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Cancer Causes and Control **12**: 231–238, 2001.

Are coffee, tea, and total fluid consumption associated with bladder cancer risk? Results from the Netherlands Cohort Study

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Received 26 May 2000; accepted in revised form 2 November 2000

Key words: bladder neoplasms, coffee, drinking behavior, epidemiology, tea, urologic neoplasms.

Abstract

Objectives: Coffee, tea, and fluid consumption have been thought to influence bladder cancer incidence. In a large prospective study, these associations were investigated.
Methods: In 1986, cohort members (55–69 years) completed a questionnaire on cancer risk factors. Follow-up was established by linkage to cancer registries until 1992. The multivariable case–cohort analysis was based on 569 bladder cancer cases and 3123 subcohort members.
Results: The incidence rate ratios (RR) for men consuming <2 cups of coffee/day was 0.89 (95% CI 0.51–1.5) using the median consumption category (4–<5 cups/day) as reference. This RR increased to 1.3 (95% CI 0.94–1.9) for men consuming ≥7 cups/day, although no clear dose–response association was found. The RRs decreased from 1.2 (95% CI 0.56–2.7) for women consuming <2 cups of coffee/day to 0.36 (95% CI 0.18–0.72) for women consuming ≥5 cups/day compared to the median consumption category (3–<4 cups/day). Men and women who abstained from drinking tea had a RR of 1.3 (95% CI 0.97–1.8) compared to those consuming 2–<3 cups of tea per day (median consumption category). The RR for men and women comparing highest to lowest quintile of total fluid consumption was 0.87 (95% CI 0.63–1.2).
Conclusion: The data suggest a possible positive association between coffee consumption and bladder cancer risk in men and a probable inverse association in women. Tea consumption was inversely associated with bladder cancer. Total fluid consumption did not appear to be associated with bladder cancer.

Introduction

Over the past four decades, several risk factors for bladder cancer, the fourth most common cancer in men, have been investigated. Many epidemiological studies and several reviews have been conducted to investigate determinants of bladder cancer [1, 2]. These studies suggested that bladder cancer is influenced by environmental factors, such as cigarette smoking and exposure to industrial chemicals, and by chronic infections with *Schistosoma haematobium*. In 1993, Viscoli *et al.* concluded, in a meta-analyses of seven studies, that coffee consumption might not have a clinically important impact on bladder cancer risk [3]. Recently, an updated meta-analysis on both coffee and tea consumption demonstrated a small elevated risk of bladder cancer for current coffee drinkers and did not identify an association for tea drinkers compared with non-drinkers [4]. The results were rather consistent across study design characteristics. In the meta-analysis, however, insufficient data were available to explore the influence of the amount of coffee and tea on bladder cancer risk. Because coffee and tea are so widely used, the association between coffee and tea consumption and bladder cancer incidence is an important concern. Furthermore, because coffee and tea consumption account for a considerable amount of daily fluid consumption, total fluid consumption is of interest, particularly given a recent analysis, which reported a negative association [5]. These results prompted us to investigate the association between coffee, tea, and total fluid consumption and bladder cancer risk in the ongoing Netherlands

Cohort Study. In this follow-up study among 120,852 men and women, which started in 1986, detailed information has been collected on dietary habits, including drinking habits, by means of a self-administered questionnaire.

Methods

Cohort

This population-based prospective cohort study on diet and cancer started in the Netherlands in September 1986. The cohort includes 58,279 men and 62,573 women aged 55–69 years at baseline. The study population originated from 204 municipal population registries throughout the country. The case–cohort approach was used for data processing and analysis [6]. Cases were enumerated from the entire cohort, while the accumulated person-years in the cohort were estimated from a subcohort sample. Following this approach, a subcohort of 3500 subjects (1688 men and 1812 women) was randomly sampled from the cohort after the baseline exposure measurement. The subcohort has been followed up for vital status information. No subcohort members were lost to follow-up, during the follow-up period. The study design has been described in detail previously [7].

