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Tobacco, alcohol use, and risks of laryngeal and lung cancer by subsite and histologic type in Turkey

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Effects of tobacco smoking and alcohol use on risks of cancers of the larynx and lung have been evaluated extensively in industrialized countries. Few studies on the effect of these risk factors have been reported from developing countries. We conducted a case-control study to evaluate risks of laryngeal and lung cancers in men by subsite and cell type in relation to smoking and alcohol drinking in Turkey, a country where smoking and alcohol consumption patterns are different from those in industrialized countries. We identified 832 laryngeal and 1,210 lung cancer cases and 829 controls with information on smoking and alcohol use (amount and duration) and histologic cell type from an oncology treatment center of a Social Security Agency hospital in Istanbul, Turkey, admitted between 1979 and 1984. Both laryngeal and lung cancer showed significant associations with smoking and alcohol drinking, but no monotonic dose-response was obtained for alcohol drinking. Among smokers, the highest risks were observed in the supraglottis region of the larynx (odds ratio [OR] = 4.1) after adjustment for age and alcohol use. Among alcohol drinkers, the highest risks were observed in the glottis region of the larynx (OR = 1.7) after adjustment for age and smoking. In the analysis by the cell type of lung cancer among ever-smokers, small cell type showed the highest risk (OR = 5.4), while it showed no association with alcohol drinking. Cumulative cigarette use (pack-years) and number of cigarettes per day showed stronger associations than years smoked for both cancer sites. The relative risks of joint exposure to smoking and alcohol were 12.2 for laryngeal cancer and 14.1 for lung cancer among heavy smokers and heavy alcohol drinkers. This study provides epidemiologic evidence from Turkey that smoking and alcohol use are associated with risks of cancers of the larynx and lung. *Cancer Causes and Control* 1997, 8, 729-737

Key words: Alcohol, histologic type, laryngeal cancer, lung cancer, men, smoking, Turkey.

Introduction

The effects of tobacco smoking and alcohol use on cancer are well established and have been reviewed extensively by the International Agency for Research on Cancer (IARC).[1,2] IARC has concluded that malignant tumors of the larynx, lung, lip, oral cavity, pharynx, bladder, kidney, esophagus, stomach, and pancreas were related causally to cigarette smoking.[1] In 1988, IARC also found sufficient evidence that the occurrence of cancers of the larynx, oral cavity, pharynx, esophagus, and liver were related causally to the consumption of alcoholic beverages.[2]

Many studies of alcohol and tobacco use have been conducted in highly industrialized American and Euro-

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pean countries. Fewer reports are available from non-industrialized countries and other areas of the world. In a recent review, Boyle *et al* [3] pointed out the importance of the new epidemic of smoking related to lung cancer in developing countries. Studies on risks of laryngeal or lung cancer and smoking and alcohol use have been reported from China,[4-10] Greece,[11] India,[12] Israel,[13] Korea,[14] Poland,[15,16] Uruguay,[17-19] Thailand,[20] and Argentina,[21] but only studies from Israel,[13] Poland,[15] and Uruguay[17] evaluated the risk by subsites of laryngeal cancer or cell types of lung cancer. To provide further information in developing countries, we conducted a case-control study of laryngeal cancer by subsite and lung cancer by cell type in relation to tobacco and alcohol use in Turkey, a country where smoking and alcohol consumption patterns are different from those in industrialized countries. No analytic studies in Turkey evaluating cancer risk patterns in relation to smoking and alcohol have been previously reported.

Materials and methods

The Social Security Agency (SSA) provides medical care to all employees (except civil servants) in Turkey. Cases and controls for this study were selected from an oncology treatment center of the SSA Okmeydani Hospital in Istanbul, Turkey. This hospital has the largest cancer therapy center (treating all sites except leukemia) in the SSA for employees in the Marmara Region of Turkey. It also provides services to some employees from other regions in Turkey.

For several years, the hospital has obtained information on occupational history, alcohol and tobacco use, from patients at admission, using a standardized data-collection instrument. Information on smoking included the number of cigarettes smoked per day and the total number of years of smoking. Frequency and duration of use of alcoholic beverages were obtained. In addition to the amount and duration measures, we calculated cumulative cigarette use (pack-years) and alcohol use (bottle[35 cl of hard liquor]-years).

