type	CS (%)	ES (%)	NS (%)	Total (%)
NSCLC	338 (78)	122 (89)	8 (88)	468 (82)
SCLC	92 (22)	15 (11)	1 (11)	108 (18)
Total	430 (74)	137 (24)	9 (2)	576 (100)
Cell subtype				
Squamous Cell	120 (44)	39 (55)	3 (50)	162 (46)
Adenocarsinoma	50 (18)	14 (20)	2 (33)	66 (19)
Large cell	4 (1.5)	- (0)	- (0)	4 (1)
Adenosquamous	1 (0.4)	- (0)	- (0)	1 (0)
Undifferantiated	8 (3)	3 (4)	- (0)	11 (3)
SCLC	92 (34)	15 (21)	1 (17)	108 (31)
Total	275 (78)	71 (20)	6 (2)	352 (100)

CS: Current smoker, ES: Ex-smoker, NS: Non-smoker,
NSCLC: Non-small-cell lung cancer, SCLC: Small-cell lung cancer.

squared test was used to compare the distribution of sex, age, education status, residence, smoking status between the study and control patients. The data were not analyzed separately for male and female subjects because of the small sample size of the female subjects. The crude odds ratio (cOR) and 95% confidence interval (95% CI) were calculated with adjustment made for demographic confounders. As the controls were not matched to the study patients, adjustment was done for age, education and residence. Unconditional logistic regression test was used for data analysis. The value was considered significant at p<0.05.

All statistical calculations were performed using the SPSS 10.0 software.

Results

Six hundred lung cancer patients and an equal number of controls were retrospectively evaluated. Table 1 shows the characteristics of the study subjects.

Table 2 shows the distribution of male cases by cell types and smoking status. In female patients, NSCLC was diagnosed in 57% (4/7) of current smokers, in 66% (2/3) of ex-smokers, and in 93% (13/14) of non-smokers and. SCLC was diagnosed in 43% (3/7) of current smokers, in 34% (1/3) of ex-smokers, and in 7% (1/14) of non-smokers. Also in females, adenocarcinoma was diagnosed in 3 of current or ex-smoker patients, in 8 of non-smoker. SCLC constituted the most common (61%) histological subtype. SCLC was diagnosed in only 2 of non-smoker patients.

Smoking habits and risk of lung cancer are shown with cORs in Table 3. The daily number of cigarettes, duration of smoking, and pack years, were all significantly associated with lung cancer risk showing a dose-response relationship as demonstrated by tests for the trend of odds ratios.

Age of onset of smoking was associated with excess risk of lung cancer. The risk estimates among short-term ex-smokers (those who quit <12 years ago) were higher than that of

ex-smokers who stopped smoking 12 or more years ago (p<0.001) (Table 3). The age of starting smoking was usually higher in non-filtered smokers (over age 20 years) as compared to filtered smokers and mixed smokers (onset at ages younger than 20 years). The risk was lowest in cases who had started smoking at an age older than 20 years in all three types of smokers and the risk showed an increase as age onset got younger age (p<0.001). In ex-smokers, the risk decreased with the number of years since quitting smoking (P<0.001).

The relation between histological types and smoking habits was investigated in cases with lung cancer whose cell subtypes were determined. Table 4 shows that the risk of lung cancer increased with number of cigarettes smoked per day and years of duration of smoking in patients with squamous cell carcinoma (SCC), small cell lung carcinoma (SCLC) and adenocarcinoma . The risk was lowest in SCC and SCLC who had quitted smoking 12 or more years ago (Table 4).

Table 5 shows that the risk of lung cancer increased with an increase in daily number of cigarettes smoked and years of duration of smoking and pack-years.

Discussion

The present study showed that cigarette smoking is an important risk factor of lung cancer also in Turkey. This risk was higher in current smokers than ex-smokers. The risk of lung cancer showed an increase in a dose-dependent manner with the number of cigarettes smoked per day and with the duration of smoking. As the number of years since quitting and age of onset of smoking increased, the risk of lung cancer showed a decrease.

