Interactions between smoking and other exposures associated with lung cancer risk in women: diet and physical activity

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Received May 15, 2006

The objective of the study is to estimate the differences in the impact of diet and physical exercise on lung cancer risk in female nonsmokers vs. smokers, and reveal interactions, if any. In a hospital based case-control study, data collected by in-person interviews from 569 female lung cancer cases and 2120 controls were analyzed using unconditional logistic regression stratifying by appropriate factors. Protective effects were observed for intake of milk/dairy products (OR=0.57, 95%CI 0.35-0.94), vegetables (OR=0.60, 95%CI 0.40-0.91), apples (OR=0.69), wine (OR=0.77), and physical exercise (OR=0.59, 95%CI 0.42-0.83) among smokers only, while no similar effects were found among nonsmokers. In contrast, the intake of black tea was associated with a protective effect (OR=0.66, 95%CI 0.47-0.94) among nonsmokers only. Comparing the effects of dietary items and physical activity on lung cancer risk among nonsmokers versus smokers, statistically significant effect modifications were found for black tea (P 0.005), and milk/dairy products (P 0.047). Borderline effect modifications emerged for physical exercise (P 0.077). Conclusions: These results indicate protective effects of some components of healthful diet and physical exercise among smokers, and of the intake of black tea among nonsmokers. The observed interactions of the impact of black tea, milk/dairy products and physical activity upon lung cancer risk in women at different levels of the smoking habit deserve further studies.

Key words: lung cancer; diet; physical activity; risk factors; interaction; epidemiology

In research carried out over the second half of the 20th century, many factors were found to be associated with lung cancer risk, and studies were implemented to identify the role and importance of these factors. Tobacco smoking was identified as the single most powerful cause of the lung cancer epidemic [1, 2]. Associations between other factors and lung cancer risk were found, including workplace agents (eg, asbestos, arsenic, chromium, nickel, and radon), environmental (passive smoking, indoor radon, heavy air pollution), lifestyle and behavioral (physical activity, diet), reproductive, genetic [3], socioeconomic and other factors [4, 5].

Current knowledge of the mechanisms of cancer suggests that all cancers are both environmental and genetic, meaning that there are multiple causes that involve exposures originating outside the body as well as hereditary and genetic changes that converge to induce the disease [6].

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In the present study, based on 569 cases – female lung cancer patients of a Prague University Hospital – and 2120 controls, we examined the relationship between diet, physical activity and the risk of lung carcinoma among nonsmoking women and compared it with smoking women. Potential interactions between smoking and other relevant factors were tested in terms of effect modification among 'nonsmokers' and 'smokers'.

Participants and Methods

Study sample and data collection.

A hospital-based case-control study of lung cancer among women was conducted in Prague University Hospital Na Bulovce, departments of pneumology, thoracic surgery, and general medicine. To be included in the study, a female patient with newly diagnosed microscopically confirmed primary lung cancer had to be admitted between April 1998-

March 2005. Controls were all women, and were spouses, relatives, or friends of other patients of the departments, with conditions unrelated to smoking. Both cases and controls had to be aged 25-89 years, and reside within the catchment area covering the north-eastern sectors of Prague and the adjacent Central Bohemia Region (10 administrative districts). Personal interviews were completed with 569 female lung cancer cases (91% of those eligible) and 2,120 controls (response rate 82%). The reasons for non-participation among 625 eligible cases included patient´s inability to cooperate during interview as a result of severe physical or mental disability (36 patients, 5.8%), refusal to be interviewed (5 subjects, 0.8%), or death shortly after admission (15 patients, 2.4%). Nonresponse among controls was due to 'no time for interview' (271 women, 10.5%), refusal to be interviewed (184 women, 7.1%), and a language barrier of mental incompetence (10 persons, 0.4%). Informed consent was obtained from all interviewed cases and controls. The interviewers were trained extensively to standardize data collection and coding techniques and to minimize inter-interviewer variation.