We identified 954 male laryngeal and 1,392 male lung cancer cases from this SSA hospital between 1979-84. This was part of a larger effort to evaluate associations between occupational risk factors and cancer. An oncologist from the hospital reviewed patient records for histologic verification and coded the diagnosis using the ICD-O classification system.[22] To investigate the potential risk differences by the different regions of the larynx, we used four-digit ICD-O codes for laryngeal subsites, specifically 161.0, 161.1, and (161.2, 161.3, and 161.9) were selected for the classification of glottis, supraglottis, and others, respectively. Female subjects were excluded from this analysis due to the small numbers and very low prevalence of smoking and alcohol use among women in Turkey. Subjects with incomplete information on age, smoking or alcohol use were also removed from the study. After these exclusions, 832 laryngeal and 1,210 lung cancers cases and 829 controls were available for the analysis. Controls included subjects with selected cancers (salivary glands, small intestine, gallbladder, peritoneum, pleura, mediastinum, bones and joints, connective tissues, testis, eye, brain, and thyroid) that are not reported to be related to smoking or alcohol use, and subjects (n = 23) found not to have cancer.

Maximum likelihood estimates of the odds ratio (OR) were used to estimate the RRs of laryngeal and lung cancers associated with smoking and alcohol use. ORs from smoking were adjusted for age (< 40, 40-59, 60+ years old), and alcohol use (never used, < 35 bottle-years, 35-90 bottle-years, > 90 bottle-years), and ORs for alcohol use were adjusted for age (< 40, 40-59, 60+) and smoking (never smoked, < 20 pack-years, 20-29 pack-years, > 29 pack-years). Gart's method[23] was used to calculate the OR and corresponding 95 percent confidence intervals (CI). Test statistics for trend were calculated using Mantel's chi-square test.[24]

Results

The distributions of subsites of laryngeal cancer cases and histologic types of lung cancer cases by smoking, alcohol drinking status, age, and socioeconomic status (SES) are presented in Table 1. The majority of the laryngeal tumors were in the supraglottis region (46 percent). Most of the laryngeal cancer cases were smokers (88 percent), while only 25 percent were alcohol drinkers. The proportion of ever-smokers and drinkers among lung cancer cases was similar to that for laryngeal cancer (88 percent smokers, and 27 percent alcohol drinkers). Only 814 lung cancer cases had histologic reports; of those, 60 percent had squamous cell carcinomas, 19 percent had small cell carcinomas, and 21 percent had 'other cell types,' including large cells and adenocarcinomas. The proportions of ever-smokers and alcohol drinkers among histologically diagnosed lung cancer cases were similar to all lung cancer cases. Of 829 control subjects, 67 percent were ever-smokers and only 13 percent were ever-alcohol-drinkers. In general, percent distributions of cases by age and by SES were similar to the distributions of controls. The majority of cases (*i.e.*, 76 percent of laryngeal cancer cases and 67 percent of lung cancer cases) and controls (72 percent) were in the lower SES category, because the Social Security Agency provides health services only for industrial workers, excluding farmers, and civil/military service workers.

Table 2 presents risks of cancers of the larynx (and its subsites) and lung (and its cell types) by amount, duration,

Table 1. Distribution of laryngeal and lung cancer cases and their controls by smoking and alcohol drinking status, Turkey

Cancer sites and controls	No. of subjects	Ever smoked	Ever drank	Age groups (yrs)			Socioeconomic status		
				> 39	40-59	60+	Low	Medium	High
Larynx (All)	832	732	207	68	506	258	634	183	15
Glottis	183	156	50	10	102	71	132	45	6
Supraglottis	385	344	91	35	243	107	301	79	5
Others	264	232	66	23	161	80	201	59	4
Lung (All)	1,210	1,068	323	79	717	414	821	321	68
Small cell	156	143	37	17	98	41	103	42	11
Squamous cell	492	434	129	25	307	160	315	150	27
Others	166	142	48	13	111	42	115	38	13
Histology unknown	396	349	109	24	201	171	288	91	17
Controls	829	536	105	118	383	328	593	206	30