Fidaner et al. (6) found that lung cancer was the most common cancer type among male patients in a study carried out in İzmir in 1993-1994. Among females, frequency of lung cancer ranked as the 6th with 5.2%. In this present hospital-based case-control study, the great majority of cases and controls were males. Zang and et al reported in their hospital based case-control study that the relative risk estimates in females were higher than males for lung cancer associated with smoking (7). In our study, male-female differences may be potentially biased findings, since the number of female patients was low. Gender differences in susceptibility to tobacco carcinogens have not yet emerged in cohort and population based case-control studies (8-10). In this study, the distribution of smoking habits of the control group corresponded to that of the general population of Turkey with similar age and sex distribution (11). The majority of our lung cancer cases were between 50-70 years of age and, as also reported by others, the risk increased with age (12).

In our study, 72.8% of the cases were current smokerss, 23.3% were ex-smokers and only 3.9% were non-smokers. By comparison, only 43% of the controls were current smokers and 32.2% of these were non-smokers at the time of interview. These figures are somewhat similar to those reported in a retrospective study by Gürsel et al (13). However, we think

Table 3. Smoking habits and the risk of lung cancer

	Current Smoker			Ex-smoker			All smokers		
	Ca/Co[c]	cOR[a]	95% CI[d]	Ca/Co[c]	cOR[a]	95% CI[d]	Ca/Co[c]	cOR[a]	95% CI[d]
Non-smoker (Reference)	23/193	1.0	-	23/193	1.0	-	23/193	1.0	-
Current smoker[a]	437/ 263	15.7	9.7-25.4	140/144	7.43	4.4-12.2	577/407	12.0	7.5-19.0
Number of cigarettes/day*									
1-9	8/13	8.5	3.0-24.0	5/6	7.5	1.9-28.4	13/19	7.1	3.0-16.9
10-19	3/44	2.8	1.2-6.0	8/19	3.2	1.2-8.3	21/63	2.8	1.4-5.5
20	228/151	14.8	8.9-24.5	59/77	5.5	3.3- 9.7	87/228	10.8	6.7-17.3
21-39	117/51	19.5	11.1-34.5	36/30	8.3	4.2-16.3	153/81	14.5	8.6-24.3
≥40	71/4	173.3	56.6-530	32/12	25.3	11-58.1	103/16	58.0	28.8-116
Trend[b]	p<0.001			p<0.001			p<0.001		
Duration of smoking (years)[a]									
1-20	10/24	3.4	1.4-8.5	6/37	1.2	0.47-3.3	16/61	2.1	1.0-4.3
21-30	54/84	5.0	2.7-9.3	37/33	9.6	5.0-18.4	91/117	6.7	3.9-11.3
31-39	148/79	14.2	8.2-24.6	44/34	10.0	5.2- 19.0	192/113	13.0	7.8-21.5
≥40	225/76	28.6	16-49.9	53/40	10.8	5.6-20.4	278/116	20.9	12.5-34.7
Trend[b]	p<0.001			p<0.001			p<0.001		
Pack-years[a]									
1-10	5/18	3.4	0.8-7.7	6/19	2.5	0.9-7.1	11/37	2.5	1.1-5.5
11-20	12/39	3.1	1.3-7.0	6/23	2.0	0.7-5.4	20/62	2.6	1.2-5.1
21-30	54/77	6.2	3.4-11.2	23/32	5.7	2.8-11.6	77/109	6.0	3.4-10.2
≥31	366/129	24.0	14.6-39.2	105/70	12.1	6.9-21.1	471/199	19.3	12.0-31.0
Trend[b]	p<0.001			p<0.001			p<0.001		
Age at start[a]									
1-10	72/22	27.6	14.1-53.9	13/12	8.4	3.3-20.8	85/34	20.0	10.9-30.4
11-15	157/77	19.7	11.5-33.7	52/45	8.8	4.7-16.0	209/122	14.7	8.9-24.1
16-19	86/56	16.0	8.9-28.7	7/22	6.4	2.9-14.2	103/78	12.3	7.1-21.0
≥20	122/108	10.0	5.9/17.0	58/65	6.0	3.7-11.8	183/173	8.4	5.1-13.7
Trend[b]	p<0.001			p<0.001			p<0.001		
Years since quitting (year)[a]									
1-5				74/51	12.0	6.7-21-4			
6-11				26/131	6.1	3.0-12.2			
≥ 12				40/62	4.4	2.3-8.0			
Trend[b]				p<0.001					