Questionnaire and definitions

The questionnaire has been described previously elsewhere [7, 8]. In brief, the questionnaire included a basic structured section on demographic characteristics; place of residence; type of house, occupation and workplace; further, a complete smoking history. Subjects were defined as current smokers if they smoked, at the time of the survey, either daily or occasionally. A daily smoker is someone who smokes at least one cigarette a day for at least three months, i.e., a total of approximately 100 cigarettes and over. An occasional smoker is someone who smokes, but not every day. Never smokers either have never smoked at all or have smoked less than 100 cigarettes in their lifetime. Ex-smokers are people who were formerly smokers but currently have not smoked for at least six months. In ex-smokers, the time since quitting was recorded. In this report, in addition to the results for all study subjects, we present results for two groups of cases and controls: Group 1, called 'nonsmokers', including never smokers + long-term ex-smokers (quit 20 or more years ago); and Group 2, called 'smokers', defined as current smokers + short-term ex-smokers (quit less than 10 years ago) (Table 1). The questionnaire included sections on exposure to environmental tobacco smoke (secondhand smoking), physical exercise (hours per week); preexisting lung disease or cancer (diagnosed by a physician at least 2 years before interview); family history of cancer among first degree relatives (parents and siblings); and menstrual and pregnancy history.

Information on dietary habits was collected with 7 food items (red meat, poultry, milk and dairy products, vegetables, apples, citrus fruit, other fruit); three nonalcoholic beverage items (black tea, green tea, coffee), and three alcoholic beverage categories (beer, wine, and spirits). The subjects were asked to try to estimate the best fitting answer reflecting the usual consumption in most years within the 10-year period before interview. One of four frequency estimates of consumption was to be selected: 1. Never, 2. Monthly or less, 3. Weekly or less, but more than once per month, or 4. Daily or several times per week. After completion of the questionnaire, the trained interviewer took

Table 1. Smoking habits and the risk of lung cancer.

	All study subjects				
Cases/ Controls	569/2120				
Smoking habits	Never smokers	Ex smokers, quit 20 or more years ago	Ex smokers, quit 10-19 years ago	Ex smokers, quit <10 years ago	Current smokers
Cases/ Controls	140/ 1166	24/112	36/149	131/197	238/ 496
Odds ratio (OR) [a]	1.00	1.78	2.42	7.91	7.16
95%CI[b]	Referent	1.08-2.93	1.57-3.74	5.77-10.85	5.45-9.42
Study groups	Group 1 "Nonsmokers"			Group 2 "Smokers"	
Cases/ Controls	164/ 1278			369/ 693	
Odds ratio (OR)[a]	1.00			6.96	
95%CI[b]	Referent			5.45-8.88	

[a]OR, odds ratio, adjusted for age, residence, and education. [b]CI, confidence interval

Table 2. Distribution of cases and controls by smoking habits, age-groups, and cell types

	All study subjects		Group 1"Nonsmokers"		Group 2"Smokers"	
Variables	Cases	Controls	Cases	Controls	Cases	Controls
Population	569	2120	164	1278	369	693
Mean age	63.0	57.2	66.7	59.4	61.3	53.0
(SD[a])	(10.1)	(12.4)	(9.9)	(12.9)	(9.7)	(10.6)
Age groups (yrs)	%	%	%	%	%	%
25-44	3.7	14.4	2.4	12.1	4.1	18.5
45-64	47.8	56.8	29.9	51.0	56.6	68.4
65-89	48.5	28.8	67.7	36.9	39.3	13.1
Cell types	*No. (%)*		*No. (%)*		*No. (%)*	
Adenocarcinoma	201 (35.3)		81 (49.4)		107 (29.0)	
Squamous cell	142 (25.0)		34 (20.7)		98 (26.5)	
Small cell	128(22.5)		16 (9.8)		104 (28.2)	
Large cell	30 (5.3)		8 (4.9)		21 (5.7)	
Carcinoma NOS[b]	68 (11.9)		25 (15.2)		39 (10.6)	
Microscopically confirmed	569 (100,0)		164 (100,0)		369 (100.0)	

[a]SD, standard deviation. [b]NOS, not otherwise specified.

basic anthropometric measures, such as standing height and weight.

Statistical methods

Descriptive statistics were used to characterize the study population. Statistical analyses were done using the unconditional logistic regression which provides results in the form of adjusted odds ratios. As the controls were not matched to cases, adjustment was done for age (in 5-year categories), residence, and education (as in Table 3), and, where appropriate, for the pack-years of smoking, as well. All adjusting variables were entered in the logistic regression as multiplicative and categorical factors. Tests for linear trend in tables were performed in equidistant categorical levels (1,2,…), even for numerical variables.

