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Lung cancer risk among nonsmoking women in relation to diet and physical activity*

A. KUBÍK¹, P. ZATLOUKAL¹, L. TOMÁŠEK², N. PAUK¹, L. PETRUŽELKA³, I. PLEŠKO^{4,5}

¹Department of Pneumology and Thoracic Surgery, e-mail: kubika@email.cz; Charles University, 3rd Faculty of Medicine, University Hospital Na Bulovce, and Postgraduate Medical Institute, 18081 Prague, ²National Radiation Protection Institute, Prague, and ³Department of Oncology, Charles University, 1st Faculty of Medicine, General Faculty Hospital, Prague, Czech Republic; ⁴National Cancer Registry, Bratislava, and ⁵Cancer Research Institute of Slovak Academy of Sciences, Bratislava, Slovak Republic

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To investigate the relationship between diet, physical activity, and the risk of lung cancer among female nonsmokers, and to compare it with female smokers in the same population, we conducted a case-control study. Data collected by personal interviews from 419 cases and 1593 controls were analyzed using unconditional logistic regression. As expected, among 130 nonsmoking cases, adenocarcinoma was the predominant cell type (49.2%), followed by squamous cell (20.2%) and small cell cancers (10.5%). The corresponding figures for 289 smoking cases were 29.3%, 27.5%, and 28.2%, respectively. Excess lung cancer risk was associated with consumption of red meat among nonsmokers (OR=2.20, 95% CI 1.07–4.51). Protective effects were observed for vegetables (OR=0.61, 95% CI 0.39–0.96), apples (OR=0.67, 95% CI 0.48–0.95), milk/dairy products (OR=0.54, 95% CI 0.32–0.93), coffee (OR=0.56, 95% CI 0.34–0.91), and wine (OR=0.69, 95% CI 0.49–0.98) among smokers only, and for black tea (OR=0.67, 95% CI 0.46–0.99) among nonsmokers only. An inverse association with risk emerged for physical exercise (or sport, walking), among smokers only. Some items of diet and physical activity appear to be important factors contributing to variation in lung cancer risk among women in the Czech Republic, however, their effects in nonsmokers may differ from those in smokers.

Key words: lung cancer, diet, physical activity, smoking, women, epidemiology

Along with tobacco use, dietary intake and physical activity are important risk factors for cancer that can be modified through lifestyle change. In the United States, evidence suggests that one third of the more than 500,000 cancer deaths occurring each year can be attributed to diet and physical activity habits, with another third due to cigarette smoking [9].

While tobacco smoke has been found to be one of the major causes of lung cancer among the female population of many developed countries, various types of epidemiological research, including ecological, case-control, prospective studies, and randomized controlled trials, have indicated that diet may be one of the cofactors in the cause of lung cancer [8]. However, the relative importance and contribu-

tion of diet and physical activity habits to the risk of cancer may vary with geographic area and socioeconomic conditions. Our case control study has been done in the Czech Republic, where the population has been consuming a typical Central European diet rich in foods from animal sources and lacking in fresh fruit and vegetables, in the second half of the past century [12].

The purpose of our hospital-based case-control study was to examine the risk of lung cancer in relation to diet and physical exercise among nonsmoking, and smoking women in the Czech Republic. This report presents results based on 451 cases and 1,710 controls, all interviewed in 1998–2002.

Material and methods

Study sample and data collection. A hospital-based casecontrol study of lung cancer among women was conducted

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Table 1. Smoking habits and the risk of lung cancer

		Smoking habits						
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	Never smokers	Quit >20 years ago	Quit10-19 years ago	Quit <10 years ago	Current smokers			
Cases/Controls	111/933	19/89	32/117	114/157	175/414			
Odds ratio (OR) ^a	1.00	1.68	2.90	8.66	6.24			
95% CI ^b	Referent	0.96-2.94	1.80-4.66	6.07–12.35	4.56-8.53			
			(Excluded from comparison)					
	Group 1 N	Ionsmokers		Group 2 Si	nokers			
Cases/Controls	13	0/1022		289	9/571			
Odds ratio (OR) ^a	1.0	00		1				
95% CI ^b	Re	eferent		5.02-8.71				