[a]cOR (crude odds ratio)	: Results are adjusted by age, education and residence.
[b]Trend	: Only calculated for smokers.
[c]Ca/Co	: Cancer/Control.
[d]95% CI	: 95% Confidence interval.

that retrospectively collected data tend to underestimate the strength of the relationship between smoking and lung cancer, since smoking histories available for analysis often fail to distinguish between ex-smokers and non-smokers, leading to misclassification.

In studies performed after 1990 in developed countries, the number of ex-smoker cases was higher when compared to our results. In a study by Roland et al, 56% of their cases with lung cancer were ex-smokers (14). In a large study performed in Western Europe, Lubin and Blot noted that 30% of 6920 male patients and 21% of 884 female patients were ex-smokers (15). In USA, the ex-smoker group has constituted a large and increasing percentage of the population for the last 10-15 years. These findings are due to the success of the anti-smoking campaigns (16).

In Turkey, cigarette smoking increased significantly between

Table 4. Histological types of lung cancer and smoking habits								
	Squamous Cell			Adenocarcinoma			SCLC		
	Ca/Co[c]	cOR[a]	95% CI[d]	Ca/Co[c]	cOR[a]	95% CI[d]	Ca/Co[c]	cOR[a]	95% CI[d]
Non-smoker (Reference)	5/193	1.0	-	10/193	1.0	-	2/193	1.0	-
Smoking status									
Current smoker	120/ 263	21	8.3-53.3	51/263	3.7	1.9-7.8	95/263	37.5	9.0-155
Ex-smoker	39/144	9.2	3.5-24.2	16/144	2.1	0.9-4.8	16/144	9.4	2.1-4.1
Number of cigarettes/day*									
1-9	5/19	12.6	3.2-49	7/19	8.6	2.8-26	0/9	-	-
10-19	3/63	1.9	0.4-8.1	5/63	1.6	0.5-5	2/63	3	0.4-22.1
20	75/228	13.4	5.2-34	28/228	2.3	1.1-5	62/228	25.9	6.2-108
21-39	42/81	19.3	7.3-51	13/81	2.9	1.1-6.9	32/81	35.3	8.2-151
≥40	34/16	99.8	33-229	14/16	17.9	6.5-49	15/16	99.9	20-485
Trend[b]	p<0.001			p<0.001			p<0.001		
Duration of smoking (years)[a]									
1-20	1/61	0.6	0.1-0.2	5/61	1.4	0.4-4.2	2/62	2.9	10.4-20
21-30	29/117	9.3	3.4-25	12/117	1.8	0.7-4.3	21/117	15.2	3.4-67
31-39	45/113	14.2	5.4-37	24/113	3.2	1.4-1.1	35/113	25.8	6.0-110
≥40	84/116	31.3	8.6-12	26/116	6.5	2.7-15.1	53/116	50.8	11.2-219
Trend[b]	p<0.001			p<0.001			p<0.001		
Age at start[a]									
1-10	33/34	37.6	13.4-104	9/34	5.2	1.9-14.2	13/34	36.7	7.8-172
11-15	52/122	17.8	6.9-46.2	32/122	5.3	2.5-11.4	37/122	30.4	7.1-128
16-19	26/78	15.2	5.6-41.7	11/78	2.7	1.6-6.7	25/78	32.5	7.4-142
≥20	48/173	10.3	4.0-26.9	15/173	1.6	6.7-3.7	36/173	18.3	4.3-77.6
Trend[b]	p< 0.001			p< 0.001			p< 0.001		
Years since quitting[a]									
Current smoker	120/263	21.2	8.4-53.9	51/263	3.8	1.8-78	95/263	37.7	9.1-156
1-5	23/51	16.4	5.9-46.1	9/51	3.6	1.3-9.5	8/51	14.5	2.3-71.3
6-11	5/31	5.9	1.6-21.8	2/31	1.2	0.2-5.8	2/31	6.1	0.8-45.4
≥12	11/62	5.5	1.8-16.6	5/62	1.2	0.4-4.4	2/62	7.3	1.4-37.5
Non-smoker	5/193	1	-	10/193	1	-	2/193	1	-
Trend[b]	p<0.001			p<0.001			p<0.001		