The comparison of relative risks between smokers (OR_2) and nonsmokers (OR_1) was based on the so called interaction in terms of the ratio of the relative risks. For statistical evaluation, the interaction was converted into a quantity:

$LR = \ln(OR_2/OR_1)$

with standard error (SE)

$SE(LR) = \sqrt{[SE(\ln(OR_2))^2 + SE(\ln(OR_1))^2]}$.

The statistical test of no interaction (LR=0) and the confidence intervals were based on a quantity z=LR/SE(LR) with approximate normal distribution.

Results

The variation in lung cancer risk by smoking habits is shown in Table 1. After adjusting for age, residence, and education, the odds ratios were 7.16 for current smokers, 7.91 for ex-smokers who stopped smoking less than 10 years ago, 2.42 for ex-smokers who stopped smoking 10-19 years ago, and 1.78 for ex-smokers who quit 20 or more years ago, all compared to never smokers. As evident, among ex-smokers, an inverse trend in the relative risk (odds ratio, OR) can be noted with years since quitting. High risk of lung cancer was observed among current smokers and ex-smokers who quitted less than 10 years ago. In contrast, the risk among women who stopped smoking 20 or more years ago was substantially lower.

Consequently, in the following part of this report, in addition to results for all study subjects (569 cases, 2120 controls), we present results comparing two groups of cases and controls: Group 1 'nonsmokers', including never smokers + long-term ex-smokers (quit 20 or more years ago); and Group 2 'smokers', containing current smokers + short-term ex-smokers (quit less than 10 years ago). The risk estimate for 'smokers' (OR=6.96) was highly contrasting in comparison to 'nonsmokers' (OR=1.00). The intermediate subgroup of ex-smokers who quit 10-19 years ago has not been included in either of the compared two groups because of substantial difference from either of them, however, the intermediate group has been included into the results for all study subjects.

The mean age of 'nonsmokers' was higher than that of smoking women, both among cases and controls (Table 2). As expected, among 164 nonsmoking cases, adenocarcinoma was the predominant cell type (49.4%), followed by squamous cell (20.7%) and small cell cancers (9.8%). Among 369 smoking cases, adenocarcinoma was diagnosed in 29.0%, followed by small cell (28.2%), and squamous cell cancers (26.5%) (Table 2).

Using odds ratios adjusted for age, risk estimates appeared elevated for rural residence among all study subjects, 'nonsmokers', and 'smokers', however, inversely associated with levels of education for all study subjects, and 'smokers' only, but not for 'nonsmokers' (Table 3).

Lung cancer risk estimates associated with food and beverage intake and physical exercise are shown in Table 4 for all study subjects. After adjustment for age, residence, education, and pack-years of smoking, a protective effect was observed for wine intake (OR=0.74, 95%CI 0.59-0.93). Fifteen per cent (86/569) of all cases, and 18% (381/2120) of controls only admitted any intake of spirits. An inverse association with the risk of lung cancer was observed for ever intake of spirits compared to never intake (OR=0.71, 95%CI 0.52-0.96). An inverse associations with the risk appeared for physical exercise (more than 1 hour per week; OR=0.67, 95%CI 0.52-0.86).

In Table 5, estimates of lung cancer risk associated with dietary items and physical exercise are given separately for Group 1 'nonsmokers', and Group 2 'smokers', and the results of the tests for interactions between smoking and other exposures are attached. In the group of 'nonsmokers', a protective effect of frequent (daily or several times per week) black tea drinking appeared (OR=0.66, 95%CI 0.47-0.94). Among 'smokers', protective effects were observed for fre-

Table 3. Socio-demographic variables and the risk of lung cancer, by smoking history

Variables	All study subjects			Group 1 "Nonsmokers"			Group 2 "Smokers"		
	Cases/ Controls	OR[a]	95%CI[b]	Cases/ Controls	OR[a]	95%CI[b]	Cases/ Controls	OR[a]	95%CI[b]
Residence									
Rural (≤100,000)	259/662	1.00	Referent	90/428	1.00	Referent	152/199	1.00	Referent
Urban (>100,000)	310/1458	0.50	0.41-0.61	74/850	0.36	0.26-0.51	217/494	0.45	0.33-0.60
Education									
Elementary	155/374	1.00	Referent	37/225	1.00	Referent	107/121	1.00	Referent
Secondary (ordinary)	215/687	0.82	0.64-1.06	71/397	1.28	0.82-1.99	135/240	0.66	0.46-0.95
Secondary (advanced)	165/832	0.59	0.45-0.76	45/496	0.84	0.52-1.37	107/279	0.51	0.35-0.73
University	34/227	0.46	0.30-0.70	11/160	0.72	0.35-1.49	20/53	0.41	0.22-0.76
Test for trend			P<0.001			P=0.175			P<0.001