Follow-up

Follow-up for incident cancer was established by record linkage to cancer registries and the Dutch national database of pathology reports [8]. The completeness of cancer follow-up was estimated to be over 96% [9]. The presented analysis is restricted to cancer incidence in 6.3 years of follow-up, from September 1986 to December 1992. After excluding prevalent cases with cancer other than skin cancer, a total of 3346 subcohort members (1630 men and 1716 women) and 619 incident cases (532 men and 87 women) with microscopically confirmed, incident carcinomas of the urinary bladder, ureters, renal pelvis, and urethra were identified. Of these cases, 584 (94.3%) were diagnosed with bladder cancer. The morphology of the bladder carcinomas was transitional cell (n = 559), squamous cell (n = 3), adenocarcinoma (n = 6), mixed (n = 1), or not specified (n = 15). The morphology of the carcinomas of ureters, renal pelvis, and urethra (n = 35) was not specified, but most probably transitional cell. Because the overwhelming majority of tumors occurred in the urinary bladder, and the renal pelvis and ureter are covered by the same urothelium as the urinary bladder, the term bladder cancer is used as a synonym for these neoplasms.

Questionnaire

At baseline, all cohort members completed a self-administered questionnaire on risk factors for cancer. The semiquantitative food-frequency section of the questionnaire concentrated on habitual consumption of food and beverages during the year preceding the start of the study. Use of beverages was addressed by questions on the consumption of water (*i.e.* tap water, mineral water), milk (*i.e.* milk, buttermilk, cocoa), juice (*i.e.* tomato, orange, others), soda and lemonade (*i.e.* cola, others), alcoholic beverages (*i.e.* beer, red wine, white wine, sherry, port, liqueur, spirits), coffee, and tea. The questionnaire covered almost all beverages consumed regularly. The questionnaire data were key entered twice and processed in a standardized manner blinded with respect to case/subcohort status in order to minimize observer bias in coding and data interpretation.

Data analysis

Fifty cases and 223 subcohort members with incomplete or inconsistent dietary data were excluded, according to criteria described previously [10]. Therefore the analyses presented are based on 569 cases (491 men and 78 women) and 3123 subcohort members (1525 men and 1598 women). Among these remaining subjects, questions on whether subjects drank coffee or tea were left blank by 0.5% (coffee) and 1.2% (tea); they were considered to be non-users. Of all included subjects, 0.8% and 2.1% reported drinking coffee or tea, respectively, but did not report how much. They were assumed to drink 4.5 cups of coffee or 3.2 cups of tea per day (*i.e.* the mean number of cups consumed by the drinkers). The standard size of a cup of coffee or tea was assessed from a pilot study to be 125 ml. The consumption of coffee and tea was categorized into strata based on the distribution in the case and subcohort groups. For categorical analyses, the median consumption stratum was chosen as reference category. We evaluated the total intake of caffeine from caffeine-containing beverages (*i.e.* coffee, tea, and cola). A cup of coffee or tea or a glass of cola (175 ml) was assumed to contain 81, 15, and 23 mg of caffeine respectively. No questions were asked on decaffeinated coffee consumption, as this item did not appear to be consumed much in the pilot study. Based on questionnaire data, we calculated total fluid consumption using information on frequency and beverage-specific serving size of the 19 specific beverages. Furthermore, total intake of water from beverages and food was calculated using the computerized Dutch food composition table [11].

Cigarettes smoking was considered as a potential confounding factor in the association between coffee/tea consumption and bladder cancer risk, since cigarette smoking is one of the most important environmental risk factors for bladder cancer [12]. Cigarette smoking was operationalized through questions on current and former cigarette smoking status at baseline (yes *vs.* no), smoking amount (cigarettes/day), and smoking duration (years of cigarette smoking) for current and former smokers. Other variables that were considered as potential confounders in multivariable analysis were: age (years); alcohol intake (g/day); coffee consumption (ml/day); tea consumption (ml/day); total water intake (ml/day); vegetables consumption (g/day); fruit consumption (g/day); current cigarette smoking (yes *vs.* no); smoking amount (cigarettes/day); smoking duration (years of cigarette smoking); occupational exposure to dye, rubber, leather, or vehicle fumes (ever *vs.* never); and first-degree family history of bladder cancer (yes *vs.* no). Incidence rate ratios (RR) and corresponding 95% confidence intervals (CI) for bladder cancer were estimated using exponentially distributed failure time regression models [13] with the Stata statistical software package. Standard errors were estimated using the robust Hubert–White sandwich estimator to account for additional variance introduced by sampling from the cohort. This method is equivalent to the variance–covariance estimator presented by Barlow [14]. Tests for dose–response trends in risk for bladder cancer were assessed by fitting ordinal exposure variables as continuous terms and performing likelihood-ratio tests between regression models with and without these variables. We confirmed constancy of the baseline hazard visually by plotting the natural logarithm of the baseline survival function against failure time. List-wise deletion of subjects with missing data on the primary determinants and confounders was applied in multivariable analyses. Sex modified the association between coffee consumption and the incidence of bladder cancer in multivariable analyses. The RRs concerning tea and total fluid consumption were similar for men and women; therefore, we conducted regression analyses for men and women separately for coffee consumption and for men and women combined for tea and total fluid consumption. Subgroup analyses conditional on smoking duration were conducted to evaluate potential coffee, tea, or total fluid by smoking interaction.