^aOR – odds ratio, adjusted for age, residence, and education; ^bCI – confidence interval.

in the Prague University Hospital Na Bulovce, departments of pneumology, thoracic surgery, and internal medicine. To be included as a case, female lung cancer patient had to be admitted between April 1998 and November 2002. Controls were all women, and were spouses, relatives, or friends of other patients hospitalized at the same department as the cases. Both cases and controls had to be aged 25-89 years, and reside within the catchment area covering the northeastern sectors of Prague and the adjacent Central Bohemia Region (10 administrative districts). Personal interviews were completed for 451 cases (89% of those eligible) and 1710 controls (response rate 79%). 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 interinterviewer variation.

Questionnaire and definitions. The questionnaire has been described previously elsewhere [20, 21]. In brief, the questionnaire included a basic structured section on demographic characteristics; place of residence; type of house, occupation and workplace; further, 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, we present the results for 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) (Tab. 1).

The questionnaire included sections on exposure to environmental tobacco smoke (passive smoking) in adult age and in childhood; physical activity (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 obstetric and gynecologic history. Information on dietary habits was collected with 9 food items (red meat, poultry, fish, milk and dairy products, fat-rich foods, vegetables, apples, citrus fruit, other fruit); four nonalcoholic beverage items (black tea, green tea, herbal tea, coffee), and three alcoholic beverage categories (beer, wine, and spirits). The subject was asked to choose one of the four frequency categories of consumption: 1. Never, 2. Monthly or less, 3. Weekly or less, but more than once per month, and 4. Daily or several times per week. The frequency estimate should reflect the average consumption within the past 10 years. After completion of the questionnaire, the trained interviewer took basic anthropometric measures, such as standing height and weight. For subjects interviewed in 2000-2002, additional questions were asked concerning physical activity 1 and 20 years before the interview.

Statistical methods. Descriptive statistics were used to characterize the study population. Statistical analyses were done using 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 10-year categories), residence, and education. All adjusting variables were entered in the logistic regression as multiplicative and categorical factors (cut points as in Tab. 2). Tests for linear trend in tables were performed in equidistant categorical levels (1, 2,...), even for numerical variables.

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

Variables	Case	es	Controls			
	Group 1	Group 2	Group 1	Group 2		
	Nonsmokers	Smokers	Nonsmokers	Smokers		
Population	130	289	1022	571		
Mean age (SD ^a)	67.2 (10.2)	61.4 (10.3)	59.5 (13.5)	52.6 (10.9)		
Age groups (yrs)	No. (%)	No. (%)	No. (%)	No. (%)		
25-34		3 (1.0)	45 (4.4)	36 (6.3)		
35-44	2 (1.5)	12 (4.1)	89 (8.7)	78 (13.7)		
45-54	17 (13.1)	61 (21.1)	234 (22.9)	234 (41.0)		
55-64	22 (16.9)	97 (33.6)	265 (25.9)	147 (25.7)		
65-74	56 (43.1)	90 (31.2)	237 (23.2)	54 (9.5)		
75–84	31 (23.9)	24 (8.3)	137 (13.4)	22 (3.8)		
85–89	2 (1.5)	2 (0.7)	15 (1.5)	´		
Cell types	No. (%)	No. (%)				
Adenocarcinoma	61 (49.2)	82 (29.3)				
Squamous cell	25 (20.2)	77 (27.5)				
Small cell	13 (10.5)	79 (28.2)				
Large cell	7 (5.6)	19 (6.8)				
Carcinoma NOS ^b	18 (14.5)	23 (8.2)				
Microscopically confirmed	124 (100.0)	280 (100.0)				
Clinical diagnosis	6 –	9 –				

^a SD – standard deviation, ^bNOS – not otherwise specified.

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 6.24 for current smokers, 8.66 for ex-smokers who stopped smoking less than 10 years ago, 2.90 for ex-smokers who stopped smoking 10-19 years ago, and 1.68 (95% CI 0.96–2.94) 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 (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 much lower, and not significantly different from that in never smokers.