[a]OR, odds ratio, adjusted for age. [b]CI, confidence interval.

quent intake of milk/dairy products (OR=0.57, 95%CI 0.35-0.94), vegetables (OR=0.60, 95%CI 0.40-0.91), apples (OR=0.69, 95%CI 0.51-0.92), and physical exercise (more than 1 hour per week; OR=0.59, 95%CI 0.42-0.83). In 'smokers', a borderline protective effect emerged for consumption of wine (OR=0.77, 95%CI 0.58-1.04).

The interactions between dietary items, physical activity and smoking ('smokers' versus 'nonsmokers') were statistically significant for black tea (P=0.005), and milk/dairy products (P=0.047). Borderline interactions (effect modifications) emerged for physical exercise (P=0.077) (Table 5).

Discussion

The concept of interaction in epidemiology is generally related to analyses of a multifactor etiology of chronic diseases and with the quantification of the joint effect of two or more potential risk factors acting in combination [9]. Such analyses sometimes use terms like synergism or antagonism. In the absence of precise knowledge of the biological mechanisms involved in the onset of the disease, synergism (or antagonism) is often used as a synonym for statistical interaction, ie. departure from additivity of the response variables of interest [9]. Another view of interaction is more general and the test of interactions is in fact the test of homogeneity of effects in different categories of a modifying factor. In our analyses, we used this view of interaction as effect modification, more precisely as a difference in the effect of a factor on disease risks depending on the presence or absence of another factor. The effect modification depends on the measure of effect used; modification of the relative risk (in case-control studies) is thus equivalent to a departure from a multiplicative model. It should be noted that sample sizes need to be at least four times larger to detect interactions than main effects of the same magnitude [10].

Our report presenting results of a hospital based case-control study on the relationship between diet, physical exercise, smoking and the risk of lung carcinoma among Czech women has certain potential limitations which should be considered before conclusions are drawn. The exposures of interest were based on self report, therefore, some recall bias is of concern. In evaluating factors of life style, potential confounding from other factors cannot be ruled out. Given the imperfect measurement of smoking history in epidemiological studies, it remains possible that the reported associations with diet or other factors could often be partly due to residual confounding by smoking. While smoking is known to be closely associated with less healthful nutrion habits [11], the associations between dietary factors and lung cancer are likely to be very weak in comparison to smoking. Therefore, it may be difficult to discern whether the dietary factors have truly been disentangled from the effects of smoking [4]. Merely controlling statistically for smoking may not be adequate, because nuances of smoking habits or susceptibility to cigarette smoke are not taken in account. In our study, all analyzed associations were adjusted for age, education, residence, and, were appropriate, in addition for tobacco consumption, which in our opinion should include large part of confounding. Smoking habits were collected from subjects by in-person interviews, and several characteristics of smoking were recorded. Our estimate of tobacco exposure was based on pack-years of cigarettes, which were categorized in analyses into four classes. Present findings were in addition checked by using continuous pack-years in logistic regression. As no substantial departure from present results emerged, we believe that residual confounding is minimal.

In the present study, a protective effect was observed for daily or several times per week intake of milk/dairy products for 'smokers' only (OR=0.57, 95%CI 0.35-0.94), however, not for the group of 'nonsmokers', the P-value of the test for interaction was statistically significant (P-value 0.047). Information on the type of milk (whole or low-fat) was not available in the present study. In a case–control study of 569 lung cancer cases (of these, 214 women) and 569 matched controls in Buffalo, subjects reporting consumption of whole milk three or more times daily had a twofold increase in lung cancer risk compared with

Table 4. Diet, alcohol consumption, physical exercise, and the risk of lung cancer.