Results

More than 96% of the subjects reported drinking coffee, and more than 85% reported drinking tea. Most subjects drank both beverages (83%). Coffee was more often consumed solely than tea (13% and 3%, respectively). The mean daily coffee consumption among coffee drinkers was higher for men (cases: 640 ml, subcohort members: 591 ml) than for women (cases: 478 ml, subcohort members: 517 ml). Conversely, tea was more consumed by female tea drinkers (cases: 474 ml, subcohort members: 431 ml) than by male tea drinkers (cases: 367 ml, subcohort members: 378 ml). The association between coffee and tea consumption was negative for cases and subcohort members ($r = -0.30$ and -0.27, respectively). Coffee and tea consumption accounted on average for 43% and 24% of the total daily fluid consumption for men, and 41% and 30% for women, respectively (data not shown).

Table 1 displays the distribution of potential risk factors for bladder cancer with respect to coffee and tea consumption among subcohort members for men and women separately. For this purpose, coffee and tea consumption were dichotomized in low and high consumption categories (lower *vs.* higher than median consumption). Number of cigarettes smoked per day, years of cigarette smoking, consumption of alcohol, and total water intake increased with increasing daily coffee consumption and not with tea consumption (except for total water intake) for both men and women. Age and the consumption of vegetables were comparable between low and high coffee and tea consumers. The consumption of fruit was negatively associated with coffee consumption and positively associated with tea consumption. Few subjects ($<3\%$) reported having a high-risk occupation or first-degree family members with bladder cancer (Table 1).

As shown in Table 2, the age- and smoking-adjusted RRs for men consuming <2 cups of coffee per day was 0.89 (CI 0.51–0.54) compared to subjects drinking 4–<5 cups of coffee per day (the median consumption category). This RR increased with increasing coffee consumption to 1.3 (CI 0.94–1.9) for men consuming ≥ 7 cups per day. However, none of the individual RRs was statistically significant. Although no clear dose–response association was found, the test for linear trend was statistically significant (p-trend < 0.01). There was no indication of a positive association between coffee consumption and bladder cancer risk for women. On the contrary, for women, the age- and smoking-adjusted RRs decreased with increasing coffee consumption from 1.2 (CI 0.56–2.7) for women drinking <2 cups of coffee per day to 0.36 (CI 0.56–2.7) for women consuming ≥ 5 cups per day, compared to the median consumption category (3–<4 cups/day) (p-trend < 0.01). When coffee consumption was modeled as a continuous term in the analyses, we also found a reduced risk for women per

Table 1. Distribution of potential risk factors for bladder cancer with respect to coffee and tea consumption among subcohort members; Netherlands Cohort Study 1986–1992

Risk factors	Coffee consumption (cups/day)				Tea consumption (cups/day)			
	Men		Women		Men		Women	
	Low (< 5) (n = 830)	High (≥5) (n = 695)	Low (< 4) (n = 594)	High (≥4) (n = 1004)	Low (< 3) (n = 851)	High (≥3) (n = 674)	Low (< 3) (n = 697)	High (≥3) (n = 901)
Mean								
Age (years)	62.0	60.6	61.9	61.0	60.8	62.1	60.9	61.8
Alcohol intake (g/day)	13.7	15.6	5.6	5.9	15.9	12.8	5.9	5.6
Total water intake (ml/day)	1982	2342	1841	2093	2041	2279	1815	2142
Vegetable consumption (g/day)	189	195	196	197	188	197	192	200
Fruit consumption (g/day)	160	147	205	191	144	168	187	203
Smoking amount (cigarettes/day)[a]	15.2	18.8	9.9	11.8	17.8	34.3	12.7	9.8
Smoking duration (years)[a]	32.0	35.0	28.4	27.6	15.8	32.3	29.8	26.1
Coffee consumption (cups/day)	3.0	6.5	2.1	5.1	5.0	4.0	4.4	3.6
Tea consumption (cups/day)	3.0	2.1	3.5	2.8	1.2	4.3	1.3	4.5
Percentage								
Non-smokers	17.2	8.8	66.0	54.9	12.0	15.1	54.4	62.6
High-risk occupation[b]	0.8	0.6	0.2	0.3	0.7	0.7	0.1	0.3
Positive family history of bladder cancer	1.6	1.3	2.5	2.2	1.4	1.5	2.4	2.2

[a] Among cigarette smokers only.
[b] Ever exposed to dye, rubber, leather, and vehicle fumes.