and cumulative exposure of smoking, adjusted for age and alcohol use. All subsites of laryngeal cancer showed elevated risks among smokers. The highest significant risk (OR = 4.1) was observed for cancer of the supraglottis. The number of cigarettes per day and pack-years showed somewhat sharper trends for larynx and lung cancers than did duration of smoking. The risk of supraglottis cancer showed the strongest association with all measures of smoking, although CIs for the various subsites overlapped. An OR of 7.9 was observed for the supraglottis among those with 21 or more pack-years of tobacco use. For lung cancer, all cell types showed significant excess risks among smokers. The greatest risk (OR = 5.4) was observed for small-cell lung cancer. Small-cell lung cancer also showed the sharpest exposure-response trend with quantitative measures of tobacco use. The number of cigarettes per day and pack-years generally showed stronger associations with the various cell types than did duration of smoking. The highest risk (OR = 13.5) was observed for small cell carcinomas associated with 21 or more cigarettes per day. Squamous and 'other cell' types of lung cancer also showed significant and monotonic dose-response relationships with smoking.

Table 3 presents risks of laryngeal and lung cancers by amount, duration, and cumulative exposure to alcohol, adjusted for age and smoking. Among laryngeal cancer subsites, the highest significant risk (OR = 1.7) was observed for the glottis. In general, the duration of alcohol use showed a stronger relationship than the other measures of alcohol use. Both laryngeal and lung cancer showed significant but non-monotonic trends with all three measures of alcohol, although risks were not nearly as high as were found for tobacco users. The only significant monotonic exposure-response relationship was between duration of alcohol use and risk of cancer of the glottis. For the glottis, the highest risk (OR = 3.3) was observed among subjects with alcohol use for 21 or more years. For the lung cancer cell types, the highest significant risk (OR = 1.9) was observed for 'other cell types,' including large cell and adenocarcinoma. Squamous and 'other cell' types showed significant but non-monotonic exposure-response relationships amount and cumulative exposure of alcohol use, while small cell carcinomas did not show any exposure-response relationship with alcohol use. Squamous cell carcinomas showed very significant monotonic exposure-response relationship with duration of alcohol use.

To eliminate the effects of nonsmokers in the reference category (non-alcohol drinkers), we evaluated alcohol-related risk of laryngeal and lung cancer among smokers only (Table 4). In addition to age, ORs were adjusted for smoking in three categories of pack-years (*i.e.*, 1-19, 20-29, and 30+). The risks were slightly lower than the RRs presented in Table 3, indicating that nonsmokers among the reference population have very little impact on risk estimates for alcohol drinking.

Table 5 presents the joint effects of smoking and alcohol on risks of laryngeal and lung cancer. The risks for laryngeal and lung cancer among heavy smokers and heavy alcohol users were 12.2 and 14.1, respectively. Both cancer sites showed monotonically increased risks with increasing smoking levels at every level of alcohol use. For alcohol use, only lung cancer showed monotonically increased risks with increasing alcohol levels at every level of smoking category. Among laryngeal subtypes, RRs were 9.9, 12.2, and 13.0 among heavy smokers and heavy alcohol drinkers for cancers of the glottis, supraglottis, and other subtypes, respectively. For lung cancer cell types, RRs of small cell, squamous cell, and other cell type were 21.7, 22.5, and 11.1, respectively, among heavy smokers and heavy alcohol drinkers.

Discussion

Tobacco and alcohol use in Turkey are not as common as in more industrialized countries, but they still have a

Table 2. Risks of laryngeal and lung cancer with subsites by ever, amount, duration, and pack-years of smoking, adjusted for age and alcohol use, Turkey