Consequently, in the following part of this report, we present results for two groups of cases and controls: Group 1, Nonsmokers, includes never smokers + long-term exsmokers (quit 20 or more years ago); and Group 2, Smokers, contains current smokers + short-term ex-smokers (quit less than 10 years ago). The risk estimate (OR) for "Smokers" was 6.6 times higher than among "Nonsmokers". For brevity, the small intermediate group of ex-smokers who quit 10–19 years ago was excluded from comparison (Tab. 1).

The mean age of "Nonsmokers" was higher than that of

smoking women, both among cases and controls (Tab. 2). The most numerous age-group among nonsmoking cases was 65–74 years, among smoking cases 55–64, among nonsmoking controls 55–64, and among smoking controls 45–54 years. As expected, among 130 nonsmoking cases, adenocarcinoma was the predominant cell type (49.2%), followed by squamous cell (20.2%) and small cell cancers (10.5%). Among 289 smoking cases, adenocarcinoma was diagnosed in 29.3%, followed by small cell (28.2%), and squamous cell cancers (27.5%) (Tab. 2).

Using odds ratios adjusted for age, risk estimates appeared elevated for rural residence among both "Nonsmokers" and "Smokers", however, inversely associated with levels of education for "Smokers" only (Tab. 3).

Risk estimates of cancer of the lung for food and beverage intake are shown in Table 4. Excess lung cancer risk was associated with consumption of red meat among "Nonsmokers" (OR=2.20, 95% CI 1.07–4.51), however, no significant increase in risk was found among "Smokers"

(OR=1.07, 95% CI 0.65–1.76).

Among "Smokers" only, protective effects were observed for several times per week or daily consumption of vegetables (OR=0.61, 95% CI 0.39–0.76), apples (OR=0.67, 95% CI 0.48–0.95), milk/dairy products (OR=0.54, 95% CI 0.32–0.93), and coffee (OR=0.56, 95% CI 0.34–0.91), no such decreases in risk were observed among "Nonsmokers" (Tab. 4).

A protective effect was apparent for drinking black tea (OR=0.67, 95% CI 0.46–0.99) in the group of "Nonsmokers" only. Drinking wine was associated with a statistically significant protective effect among "Smokers" (OR=0.69, 95% CI 0.49–0.98), while the risk of lung cancer was similarly reduced even for wine intake among "Nonsmokers", however, the latter statistical association was not statistically significant (OR=0.65, 95% CI 0.41–1.03).

Among "Smokers" only, physical exercise (or sport, walking, within recent ten years) was inversely associated with lung cancer risk (Tab. 5). Among "Smokers", for the category of physical exercise (or sport, walking) of more than 6 hours per week the odds ratio was 0.48 (95% CI 0.32–0.71), compared to 0–2 hours per week.

The questionnaire used in the years 2001–2003 included additional questions on physical exercise (or sport, walking) one and twenty years before the interview. In group 2, Smokers, similar statistically nonsignificant decreases in lung cancer risk were observed for physical exercise 1 year,

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

		Group 1 No	nsmokers			Group 2 Smokers		
Variables	Cases	Controls	OR^a	95% CI ^b	Cases	Controls	OR^a	95% CI ^b
Residence								
Rural (≤100,000)	68	347	1.00	Referent	116	164	1.00	Referent
Urban (>100,000)	62	675	0.41	0.28-0.61	173	407	0.42	0.30-0.59
Education								
Elementary	31	192	1.00	Referent	94	104	1.00	Referent
Secondary (ordinary)	55	314	1.30	0.80 - 2.12	102	194	0.59	0.40-0.89
Secondary (advanced)	36	387	0.90	0.52 - 1.54	80	225	0.46	0.31-0.69
University	81	29	0.69	0.30 - 1.60	13	48	0.31	0.15-0.62
Test for trend				P=0.287				P<0.001

^aOR – odds ratio, adjusted for age; ^bCI – confidence interval.