Table 2. Adjusted incidence rate ratios (RR) for bladder cancer according to coffee consumption in categorical and continuous analyses; Netherlands Cohort Study 1986–1992

Coffee consumption (cups/day)	Cases in cohort	Person-years in subcohort	RR (95% CI)[a]	RR (95% CI)[b]	RR (95% CI)[c]
Men					
0–<2	23	628	0.83 (0.50–1.36)	0.89 (0.51–1.54)	0.92 (0.53–1.60)
2–<3	32	907	0.69 (0.44–1.07)	0.72 (0.45–1.13)	0.74 (0.47–1.17)
3–<4	61	961	1.24 (0.86–1.79)	1.27 (0.87–1.87)	1.27 (0.86–1.87)
4–<5	119	2463	1.00 (reference)	1.00 (reference)	1.00 (reference)
5–<6	72	1432	1.12 (0.80–1.58)	0.98 (0.68–1.40)	0.96 (0.67–1.38)
6–<7	91	1456	1.43 (1.04–1.98)	1.25 (0.89–1.76)	1.19 (0.84–1.68)
≥7	93	1302	1.76 (1.27–2.44)	1.33 (0.94–1.90)	1.25 (0.87–1.78)
p-Value for linear trend			<0.01	<0.01	0.06
Coffee increment, 1 cup/day			1.09 (1.05–1.13)	1.04 (1.00–1.09)	1.03 (0.98–1.08)
Women					
0–<2	11	773	1.11 (0.52–2.40)	1.23 (0.56–2.73)	1.16 (0.51–2.62)
2–<3	13	1293	0.78 (0.38–1.60)	0.84 (0.40–1.76)	0.82 (0.39–1.72)
3–<4	20	1573	1.00 (reference)	1.00 (reference)	1.00 (reference)
4–<5	17	3144	0.43 (0.22–0.83)	0.44 (0.22–0.86)	0.44 (0.22–0.86)
≥5	17	3064	0.44 (0.23–0.86)	0.36 (0.18–0.72)	0.37 (0.19–0.72)
p-Value for linear trend			<0.01	<0.01	<0.01
Coffee increment, 1 cup/day			0.87 (0.75–1.01)	0.83 (0.72–0.96)	0.84 (0.72–0.97)

[a] Adjusted for age (years).
[b] Adjusted for age (years), number of cigarettes/day, and years of cigarette smoking.
[c] Adjusted for age (years), number of cigarettes/day, years of cigarette smoking, and tea consumption (ml/day).

cup of coffee consumed per day. Simultaneous inclusion of both coffee and tea consumption in one regression model (Table 2) or additional correction for current cigarette smoking, alcohol intake, total water intake, vegetables consumption, fruit consumption, occupational exposure, and family history of bladder cancer did not

essentially change the risk estimates for coffee consumption (data not shown).

Tea consumption was inversely associated with bladder cancer risk, irrespective of the number of cups consumed per day (Table 3). Men and women consuming 0, <2, 3–<4, 4–<5, and ≥ 5 cups of tea per day had age-, sex-, and smoking-adjusted RRs of 1.3 (CI 0.97–1.8), 0.95 (CI 0.67–1.3), 0.81 (CI 0.58–1.1), 0.81 (CI 0.59–1.1), and 0.93 (CI 0.66–1.3) compared to the median consumption category (2–<3 cups/day), respectively (p-trend < 0.01). The risk of bladder cancer decreased by 5% for every increment of one cup of tea per day in continuous analysis. Neither adjustment for coffee consumption (Table 3) nor adjustment for current cigarette smoking and other potential risk factors changed these results. Because coffee consumption for women, and tea consumption for men and women, appeared to be inversely associated with bladder cancer risk, we investigated the combined effect of coffee and tea consumption. We found no significant interaction effect between coffee and tea consumption on bladder cancer risk for men and women (data not shown).