Cancer sites	Ever smoked	Number of cigarettes per day				Duration of smoking (years)				Pack-years			
	OR[a] (*n*[b]) (CI)	1-10 OR (*n*) (CI)	11-20 OR (*n*) (CI)	21+ OR (*n*) (CI)	*P* for trend	1-10 OR (*n*) (CI)	11-20 OR (*n*) (CI)	21+ OR (*n*) (CI)	*P* for trend	1-10 OR (*n*) (CI)	11-20 OR (*n*) (CI)	21+ OR (*n*) (CI)	*P* for trend
Larynx (All)	3.5 (732) (2.6-4.4)	1.6 (45) (0.9-2.6)	3.5 (470) (2.6-4.8)	6.6 (202) (4.2-10.3)	< 0.001	1.1 (22) (0.6-1.9)	4.8 (126) (3.1-7.4)	4.1 (284) (2.8-6.0)	< 0.001	1.9 (77) (1.3-3.0)	4.4 (155) (2.9-6.7)	6.0 (197) (3.8-9.5)	< 0.001
Glottis	2.7 (156) (1.7-4.4)	1.0 (8) (0.4-2.7)	2.8 (103) (1.7-4.7)	4.9 (43) (2.5-9.9)	< 0.001	0.8 (4) (0.2-2.6)	4.0 (31) (2.0-7.9)	2.2 (47) (1.2-4.1)	< 0.001	1.4 (14) (0.6-3.0)	3.0 (31) (1.5-6.0)	3.6 (37) (1.8-7.3)	< 0.001
Supraglottis	4.1 (344) (2.7-6.0)	1.7 (23) (0.9-3.3)	4.1 (220) (2.7-6.2)	7.1 (92) (4.1-12.3)	< 0.001	0.9 (8) (0.4-2.1)	4.9 (58) (2.8-8.4)	5.5 (150) (3.4-8.9)	< 0.001	2.3 (40) (1.3-4.0)	4.8 (68) (2.8-8.1)	7.9 (106) (4.6-13.7)	< 0.001
Other subsites	3.5 (232) (2.3-5.5)	1.6 (14) (0.8-3.5)	3.5 (147) (2.2-5.5)	6.6 (67) (3.5-12.0)	< 0.001	1.5 (10) (0.6-3.5)	4.2 (37) (2.3-6.9)	4.0 (87) (2.3-6.9)	< 0.001	1.9 (23) (1.0-3.6)	4.8 (56) (2.6-8.6)	4.8 (54) (2.5-9.1)	< 0.001
Lung (All)	3.3 (1,068) (2.6-4.4)	2.2 (101) (1.4-3.3)	3.1 (614) (2.3-4.1)	6.6 (317) (4.4-10.2)	< 0.001	1.0 (32) (0.6-1.7)	3.8 (158) (2.6-5.7)	4.9 (466) (3.5-7.0)	< 0.001	1.8 (110) (1.2-2.6)	4.3 (226) (3.0-6.4)	6.8 (313) (4.4-10.4)	< 0.001
Small cell	5.4 (143) (2.9-10)	1.7 (6) (0.6-5.2)	5.0 (85) (2.6-9.8)	13.5 (48) (6.1-30.0)	< 0.001	1.7 (6) (0.5-5.3)	7.0 (25) (3.2-15.6)	8.4 (58) (4.0-17.6)	< 0.001	2.8 (17) (1.2-6.6)	7.8 (35) (3.6-17.2)	12.9 (36) (5.3-29.0)	< 0.001
Squamous cell	3.6 (434) (2.6-5.0)	2.6 (47) (1.5-4.6)	3.2 (247) (2.2-4.6)	7.0 (126) (4.1-12.0)	< 0.001	1.2 (15) (0.6-2.5)	3.9 (70) (2.3-6.7)	4.9 (199) (3.2-7.5)	< 0.001	1.8 (44) (1.1-3.0)	4.4 (94) (2.7-7.0)	7.1 (143) (4.2-11.8)	< 0.001
Other cells	2.6 (142) (1.7-4.2)	1.8 (14) (0.8-4.1)	2.7 (91) (1.6-4.7)	3.2 (32) (1.4-7.0)	< 0.001	0.8 (5) (0.3-2.5)	3.3 (26) (2.2-7.5)	4.1 (69) (2.2-7.5)	< 0.001	2.3 (26) (1.2-4.5)	4.3 (41) (2.3-8.3)	3.5 (33) (1.6-7.7)	< 0.001

[a] ORs (odds ratios) compared with subjects who never smoked.
[b] Number of subjects.
[c] CI = 95% confidence interval.