	All study subjects (569 cases, 2120 controls)					
Adjusted for:			*age, res, edu* [a]		*age, res, edu, py* [b]	
Variables	Cases	Controls	OR [a]	95%CI [c]	OR [b]	95%CI [c]
Red meat [d]	263	912	1.32	1.08 – 1.61	1.20	0.97 – 1.49
Poultry [d]	343	1312	0.94	0.77 – 1.15	0.93	0.75 – 1.15
Milk, dairy products [d]	523	1983	0.70	0.49 – 1.01	0.80	0.54 – 1.20
Vegetables [d]	479	1903	0.62	0.46 – 0.82	0.76	0.56 – 1.05
Apples [d]	386	1635	0.62	0.50 – 0.76	0.81	0.64 – 1.03
Citrus fruits [d]	350	1309	1.01	0.83 – 1.24	1.11	0.89 – 1.38
Other fruits [d]	338	1315	0.97	0.79 – 1.18	1.01	0.81 – 1.25
Black tea [d]	263	1022	0.93	0.76 – 1.13	0.99	0.80 – 1.23
Green tea [f]	188	805	0.84	0.68 – 1.03	0.92	0.73 – 1.15
Coffee [d]	466	1726	1.18	0.92 – 1.52	0.85	0.64 – 1.12
Beer [f]	254	944	0.96	0.79 – 1.17	1.01	0.82 – 1.25
Wine [f]	192	917	0.79	0.64 – 0.97	0.74	0.59 – 0.93
Spirits [f]	86	381	0.94	0.72 – 1.23	0.71	0.52 – 0.96
Physical exercise, sport, or walking [g]	420	1747	0.61	0.48 – 0.77	0.67	0.52 – 0.86

[a] OR, odds ratio, adjusted for age, residence and education.
[b] OR, odds ratio, adjusted for age, residence, education and pack-years of smoking.
[c] CI, confidence interval.
[d] Daily or several times per week
[e] Weekly or less, but more than once per month / Daily or several times per week
[f] Monthly or less / Weekly or less / Daily or several times per week.
[g] Physical exercise, sport, or walking, more than 1 hour per week.

those who reported never drinking whole milk. The same frequency of low-fat milk intake was associated with a significant protective effect [12]. In a population-based study of 413 matched case–control pairs of non-smoking subjects in New York State, consumption of greens, fresh fruits and cheese was associated with a significant dose-dependent reduction in risk for lung cancer, whereas consumption of whole milk was associated with a significant dose-dependent increase in risk [13]. In a case-control study of 982 lung cancer cases (of these, 315 women) and 1486 population controls, Darby et al. [14] observed an increase in risk associated with increasing consumption of whole milk but not of skimmed milk. In the study of Darby et al., there was no evidence of an association with lung cancer risk for cheese consumption. In contrast, in a German study of 234 non-smoking female lung cancer cases and 535 controls, protective effects with high intakes of cheese, milk and other dairy products were observed, showing a statistically significant trend with consumption of cheese [15].

The effect of black tea on inhibiting tumorigenesis that has been observed in some studies and has been supposed to be related to the high content of some flavonoids, particularly quercetin, which is also present in onions and apples, and has been found to constitute 75% of the total flavonoid intake of the average Dutch subject [16]. In the present study, we found a significantly decreased risk of lung cancer for women in group 1 – 'nonsmokers' consuming black tea daily or several times per week (OR=0.66, 95%CI 0.47-0.94), while no significant association was observed among 'smokers' (OR=1.24, 95%CI 0.93-1.65), resulting in the test of interaction P-value 0.005 (Table 5). In the literature, data on risk of lung cancer among tea drinkers are scanty. In a review of the epidemiological evidence, Blot et al. [17] quoted 3 case-control, and 4 cohort studies, however, in all of them except one no association was noted. The one significant association reported came from a cohort study of British men, showing rising risks of lung cancer with increasing consumption of tea [18]. Most of this trend, however, seems related to confounding factors, especially the rising prevalence of cigarette smoking with rising tea intake. In a case-control study among never smoking women in eight Canadian provinces (161 cases and 483 population controls), a significant inverse association was found between consumption of tea and the risk of lung cancer [19]. In a population based case-control study among women in Shanghai, China (649 cases 675 controls) the consumption of green tea was associated with reduced risk of lung cancer among nonsmoking women (OR=0.65, 95%CI 0.45-0.93), and the risk decreased with increasing consumption, however, little association was found among women who smoked (OR=0.94, 95%CI 0.40-2.22) [20].

Reviewing the scientific evidence on the role of physical activity in cancer prevention, Friedenreich and Orenstein [21] identified 11 studies examining physical activity as a risk factor of lung cancer, of which 8 found a risk reduction. In the report of the IARC Working Group on the Evaluation of Cancer Preventive Strategies [22], five cohort studies and two case-control studies have been listed. In all of the cohort stud-

Table 5. Diet, alcohol consumption and the risk of lung cancer, by smoking history. Test for interactions.