Most of the daily caffeine intake was derived from coffee (85.0%) and tea (14.5%) consumption. For men, the age- and smoking-adjusted risk of bladder cancer increased with increasing caffeine intake to 1.5 (CI 1.0–2.1), comparing highest to lowest quintile of caffeine intake (p-trend = 0.03) (Table 4). For women, conversely, a negative dose–response trend was found (p-trend < 0.01). The RR for women in the highest quintile of caffeine intake was 0.50 (CI 0.25–1.0) compared to women in the lowest consumption quintile (p-trend < 0.01) (Table 4).

Neither total fluid consumption from beverages only nor total water intake from food and beverages combined was associated with the incidence of bladder cancer (Table 5). None of the age-, sex- and smoking-adjusted risks for subjects categorized by quintiles of consumption differed significantly from the lowest consumption quintile. The RRs per 100 ml increment per day were around unity (all p-trends > 0.70). The results for total fluid consumption and total water intake persisted after additional adjustment for coffee and tea consumption (Table 5) and other potential risk factors for bladder cancer (data not shown).

Almost none of the RRs were notably altered after adjustment for smoking. Cigarette smoking duration, however, was found to be a statistically significant effect modifier in the association between bladder cancer and coffee and tea consumption (p-interaction coffee < 0.01, p-interaction tea = 0.05) (data not shown). Coffee consumption was inversely associated with bladder cancer risk for men smoking cigarettes for < 20 years, although not statistically significant. Never smokers and men who had smoked cigarettes over a longer period than 20 years had increasing risks of bladder cancer with increasing coffee consumption. An inverse association between tea consumption and bladder cancer risk was most pronounced in men and women who smoked cigarettes for <20 years and > 40 years. The results for total fluid consumption were similar for different classifications of smoking duration (p-interaction = 0.24). These stratum-specific results, however, are based on small numbers (data not shown).

Discussion

The results of this prospective cohort study support a possible positive association between coffee consumption and male bladder cancer, mainly confined to the higher consumption categories (*i.e.* ≥7 cups/day). For women, an inverse association was found. Tea consumption was inversely associated with bladder cancer for

Table 3. Adjusted incidence rate ratios (RR) for bladder cancer according to tea consumption in categorical and continuous analyses; Netherlands Cohort Study 1986–1992

Tea consumption (cups/day)	Cases in cohort	Person-years in subcohort	RR (95% CI)[a]	RR (95% CI)[b]	RR (95% CI)[c]
No tea consumption	115	2422	1.45 (1.09–1.94)	1.31 (0.97–1.78)	1.30 (0.96–1.78)
<2	70	2318	0.96 (0.69–1.33)	0.95 (0.67–1.34)	0.95 (0.67–1.34)
2–<3	155	4625	1.00 (reference)	1.00 (reference)	1.00 (reference)
3–<4	71	2914	0.80 (0.58–1.10)	0.81 (0.58–1.13)	0.81 (0.58–1.13)
4–<5	80	3631	0.69 (0.51–0.94)	0.81 (0.59–1.12)	0.81 (0.59–1.12)
≥ 5	78	3086	0.88 (0.64–1.20)	0.93 (0.66–1.29)	0.93 (0.66–1.30)
p-Value for linear trend			<0.01	<0.01	<0.01
Tea increment, 1 cup/day			0.92 (0.87–0.97)	0.95 (0.89–1.00)	0.95 (0.90–1.00)

[a] Adjusted for age (years) and sex.
[b] Adjusted for age (years), sex, number of cigarettes/day, and years of cigarette smoking.
[c] Adjusted for age (years), sex, number of cigarettes/day, years of cigarette smoking, and coffee consumption (ml/day).

Table 4. Adjusted incidence rate ratios (RR) for bladder cancer according to caffeine intake in categorical and continuous analyses; Netherlands Cohort Study 1986–1992

Caffeine quintiles	Men		Women	
	Range (median) in mg/day	RR[a] (95% CI)	Range (median) in mg/day	RR[a] (95% CI)
1 (low)	0–274 (208)	1.00 (reference)	0–252 (193)	1.00 (reference)
2	275–357 (340)	1.25 (0.87–1.80)	253–340 (289)	0.95 (0.51–1.76)
3	358–436 (400)	1.14 (0.79–1.63)	341–385 (370)	0.59 (0.29–1.19)
4	437–520 (488)	1.23 (0.85–1.78)	386–487 (430)	0.31 (0.12–0.79)
5 (high)	521–2438 (629)	1.47 (1.03–2.12)	488–1309 (543)	0.50 (0.25–1.00)
p-Value for linear trend		0.03		< 0.01
Increment, 100 mg/day		1.04 (0.98–1.10)		0.80 (0.67–0.96)

[a] Adjusted for age (years), number of cigarettes/day, and years of cigarette smoking.