Table 3. Risks of laryngeal and lung cancer with subsites by ever, amount, duration, and bottle-years of alcohol use, adjusted for age and smoking, Turkey

Cancer sites	Ever drank	Amount of alcohol per week (cl/week)				Duration of alcohol drinking (yrs)				Bottle-years (35 cl of hard liquor-yrs)			
	OR[a] (*n*[b]) (CI)	1-35 OR (*n*) (CI)	36-140 OR (*n*) (CI)	141+ OR (*n*) (CI)	*P* for trend	1-10 OR (*n*) (CI)	11-20 OR (*n*) (CI)	21+ OR (*n*) (CI)	*P* for trend	1-34 OR (*n*) (CI)	35-90 OR (*n*) (CI)	91+ OR (*n*) (CI)	*P* for trend
Larynx (All)	1.6 (207)	1.7 (46)	1.8 (85)	1.5 (41)		1.8 (30)	1.5 (59)	2.0 (40)		1.3 (32)	2.4 (54)	1.4 (35)	
	(1.2-2.1)	(1.0-3.2)	(1.1-2.9)	(0.8-2.9)	< 0.001	(0.9-3.6)	(0.9-2.6)	(0.9-4.5)	0.004	(0.7-2.6)	(1.2-4.6)	(0.7-2.8)	0.007
Glottis	1.7 (50	2.3 (15)	1.7 (18)	1.5 (9)		1.3 (8)	2.5 (15)	3.3 (10)		1.3 (7)	2.3 (13)	1.8 (10)	
	(1.1-2.6)	(1.0-5.3)	(0.8-3.4)	(0.6-3.6)	0.032	(0.3-5.3)	(1.1-5.7)	(1.2-9.1)	0.006	(0.5-3.7)	(0.9-5.6)	(0.7-4.6)	0.013
Supraglottis	1.5 (91)	1.3 (15)	1.6 (40)	1.3 (16)		1.6 (11)	1.1 (22)	1.9 (18)		1.2 (13)	1.8 (22)	1.0 (13)	
	(1.1-2.1)	(0.6-3.0)	(0.9-2.9)	(0.6-2.8)	0.033	(0.6-4.1)	(0.6-2.0)	(1.0-3.6)	0.068	(0.5-2.9)	(0.8-3.8)	(0.4-2.4)	0.142
Others	1.5 (66)	1.8 (16)	1.9 (27)	1.6 (16)		2.2 (11)	1.7 (22)	2.3 (12)		1.6 (12)	2.7 (19)	1.4 (12)	
	(1.0-2.4)	(0.8-3.9)	(1.0-3.5)	(0.7-3.5)	0.007	(0.8-6.2)	(0.8-3.6)	(0.8-6.6)	0.008	(0.7-3.7)	(1.3-6.2)	(0.6-3.3)	0.010
Lung	1.6 (323)	1.6 (60)	1.7 (119)	1.7 (81)		1.8 (43)	1.6 (97)	2.1 (62)		1.7 (59)	1.9 (66)	1.6 (65)	
	(1.2-2.1)	(0.8-2.9)	(1.1-2.7)	(1.0-2.9)	< 0.001	(0.9-3.5)	(1.0-2.7)	(1.0-4.5)	0.001	(0.9-3.0)	(1.0-3.7)	(0.9-3.0)	0.004
Small cell	1.3 (37)	1.8 (9)	1.2 (13)	0.8 (5)		2.0 (7)	1.2 (11)	1.6 (6)		1.7 (8)	1.8 (10)	0.7 (4)	
	(0.8-2.1)	(0.7-4.6)	(0.6-2.6)	(0.2-2.3)	0.419	(0.7-5.8)	(0.5-2.7)	(0.5-5.3)	0.139	(0.6-4.5)	(0.7-4.6)	(0.2-2.4)	0.298
Squamous cell	1.6 (129)	1.7 (27)	1.6 (47)	1.8 (35)		1.6 (14)	1.7 (41)	2.7 (32)		1.9 (28)	1.7 (21)	1.9 (32)	
	(1.1-2.2)	(0.8-3.5)	(0.9-2.8)	(1.0-3.6)	0.003	(0.7-4.0)	(1.0-3.1)	(1.2-6.2)	<0.001	(1.0-3.9)	(0.8-3.9)	(1.0-3.9)	0.003
Others	1.9 (48)	2.0 (10)	1.9 (17)	1.8 (11)		2.2 (7)	1.8 (11)	1.7 (6)		1.6 (7)	2.6 (13)	1.4 (7)	
	(1.2-2.9)	(0.8-5.0)	(0.9-3.8)	(0.8-4.3)	0.008	(0.7-6.3)	(0.8-3.7)	(0.5-5.7)	0.021	(0.6-4.3)	(1.1-6.3)	(0.5-3.7)	0.025

[a] ORs (odds ratios) compared with subjects who never drank.
[b] Number of subjects.
[c] CI = 95% confidence interval.