Table 4. Diet, alcohol consumption and the risk of lung cancer, by smoking history

		Group 1 No	Group 1 Nonsmokers			Group 2 Smokers		
Variables	Cases	Controls	OR^a	95% CI ^b	Cases	Controls	OR^a	95% CI ^b
Red meat ^d	121	874	2.20	1.07-4.51	256	509	1.07	0.65-1.76
Poultry ^d	123	992	0.68	0.28 - 1.67	281	553	1.61	0.64-4.05
Fish ^d	88	705	1.09	0.72 - 1.65	202	369	1.33	0.94-1.88
Milk, dairy products ^c	123	959	1.29	0.56-2.96	258	522	0.54	0.32-0.93
Fat-rich foods ^d	54	501	0.88	0.60-1.30	143	336	0.81	0.59-1.12
Vegetables ^c	117	907	1.19	0.63 - 2.27	233	507	0.61	0.39-0.96
Apples ^c	106	827	1.02	0.62 - 1.67	182	425	0.67	0.48-0.95
Citrus fruits ^c	85	678	0.96	0.64-1.44	184	361	1.00	0.72 - 1.39
Other fruits ^d	121	957	1.01	0.48-2.13	256	532	0.60	0.34-1.04
Black tea ^d	69	631	0.67	0.46-0.99	163	293	1.22	0.89-1.67
Green tea ^e	40	372	0.88	0.58 - 1.34	87	175	1.16	0.82 - 1.64
Herbal tea ^c	89	670	1.13	0.75 - 1.71	169	317	1.04	0.76-1.43
Coffee ^c	91	761	0.90	0.59-1.38	246	521	0.56	0.34-0.91
Beer ^e	48	406	0.83	0.56-1.23	116	221	1.14	0.82-1.57
Wine ^e	29	355	0.65	0.41-1.03	80	241	0.69	0.49-0.98
Spirits ^e	8	130	0.55	0.25-1.18	42	101	0.82	0.53-1.27

^aOR – odds ratio, adjusted for age, residence and education; ^bCI – confidence interval; ^cDaily or several times per week; ^d(Weekly or less, but more than once per month)+(Daily or several times per week); ^c(Monthly or less)+(Weekly or less)+(Daily or several times per week).

and 20 years before the interview. No such variations in risk were apparent among "Nonsmokers".

Discussion

Few data are available to explain the on-going increase in lung cancer mortality among women in the Czech Republic, a Central European country with a population of over 10 million, 5726 deaths from lung cancer (of these, 1246 in women), and a per caput sale of 1882 cigarettes in the year 2000 [10, 19]. The overwhelming contribution of cigarette smoking as a cause of lung cancer imposes challenges to detecting the role that other lifestyle factors, such as diet, may play in the etiology of lung cancer [2]. Associations

between dietary factors and lung cancer risk are likely to be very weak, while tobacco smoke is far and away the most important cause of lung cancer.

Some studies have suggested that diet may vary in relation to smoking habits and physical activity. Nutrient intakes, and circulating levels of nutrients of smokers were found to be different from those of nonsmokers [23, 26]. A correlation between physical activity and dietary behaviors were found in a cross-sectional study of 1322 male and female participants interviewed in a large managed-care organization in Boston, Massachusetts. Suboptimal diet and sedentary behavior tended to cluster in individuals who were less educated, not married, and of nonwhite race [14].

While there are over 200 studies on the association be-

Table 5. Physical activities^{a,b} and the risk of lung cancer, by smoking history

Variables		Group 1 Nonsmokers			Group 2 Smokers			
	Cases	Controls	ORc	95% CI ^d	Cases	Controls	ORc	95% CI ^d
Physical exercise ^a								
(within recent 10 year)								
0–2 hours/week	40	280	1.00	Referent	126	167	1.00	Referent
3–6 hours/week	51	357	1.08	0.67 - 1.73	89	180	0.70	0.47-1.03
>6 hours/week	39	385	0.74	0.45 - 1.22	74	224	0.48	0.32-0.71
Test for trend				P=0.210				P<0.001
Other physical activities	s^{b}							
(within recent 10 year)								
0–2 hours/week	48	389	1.00	Referent	128	217	1.00	Referent
3–6 hours/week	24	268	0.83	0.48 - 1.44	68	145	0.82	0.54-1.25
>6 hours/week	58	365	1.22	0.77 - 1.92	93	209	0.71	0.49-1.04
Test for trend				P=0.358				P=0.074
Physical exercise ^a								
(1 year before interview	v)							
0–2 hours/week	39	228	1.00	Referent	89	137	1.00	Referent
3–6 hours/week	28	188	1.00	0.57 - 1.77	39	101	0.78	0.46-1.31
>6 hours/week	21	166	1.01	0.54-1.86	36	114	0.63	0.37-1.05
Test for trend				P=0.980				P=0.069
Physical exercise ^a								
(20 years before intervi	ew)							
0–2 hours/week	20	122	1.00	Referent	48	84	1.00	Referent
3–6 hours/week	25	155	1.06	0.53-2.11	50	101	0.89	0.51-1.55
>6 hours/week	43	305	1.04	0.56-1.94	66	167	0.73	0.44-1.23
Test for trend				P=0.914				P=0.227