	Group 1 'nonsmokers'				Group 2 'smokers'				Test for interactions		
Variables	Cases	Cont-rols	OR [a]	95%CI [b]	Cases	Cont-rols	OR [a]	95%CI [b]	Ratio OR2/OR1	95%CI [b]	P-vaIue [c]
Red meat [d]	69	529	1.24	0.88 – 1.77	176	315	1.26	0.95 – 1.67	1.02	0.65 – 1.59	0.943
Poultry [d]	91	771	0.84	0.59 – 1.19	229	434	1.03	0.77 – 1.39	1.23	0.78 – 1.94	0.374
Milk, dai ry products [d]	157	1204	1.48	0.65 – 3.38	332	638	0.57	0.35 – 0.94	0.39	0.15 – 1.01	0.047
Veget-ables [d]	146	1146	0.97	0.56 – 1.68	300	619	0.60	0.40 – 0.91	0.62	0.31 – 1.23	0.161
Apples [d]	128	1010	0.87	0.57 – 1.32	227	507	0.69	0.51 – 0.92	0.79	0.47 – 1.32	0.366
Citrus fruits [d]	106	812	1.06	0.74 – 1.52	218	413	1.06	0.79 – 1.41	1.00	0.63 – 1.59	1.000
Other fruits [d]	98	797	0.99	0.69 – 1.40	215	433	0.96	0.72 – 1.28	0.97	0.61-1.53	0.893
Black tea [d]	69	665	0.66	0.47 – 0.94	174	286	1.24	0.93 – 1.65	1.88	1.20 – 2.95	0.005
Green tea [f]	58	503	0.90	0.63 – 1.30	117	231	1.02	0.75 – 1.38	1.13	0.71 – 1.82	0.597
Coffee [d]	117	974	0.86	0.59 – 1.26	319	629	0.76	0.49 – 1.19	0.88	0.49 – 1.58	0.672
Beer [f]	78	582	1.01	0.72 – 1.42	167	291	1.17	0.88 – 1.55	1.16	0.74 – 1.80	0.506
Wine [f]	54	520	0.89	0.61 – 1.30	127	320	0.77	0.58 – 1.04	0.87	0.54 – 1.40	0.544
Spirits [f]	18	206	0.81	0.47 – 1.40	65	140	0.84	0.58 – 1.21	1.18	0.75 – 1.87	0.455
Physical exercise [g]	133	1061	0.97	0.62 – 1.52	263	559	0.59	0.42 – 0.83	0.61	0.35 – 1.07	0.077

[a] OR, odds ratio, adjusted for age, residence and education.
[b] CI, confidence interval.
[c] P-value (test for interaction)
[d] Daily or several times per week
[e] Weekly or less, but more than once per month / Daily or several times per week
[f] Monthly or less / Weekly or less / Daily or several times per week.
[g] Physical exercise, sport, or walking, more than 1 hour per week.

ies, a lower risk of lung cancer was associated with physical activity. The largest studies were the Harvard Health Alumni Study [23], and a population-based cohort study in Norway [24]. The Norwegian scientists measured both recreational and occupational activity, and found a 30% decreased risk when these activities were combined into a total activity variable for the male study subjects, but no comparable risk decrease was observed for females. In our study, an inverse association was found between lung cancer risk and time (hours/week) devoted to physical exercise among smoking women (OR=0.59, 95%CI 0.42-0.83), while no significant decrease in risk appeared among nonsmokers, The P-value of the test for interaction was 0.077 (Table 5). It should be noted that if all study subjects were evaluated together (569 cases, 2120 controls), significant inverse statistical association of physical exercise with lung cancer risk was found (OR=0.67, 95%CI 0.52-0.86) (Table 4).

In conclusion, our findings support the opinion that diet and physical exercise are important factors contributing to variation in risk among women in the Czech Republic; their importance seems to vary in relation to status of smoking, the dominant factor in the aetiology of lung cancer. In the present study, a protective effect was observed among nonsmoking women frequently drinking black tea. Among smoking women, protective effects appeared for milk/dairy products, vegetables, apples and physical exercise, while the inverse statistical association for wine was not significant. The observed interactions (effect modifications) of the impact of some dietary items upon lung cancer risk in women at different levels of the smoking habit deserve further studies.