Table 4. Risks of laryngeal and lung cancers among smokers only with amount, duration, and bottle-years of alcohol use, adjusted for age and smoking, Turkey

Cancer sites	Amount of alcohol per week (cl/wk)				Duration of alcohol drinking (yrs)				Bottle-years (35 cl of hard liquor-yrs)			
	1-35 OR (*n*) (CI)	36-140 OR (*n*) (CI)	141+ OR (*n*) (CI)	*P* for trend	1-10 OR (*n*) (CI)	11-20 OR (*n*) (CI)	21+ OR (*n*) (CI)	*P* for trend	1-34 OR (*n*) (CI)	35-90 OR (*n*) (CI)	91+ OR (*n*) (CI)	*P* for trend
Larynx	1.7 (45)	1.6 (82)	1.3 (41)	—	1.6 (30)	1.5 (59)	1.8 (40)	—	1.3 (32)	2.3 (54)	1.3 (35)	—
	(0.9-3.3)	(1.0-2.6)	(0.7-2.5)	0.023	(0.8-3.4)	(0.9-2.7)	(0.8-4.1)	0.008	(0.7-2.6)	(1.1-3.8)	(0.6-2.7)	0.013
Lung	1.5 (59)	1.6 (117)	1.3 (80)	—	1.7 (43)	1.5 (95)	1.9 (62)	—	1.6 (59)	1.8 (65)	1.3 (64)	—
	(0.8-2.9)	(1.0-2.5)	(0.8-2.4)	0.016	(0.8-3.4)	(0.9-2.5)	(0.9-4.2)	0.006	(0.9-3.0)	(1.0-3.5)	(0.7-2.6)	0.019

[a] ORs (odds ratios) compared with subjects who never drank.
[b] Number of subjects.
[c] CI = 95% confidence interval.

Table 5. Joint effects of cigarette smoking and alcohol drinking on risks of laryngeal and lung cancer by subtype and histologic cell type, Turkey; odds ratio (number of subjects) and 95% confidence interval

Laryngeal cancer (any cell type)

	Never smoked	1-20 cigarettes per day	21+ cigarettes per day
Never drank	1.0 (99)	3.0 (398) (2.2-4.1)	6.2 (123) (3.9-9.9)
1-20 yrs drank	— (—)	5.6 (64) (3.2-9.8)	6.0 (25) (2.5-14.3)
21+ yrs drank	— (—)	5.2 (20) (1.9-15.1)	12.2 (20) (3.1-57.6)

Lung cancer (any cell type)

	Never smoked	1-20 cigarettes per day	21+ cigarettes per day
Never drank	1.0 (142)	2.8 (549) (2.1-3.6)	6.1 (175) (4.0-9.3)
1-20 yrs drank	— (—)	4.4 (82) (2.6-7.3)	8.5 (56) (2.5-14.3)
21+ yrs drank	— (—)	5.2 (28) (2.0-14.6)	14.1 (34) (3.9-61.2)

Laryngeal cancer (glottis)

	Never smoked	1-20 cigarettes per day	21+ cigarettes per day
Never drank	1.0 (27)	2.3 (79) (1.4-3.8)	4.6 (27) (2.3-9.4)
1-20 yrs drank	— (—)	5.8 (19) (2.6-13.4)	2.2 (4) (0.5-8.9)
21+ yrs drank	— (—)	4.9 (6) (1.2-19.5)	9.9 (4) (1.5-83.0)

Lung cancer (small-cell)

	Never smoked	1-20 cigarettes per day	21+ cigarettes per day
Never drank	1.0 (13)	4.2 (74) (2.2-8.1)	13.0 (31) (5.9-29.3)
1-20 yrs drank	— (—)	5.5 (9) (1.9-15.9)	14.4 (9) (4.2-49.8)
21+ yrs drank	— (—)	14.5 (4) (2.3-95.2)	21.7 (2) (1.3-351.6)

Laryngeal cancer (supraglottis)