^aPhysical exercise, or sport, walking; ^bOther non-occupational physical activities (e.g., in the garden, house); ^cOR – odds ratio, adjusted for age, residence and education; ^dCI – confidence interval.

tween vegetables, fruits and lung cancer, considerably fewer studies refer to lung cancer risk related to meats, poultry, fish, dairy products, alcohol and others [7]. The results on the role of meat in lung cancer risk have been inconsistent. Some studies showed an association between meat consumption and lung cancer risk [28], while others did not [3]. In a case-control study of 234 nonsmoking female lung cancer cases and 535 controls in Germany [18], a non-significantly 1.6 fold increased lung cancer risk was associated with daily consumption of meat (OR=1.61, 95% CI 0.90-2.89). In the present study, we found a significantly increased risk of lung cancer for women in group 1 "Nonsmokers" (OR=2.20, 95% CI 1.07-4.51) consuming red meat at a higher frequency than once per month, however, not for group 2 "Smokers" (OR=1.07, 95% CI 0.65-1.76). In a recent multicenter case-control study of 506 non-smoking lung cancer cases and 1045 controls in 8 centers in Europe [6], excess risk associated with meat consumption was restricted to squamous and small cell carcinomas, but was not apparent for adenocarcinomas. The inconsistencies in studies across continents might be due, in part, to different cooking methods. Burning or charring food is known to create many substances that are mutagenic. In meats cooked at high temperatures, several heterocyclic amines were found, however, the intake of some of them was not associated with lung cancer risk, while 2-amino-3,8-dimethylimidazo[4,5f]quinoxaline was associated with increased risk of lung cancer for nonsmokers and light/moderate smokers, but not for heavy smokers [29].

In the present study, we found an inverse relationship between frequent (daily or several times per week) intake of milk/dairy products and the risk of lung cancer for women in group 2 "Smokers" (OR=0.54, 95% CI 0.32-0.93), however, not for group 1 "Nonsmokers" (OR=1.29, 95%CI 0.56–2.96). In the German study of 234 nonsmoking 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 [18]. Information on the type of milk (whole, or reduced-fat) was not available in the German or our studies. 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 3 or more times daily had a 2-fold increase in lung cancer risk compared to those who reported never drinking whole milk. The same frequency of intake reduced-fat milk was associated with a significant protective effect [25]. In a population-based study of 413 matched case-control pairs of nonsmoking 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 [24].

The inverse relationship between intake of vegetables and fruits and risk of lung cancer represents one of the best established associations in the field of nutritional epidemiology [35]. In a review of over 200 studies that examined the relationship between fruit and vegetable intake and 10 types of cancer, including lung cancer, a statistically significant protective effect of fruit and vegetable consumption was found in 128 of 156 dietary studies in which results were expressed in terms of relative risk [4]. In a prospective study of 77 283 women in the Nurses' Health Study and 47 778 men in the Health Professionals' Follow-up Study higher fruit and vegetable intakes were associated with lower risks of lung cancer in women but not in men [11]. In a hospitalbased case-control study in women in Barcelona, Spain, a reduction in risk, adjusted for smoking habits, was found for the intake of yellow/orange vegetables (mainly carrots) and tomatoes [1]. In a population-based case-control study of non-smoking 124 cases and 235 controls (of these, more than two thirds were women) in Stockholm, Sweden, a protective effect was suggested for vegetables, mediated primarily by carrots, and non-citrus fruits [27]. In the present study, we found significant inverse relationships between the risk of lung cancer and frequent intake (daily or several times per week) of vegetables (OR=0.61, 95% CI 0.39-0.96) and apples (OR=0.67, 95% CI 0.48–0.95), and a statistically nonsignificant inverse association with intake of other noncitrus fruits (OR=0.60, 95% CI 0.34–1.04) for group 2 "Smokers" only, no such protective effects were apparent among "Nonsmokers".