[a]cOR (crude odds ratio) : Results are adjusted by smoking variables, age, education and residence.
[b]Trend : Only calculated for smokers.
[c]Ca/Co : Cancer/Control.
[d]95% CI : 95% Confidence interval.

1970 to 1985 and the frequency of smokers is high when compared with European countries (3). A survey performed on university students aged between 20 and 24 revealed that 47% of the females and 31% of the males were current smokers (17,18). One of the striking findings in our study is the low rate (4%). of females among lung cancer cases The rate among female patients was reported as 5.2% and 8% in other Turkish studies (5,13). These findings show that the number of male smokers are significantly higher than the number of female smokers. With the increase of the number of young female smokers, it is expected that cases with lung cancer among females will increase in coming years.

The risk of lung cancer for current smokers is higher than for ex-smokers. As the number of cigarettes smoked per day, duration of cigarette smoking and number of pack-years smoked increase, the risk of lung cancer also increases at the same rate for current smokers and ex-smokers. Our data show that the risk of lung cancer was highest when the number of cigarettes smoked per day was 40 or more, duration of cigarette use was 40 or more years and number of pack-years was 31 or more. The group who smoked 1.9 cigarettes per day showed a high risk, but this finding may be related to the low

Table 5. Cigarette types and the risk of lung cancer

	Filtered only			Non-filtered only			Mixed		
	Ca/Co[c]	cOR[a]	95% CI[d]	Ca/Co[c]	cOR[a]	95% CI[d]	Ca/Co[c]	cOR[a]	95%CI[d]
Non-smoker (Reference)	23/193	1.0	-	23/193	1.0	-	23/193	1.0	-
Smoking status[a]									
Current smoker	127/137	12	6.7-21.8	25/25	7.4	3.4-15.7	227/87	22.8	13-38.9
Ex-smoker	37/52	7.5	3.9-14.3	17/47	2.7	1.2-5.8	61/36	15.8	8.3-29.9
Number of cigarettes/day*									
1-9	10/16	8.5	3.2-22.8	1/0	-	-	2/2	10.6	1.2-90.4
10-19	5/40	1.3	0.4-3.8	1/7	0.1	0.1-8.6	7/11	6.8	2.3-20.4
20	81/100	10.6	5.7-19.7	19/48	3.0	1.4-6.4	141/70	18.1	10.4-31.7
21-39	35/26	10.7	7.8-35.7	12/13	6.8	2.6-18	78/35	18.8	10-35.2
≥40	33/7	55.2	20-178	9/4	20.5	5.3-78	53/5	128	42-391
Trend[b]		p<0.001			p<0.001			p<0.001	
Duration of smoking (years)[a]									
1-20	13/48	2.8	1.2-6.3	8/1	0.5	0.06-4.2	0/1	-	-
21-30	49/97	5.3	2.8-10	11/6	4.5	1.4-13.9	9/27	29.1	11.6-72
31-39	79/35	23.4	12.6-45.7	14/13	7.2	2.8-15.2	57/89	12.2	6.8-22
≥40	23/9	23.8	9.4-60.2	35/22	5.4	2.5-11.9	57/168	29.7	16.3-54
Trend[b]		p<0.001			p<0.001			p<0.001	
Pack-years[a]									
1-10	10/31	3.5	1.4-8.6	0/8	-	-	1/1	6.1	0.3-108
11-20	10/46	2.3	0.98-5.5	2/7	1.8	0.33-9.6	5/5	12.8	3.2-51.6