	Never smoked	1-20 cigarettes per day	21+ cigarettes per day
Never drank	1.0 (40)	3.6 (195) (2.4-5.4)	7.0 (56) (4.0-12.4)
1-20 yrs drank	— (—)	4.7 (23) (2.3-9.8)	5.3 (10) (1.9-15.1)
21+ yrs drank	— (—)	5.6 (9) (1.6-19.7)	12.2 (9) (3.1-57.6)

Lung cancer (squamous cell)

	Never smoked	1-20 cigarettes per day	21+ cigarettes per day
Never drank	1.0 (58)	2.9 (225) (1.9-4.1)	6.5 (72) (3.8-11.2)
1-20 yrs drank	— (—)	5.0 (34) (2.5-9.8)	7.8 (19) (3.0-20.6)
21+ yrs drank	— (—)	6.5 (14) (2.2-20.7)	22.5 (18) (5.1-125.6)

Laryngeal cancer (others)

	Never smoked	1-20 cigarettes per day	21+ cigarettes per day
Never drank	1.0 (32)	2.9 (124) (1.9-4.7)	6.0 (40) (3.2-11.3)
1-20 yrs drank	— (—)	6.0 (22) (2.8-12.8)	7.1 (11) (2.5-20.2)
21+ yrs drank	— (—)	4.1 (5) (1.0-16.9)	13.0 (7) (2.4-82.2)

Lung cancer (others)

	Never smoked	1-20 cigarettes per day	21+ cigarettes per day
Never drank	1.0 (24)	2.5 (79) (1.4-4.1)	2.7 (12) (1.2-6.3)
1-20 yrs drank	— (—)	4.9 (15) (2.1-11.3)	5.4 (7) (1.6-17.6)
21+ yrs drank	— (—)	4.3 (3) (0.7-23.6)	11.1 (3) (1.5-91.1)

[a] OR = odds ratio.
[b] *n* = number of subjects.
[c] CI = 95% confidence interval.

considerable impact on the public's health. Turkey ranks 39th out of 110 countries with regard to *per capita* cigarette consumption (1,305 manufactured cigarettes *per capita*) compared with the US, which ranks fifth (2,678 *per capita*).[1] The use of filtered cigarettes in Turkey has grown from 18 percent in 1973 to 76 percent in 1982.[1] We did not have information on the type of tobacco the subjects consumed; however, Turkish tobacco is aromatic and the method of curing is a combination of sun-curing and air-curing.[1] Although alcohol is not prohibited in

Turkey, the consumption is not generally socially acceptable because of religious reasons. Production and sales of alcoholic beverages are carried out by the state monopoly. The average annual consumption of alcoholic beverages is 1.0 liter ethanol per person, compared with the US with 8.0 liters ethanol per person or France with 13.3 liters ethanol per person.[2] According to the government sources,[25] out of 371 million liters/year of alcoholic beverage sales, 68 percent are beer, 12 percent are wine, and 20 percent are hard liquor (16 percent raki [distilled drink made from grapes], two percent vodka, two percent gin and other spirits).

In this case-control study of laryngeal and lung cancer, all subsites of laryngeal cancer and cell types of lung cancer showed significant dose-response relationships with the various quantitative measures of smoking. The observed RRs of laryngeal and lung cancer among ever-smokers, however, were smaller than those observed in the industrial countries.[1] This may be due to the smaller percentages (27 to 30 percent) of heavy smokers (*i.e.*, 21+ cigarettes/day) than typically found in developed countries[1] (48 to 52 percent). In our study, we observed that the number of cigarettes per day and pack-years measures showed stronger associations than duration of smoking. The relatively weaker association by the duration of smoking may be a result of a lower response rate to the questions related to the duration of smoking (60 percent of smokers) than the amount of cigarettes per day (97 percent of smokers) or potential errors in the collection of the duration information. In this study, we did not have detailed smoking information such as starting age, filtered/non-filtered cigarette, blond *cf* black tobacco use, and inhalations status. Our exposure measures were limited to the duration of smoking and the average number of cigarettes per day.

We observed similar risk for cancer of the supraglottis from smoking with the findings of others.[1,26-37] In another report,[38] however, risk for glottis cancer was slightly higher than the risk for supraglottis cancer.

Similar to the previously reported studies[1,11,39-45] of lung cancer and smoking by cell type, we observed stronger associations for small- and squamous-cell lung cancer than 'other cell' types with smoking. Number of cigarettes per day and pack-years showed stronger associations with each cell type, except 'other types.' A relatively weaker association between smoking and the 'other cell' type may reflect the heterogeneity of cell types in this category. Adenocarcinoma and large cell types were included in the 'other cell' types of lung cancer, because of small numbers.