Data on risk of lung cancer among tea drinkers are scanty. In a review of the epidemiological evidence BLOT et al [5] quoted 3 case-control, and 4 cohort studies, however, in all of them except for 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 [17]. Most of this trend, however, seems related to confounding factors, especially the rising prevalence of cigarette smoking with the 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 [15]. 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) [36]. In the present study, black tea drinking, at a higher frequency than once per month, was inversely associated with lung cancer risk among "Nonsmokers" (OR=0.67, 95% CI 0.46–0.99), while no significant association was found among "Smokers" (OR=1.22, 95% CI 0.89–1.67).

Studies on association between coffee drinking and lung cancer risk are scarce [31]. In a Norwegian cohort study of 43,000 subjects, some increase in lung cancer risk among men, but not in women was found [30]. In our study, coffee drinking daily or several times per week was significantly inversely associated with the risk of lung cancer among "Smokers".

Physical activity is important in the prevention of a variety of diseases and conditions [33]. Because occupational physical activity is now uncommon in westernized countries, many countries monitor only leisure-time physical activity [16]. Physical activity is one of the factors related to cancer that can be modified through lifestyle change. The evidence for decreased risk with increased physical activity has been classified as convincing for breast and colon cancers, probable for prostate cancer, and possible for lung and endometrial cancers. Hypotheses on biological mechanisms include changes in endogenous sexual and metabolic hormone levels and growth factors, decreased obesity, and possibly changes in the immune function [13]. With regard to lung cancer, Norwegian investigators [32] hypothesized that increased pulmonary ventilation and perfusion could reduce carcinogenic agent-airway interaction time, concentration of such agents in the airways, as well as diminish amount and influence location of particle deposition in the airways. Recommendations for individual choices of the American Cancer Society [9] include engaging in at least moderate physical activity for 30 minutes or more on five or more days of the week.

In a review of scientific evidence on physical activity and cancer prevention FRIEDENREICH and ORENSTEIN [13] 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 [16], five cohort studies and two case-control studies have been listed. In all of the cohort studies, a lower risk of lung cancer was associated with physical activity. The largest studies were the Harvard Health Alumni Study [22], and a population-based cohort study in Norway [32]. 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. The Norwegian study indicates that four hours per week of hard leisure-time activity can reduce lung cancer risk independently after adjustment for smoking and other possible risk factors [16].

In our study, an inverse association was found among

"Smokers" between lung cancer risk and time (hours/week) devoted to physical exercise (or sport, walking, within recent 10 years). During the ongoing investigation we have realized that preclinical cancer is a well-known cause of weight loss and may also lead to a reduction in physical activity. Lack of physical activity shortly before diagnosis of lung cancer may more likely be the result, rather than the cause, of preclinical disease. Therefore, two additional questions were affixed to the questionnaire, related to physical exercise (sport, walking) one year prior to diagnosis, and twenty years prior to diagnosis. Using these two additional questions in 2000-2002, a statistically nonsignificant inverse association of lung cancer risk with physical exercise 1 and 20 years before interview was found among "Smokers", however, not among "Nonsmokers" (Tab. 5). If the assessment of physical activity were too close to the point of clinical disease, an accurate picture of the relationship between physical activity and lung cancer could not be obtained. Another serious problem in case-control studies is that many factors can influence the recall or reporting of physical activity and diet [16].

In conclusion, the evidence of a beneficial effects of physical activity and healthful diet on cancer risk is accumulating, although for lung cancer it has been classified as possible and remains inconclusive. In the present study of factors related to lung cancer risk among women in the Czech Republic, a positive association with lung cancer risk for red meat, and an inverse association with black tea were found in nonsmokers. Among smokers, inverse associations appeared for vegetables, apples, milk/dairy products, coffee, wine, and physical exercise. To obtain more specific results, further studies, with updated design, are needed. In a recent guest editorial [34], WILLETT pointed out that after avoidance of tobacco staying lean and active provides the greatest potential for minimizing cancer risk.

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