This work was supported by the Internal Grant Agency (IGA) of the Ministry of Health of the Czech Republic grant # NR/8411-3.

References

[1] IARC Monographs on the Evaluation of Carcinogenic Risks to Humans, Vol 83. Tobacco smoke and involuntary smoking. Lyon: IARC Press, 2004.

[2] Samet JM. Epidemiology of lung cancer. New York, NY: Marcel Dekker, 1994.

[3] Shields PG. Molecular epidemiology of smoking and lung cancer. Oncogene 2002; 21: 6870-6.

[4] Ekberg-Aronsson M, Nilsson PM, Nilsson J-A, et al. Socioeconomic status and lung cancer risk including histologic subtyping – A longitudinal study. Lung Cancer 2006; 51: 21—29.

[5] Alberg AJ, Samet JM. Epidemiology of lung cancer. Chest 2003; 123: 21S-49S.

[6] Clapp RW, Howe GK, Jacobs M. Environmental and occupational causes of cancer re-visited. J Publ Health Policy 2006; 27: 61-76.

[7] Kubik A, Zatloukal P, Boyle P, et al. A case-control study of lung cancer among Czech women. Lung Cancer 2001; 31: 111-122.

[8] Kubik AK, Zatloukal P, Tomasek L, et al. Lung cancer risk among Czech women: A case-control study. Prev Med 2002; 34: 436-444.

[9] Kupper LL, Hogan MD. Interactions in epidemiologic studies. Am J Epidemiol 1978; 108: 447-453.

[10] Smith P, Day NE. The desing of case-control studies: The influence of confounding and interactions effects. Int J Epidemiol 1984; 13: 356-365.

[11] Morabia A, Wynder EL. Dietary habits of smokers, people who never smoked, and exsmokers. Am J Clin Nutr 1990;52:933-937.

[12] Mettlin C. Milk drinking, other beverage habits and lung cancer risk. Int J Cancer 1989; 43: 608-612.

[13] Mayne ST, Janerich DT, Greenwald P, et al. Dietary beta carotene and lung cancer risk in U.S. nonsmokers. J Natl Cancer Inst 1994; 86: 33-38.

[14] Darby S, Whitley E, Doll R, et al. Diet, smoking and lung cancer: a case-control study of 1000 cases snd 1800 controls in South-West England. Br J Cancer 2001; 84: 728-735.

[15] Kreuzer M, Heinrich J, Kreienbrock L, et al. (2002). Risk factors for lung cancer among nonsmoking women. Int J Cancer 2002; 100: 706-713.

[16] Hertog MGI, Hollman PCH, Krombhout D. Determination of potentially anticarcinogenic flavonoids in foods and preliminary results of daily intake in the Netherlands. In: Waldron KW, Johnson IT, Fenwick GR, editors. Food and cancer prevention: chemical and biological aspects. Cambridge: Royal Society of Chemistry, 1993: 198-202.

[17] Blot WJ, Chow W-H, McLaughlin JK. Tea and cancer: a review of the epidemiological evidence. Eur J Cancer Prevention 1996; 5: 425-438.

[18] Kinlen LJ, Willows AN, Goldblatt P, et al. Tea consumption and cancer. Br J Cancer 1988;58: 397-401.

[19] Hu J, Mao Y, Dryer D, et al.(2002). Risk factors for lung cancer among Canadian women who have never smoked. Cancer Detect Prev 2002; 26: 129-138.

[20] Zhong L, Goldberg MS, Gao YT, et al. A population-based case-control study of lung cancer and greeen tea consumption among women living in Shanghai, China. Epidemiology 2001; 12: 695-700.

[21] Friedenreich CM, Orenstein MR. Physical activity and cancer prevention: etiologic evidence and biological mechanisms. J Nutr 2002; 132(11Suppl): 3456S-64S.

[22] IARC Working Group on the Evaluation of Preventive Strategies. Weight Control and Physical Activity. International Agency for Research on Cancer Handbooks of Cancer Prevention Volume 6. Lyon: IARC Press, 2002.

[23] Lee I-M, Sesso HD, Paffenbarger RS, Jr. Physical activity and risk of lung cancer. Int J Epidemiol 1999; 28: 620–625.

[24] Thune I, Lund E. The influence of physical activity on lung cancer risk. A prospective study. Int J Cancer 1997; 70: 57-62.