The relationships between alcohol and laryngeal or lung cancer were inconsistent and much weaker than the links with smoking. The maximum risks of both laryngeal and lung cancer occurred in the medium exposure category for both the amount of alcohol use and cumulative measures of alcohol drinking. This could either reflect the lack of an association or indicate possibly underreporting of alcohol use. Duration of alcohol use showed more consistent association than the other measures of alcohol, suggesting that the reporting of duration may be more accurate than the reporting of the amount.

The relationship between alcohol drinking and laryngeal cancer has been well documented.[2,14,15,19,26-38,46-50] We found significant excess risk for both the glottis (intrinsic) and supraglottis (extrinsic) among alcohol drinkers. Similar results have been reported in a case-control study in Denmark,[38] in an IARC international case-control study[31] conducted in Italy, Spain, Switzerland, and France, and in another case-control study in Spain.[37] Other studies, however, have reported a stronger effect of alcohol on the risk for supraglottis than for glottis.[28,30,32]

We did not find a monotonic dose-response relationship between alcohol use and the risk of lung cancer. It has been concluded by the IARC[2] and other investigators[47,49-52] that there is no strong evidence for the causal relationship between the consumption of alcoholic beverages and lung cancer, however, some studies[18,46,53,54] observed significant and monotonic association between alcohol and lung cancer, even after adjustment for smoking. We observed significant excess risk among alcohol drinkers for squamous and other types of lung cancer, but not with small cell. The dose-response relationships using several exposure measures of alcohol however, were inconsistent. The only significant monotonic relationship was between duration of alcohol consumption and squamous cell lung cancer. Even though we adjusted the observed alcohol risk for smoking, the possibility of residual confounding cannot be ruled out. This problem is enhanced in our study because the prevalence of alcohol use was relatively low compared with industrialized countries. Associations between alcohol and cancers may be explained by micronutrient deficiencies that occur among heavy alcohol drinkers.[18,52,55] Our data provide only a suggestive evidence on the association between alcohol use and lung cancer.

Similar to the previous studies,[14,28,31,32,56-61] joint exposure to smoking and alcohol enhanced the risks of these cancers, but formal tests of interaction were not carried out because all alcohol drinkers also smoked in this study, and there were few subjects in the categories of heavy smokers and heavy alcohol drinkers. We observed monotonically increased risk of lung cancer, particularly for small- and squamous-cell carcinomas, with increasing level of alcohol use at each level of smoking categories. Similarly, we observed monotonically increased risk of lung cancer in every cell type with increasing level of smoking at each level of alcohol use, suggesting that the effects of alcohol and smoking on lung cancer risk may be distinct and separate.

In summary, both laryngeal and lung cancer showed significant associations with smoking in this Turkish population. Alcohol drinking was associated with the risks of laryngeal and lung cancer, but exposure-response relationships were not consistent in every measure of alcohol. Overall risks for ever-smokers were smaller than observed in studies from developed countries. For smoking, the strongest associations were observed in the supraglottis region of the larynx, while for alcohol drinking, the strongest associations were observed in the glottis region of the larynx. Among various exposure measures, number of cigarettes per day and pack-years showed stronger associations for both cancer sites than duration of smoking. On the other hand, duration of alcohol use showed the strongest association with both laryngeal and lung cancer. In the analysis by the cell type of lung cancer and smoking, similar to the previously reported studies, small and squamous cell types were affected more than the 'other cell' types. Only squamous-cell lung cancer was associated with alcohol. This study provides epidemiologic evidence from Turkey that smoking and alcohol use are associated with risks of cancers of the larynx and lung. Although the data collection was carried out about 13 years ago, the results of this study point out the importance of adverse effects of smoking in Turkey and in developing countries, because the use of tobacco is still increasing in Turkey[62] and in other developing countries [3] while it is decreasing in industrialized countries.[63] The use of tobacco in public places in Turkey has been rising in recent decades, creating important public health problems even for nonsmokers. Further studies are needed particularly on the effects of passive smoking in developing countries where smoking prevalence is increasing more rapidly than at in industrialized countries.

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