21-30	38/81	5	2.9-9.8	5/13	2.9	0.9-2.7	20/12	13.7	5.7-32.8
≥31	106/31	37.1	19-72	35/47	6.3	3.1-12.8	259/105	22.9	13.4-39
Trend[b]		p< 0.001			p< 0.001			p< 0.001	
Age at start[a]									
1-10	13/5	35.6	10.6-119	9/8	8.6	2.8-26.2	41/12	29	13-66.0
11-15	47/47	14.5	7.0-27.9	11/19	4.8	2.8-12.3	110/52	19.3	10.8-34
16-19	29/44	9.6	4.6-20.0	5/7	4.1	1.1-14.7	60/24	22.9	12.6-45
≥20	75/93	8.2	4.5-14.0	17/38	3.4	1.5-7.5	70/35	18.2	9.6-34.5
Trend[b]		p<0.001			p<0.001			p<0.001	
Years since quitting[a]									
Current smoker	127/137	12.7	6.9-12.4	25/25	7.4	3.4-15.9	220/87	22.9	13.4-39.1
1-5	22/23	12.4	5.5-27.7	6/11	4	1.2-10.9	35/15	21.2	9.7-46.6
6-11	9/9	8.7	3-25.5	2/12	1	0.2-5.2	10/7	13.4	4.3-41.3
≥12	6/20	2.6	0.9-7.6	9/24	3.1	1.2-8.1	16/14	10.6	4.3-26.2
Non-smoker	23/193	1	-	23/193	1	-	16/14	1.0	-
Trend[b]		p<0.001			p<0.001			p<0.001	

[a] cOR (crude odds ratio) : Results are adjusted by age, education and residence.
[b] Trend : Only calculated for smokers.
[c] Ca/Co : Cancer/Control.
[d] 95% CI : 95% Confidence interval.

number of cases in this group.
In a case-control study performed by Matos et al., number of cigarettes smoked per day, duration of cigarette smoking and pack-year were similarly reported as important risk factors for lung cancer (19). Peto et al. compared the number of cigarettes smoked per day and duration of cigarette smoking and reported that the duration of cigarette smoking is a more important risk factor than the number of cigarettes smoked per

day (20). The study performed by Flanders et al. confirmed that duration of cigarette smoking is far more important than the number of cigarettes smoked per day in predicting lung cancer risk in American males regardless of age. This study also provides new evidence that a qualitatively similar pattern holds for women (21).

Those who start smoking earlier in life are most likely to develop lung cancer (22,23). In this study, most of the cases diagnosed as lung cancer had started to smoke between 11 and 15 years of age. We found that the patients who had started smoking at ages younger than 11 years have a higher risk than cases who were 20 years or older at start. The risk of lung cancer decreases among those who quit smoking (24). The risk of lung cancer is highest in the first years after quitting smoking due to "sick quitter effect" (25). The cOR was 12 (95% CI, 6.7-21) for a period of abstinence of 1-5 years. However, our study showed that even for periods of abstinence of 12 years or longer, the risk of lung cancer among ex-smokers remains elevated compared to non-smokers. These findings show that anti-cigarette campaigns must be directed towards young population in Turkey.

Forty-nine percent of cases diagnosed as lung cancer smoked mixed (both filtered and nonfiltered) cigarettes. There are several reasons for this. Firstly, the cigarettes first produced in Turkey were non-filtered. Secondly, filtered cigarettes were not available in rural areas until recent years. Also, filtered cigarettes are more expensive. Another finding in this study was that only non-filtered cigarette smokers have a lower risk than only filtered cigarette smokers. However, most of the only non-filtered smokers had started smoking at age 20 years or at older ages, most of them had quit smoking and time of duration after quitting was 12 years or more, while most smokers of mixed cigarettes had started smoking at younger ages, duration of smoking was longer in this group and most had quit smoking only recently, after appearance of disease symptoms. It was found that risks associated with number of cigarettes smoked per day, duration of smoking and pack-years were similar in filtered, non-filtered and mixed cigarette smokers.

Some epidemiologic data, coming primarily from case-control studies, suggest that filtered cigarettes slightly reduce the risk of lung cancer associated with cigarette smoking compared to non-filtered cigarettes (26-32). Similar findings were obtained in subsequent case-control studies that have contrasted the use of either filter cigarettes across the cumulative smoking history with non-filter cigarettes (32,33). Determination of the tar, nicotine, and carbon monoxide content in locally produced cigarettes in Turkey indicates that in most brands the tar and carbon monoxide content are higher than that in imported cigarettes. Thus, locally produced cigarettes smoked over many years could also be a contributory factor in the increased risk relative to filtered cigarettes (34). Although we did not evaluate inhalation parameters in our study, we can speculate that another cause of increased risk could be related to smoking patterns such as more frequent and deeper puffs. The finding of a higher risk in the mixed cigarettes group in this study probably results from the small sample size of the control subjects.

Epidemiological studies over the past several decades have shown that histological types of lung cancer vary in their respective etiologies. Adenocarcinoma is more common in females than males (35). In this study, among 430 male cases, NSCLC was detected in 78% of current smokers, in 89% of ex-smokers, in 88% of non-smokers. SCC was the most common histological subtype among the 352 male patients analyzed for subtypes. The proportion of adenocarcinoma in non-smokers (33%) was higher than adenocarcinoma in current smokers (18%) and ex-smoker (20%).

Gürsel et al (13) found that SCC was the most common cancer type (46%) among male current smokers with lung cancer. Our findings are very similar. However, Matos et al found that adenocarcinoma was the most common cancer type in male patients with lung cancer (19). Kreyberg et al estimated that the most common histological types related with smoking were SCC and SCLC and stated that smoking was a lower risk factor for adenocarcinoma (36). Brownson et al showed that smoking was the cause of most cases of adenocarcinoma (37). In our study, the histological types SCC, adenocarcinoma and SCLC were all found to be significantly associated with cigarette smoking. For current and ex-smokers, the pooled estimates for SCC or SCLC were higher than that for adenocarcinoma, indicating that adenocarcinoma had the lowest relation with cigarette smoking. On the other hand, recent studies indicate that cigarette smoking can be more strongly associated with death from lung adenocarcinoma than that reported in previous studies (38).

We believe that this present study offers some valuable data, since it was based on prospectively collected smoking histories. Also, the high response rate to the interviews and all patients being consecutive cases who have presented to the same hospital, thus eliminating selection bias, are points which we believe strengthen the validity of our findings. We should also list the limitations of the study, which were: 1) The number of female cancer cases is too small to allow for detailed separate analysis. 2) Some subgroups are too small and the sample size of cases and controls are open to bias. This resulted in the OR values with relatively wide confidence interval. 3) Inhalation patterns were not included in the questionnaire. 4) The ORs were not calculated with adjustment made for smoking variables.

In conclusion, as is true for other countries, smoking is an important risk factor of lung cancer in Turkey. The risk is higher in current smokers. The number of cigarettes smoked per day, duration of smoking, pack-years, age of starting and time lapse after quitting smoking stand out as important risk factors.

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