Table 5. Incidence rate ratios (RR) for bladder cancer according to total fluid consumption (from beverages) and total water intake (from food and beverages) in categorical and continuous analyses; Netherlands Cohort Study 1986–1992

Quintiles	Total fluid consumption			Total water intake		
	Range (median) in mg/day	RR (95% CI)[a]	RR (95% CI)[b]	Range (median) in mg/day	RR (95% CI)[a]	RR (95% CI)[b]
1 (low)	12–984 (846)	1.00 (reference)	1.00 (reference)	340–1686 (1516)	1.00 (reference)	1.00 (reference)
2	985–1181 (1086)	0.81 (0.54–1.21)	0.83 (0.55–1.25)	1687–1916 (1807)	0.78 (0.56–1.09)	0.80 (0.57–1.11)
3	1181–1372 (1286)	0.70 (0.47–1.07)	0.74 (0.48–1.13)	1917–2130 (2020)	0.82 (0.59–1.14)	0.86 (0.61–1.21)
4	1373–1614 (1480)	0.97 (0.66–1.43)	1.04 (0.69–1.56)	2131–2435 (2268)	0.86 (0.62–1.18)	0.91 (0.63–1.30)
5 (high)	1615–4647 (1827)	0.87 (0.63–1.21)	0.91 (0.65–1.29)	2436–5352 (2682)	0.88 (0.64–1.21)	0.94 (0.64–1.39)
p-Value for linear trend		0.99	0.77		0.70	0.88
Increment, 100 ml/day		1.00 (0.97–1.03)	1.01 (0.98–1.05)		0.99 (0.97–1.01)	1.00 (0.97–1.03)

[a] Adjusted for age (years), sex, number of cigarettes/day, and years of cigarette smoking.
[b] Adjusted for age (years), sex, number of cigarettes/day, years of cigarette smoking, coffee consumption (ml/day), and tea consumption (ml/day).

both men and women, irrespective of consumption frequency. The results do not suggest an association between total fluid consumption and bladder cancer.

One strength of this and other prospective studies is that exposure was assessed before diagnosis of bladder cancer. Therefore, recall bias is not likely to have influenced our results. Furthermore, selection bias is not likely, because the follow-up of cases and subcohort members was almost complete [9, 15]. The measurement of coffee, tea, and total fluid intake has not been validated. However, subjects with incomplete or inconsistent food-frequency questionnaires were excluded from analyses [10]. The relatively large number of bladder cancer cases in this study was another important strength. To ensure that the results were not influenced by changes in exposure by subjects with preclinical bladder cancer, we conducted analyses with and without cases diagnosed in the first one or two years of follow-up. Results from these analyses were similar.

A potentially more realistic threat to the interpretation of the observed associations is residual confounding by risk factors for bladder cancer that happen to be associated with coffee, tea, or total fluid consumption. Multivariable analyses showed that the estimates of the RRs for coffee, tea, and total fluid consumption were not confounded by current cigarette smoking, total consumption of alcohol, coffee (for tea and total fluid analyses), tea (for coffee and total fluid analyses), water, vegetables and fruit, high-risk occupation, and positive family history of bladder cancer. Age, sex, smoking amount, and smoking duration were found to be important determinants. We modeled cigarette smoking habits such that they best explained bladder cancer. This resulted in a model including number of years smoked and habitual number of cigarettes smoked per day, both as continuous variables. When we added the smoking variables to an age- and sex- (for tea and total fluid analyses) adjusted model, the RR estimates changed

only slightly. We therefore believe that the associations observed were not entirely due to residual confounding by smoking, although we cannot exclude some influence due to misclassification of the smoking variables.

The mean coffee and tea consumption measured in this study is similar to the mean intake measured in previous food consumption surveys conducted in the Netherlands [16, 17]. In accordance with previous studies [4], our results suggested a positive association between coffee consumption and male bladder cancer risk. Although no clear dose–response association was found, the test for linear trend was strongly statistically significant. Therefore, we expect the observed nonlinear association to be the result of chance. For women, we found an inverse association between coffee consumption and bladder cancer risk, which was statistically significant. At present, the biological mechanism that might explain this discrepancy between men and women remains unclear and needs further investigation. Previous epidemiological studies on coffee consumption associated with bladder cancer were primarily based on case–control data, although three prospective studies have been conducted [5, 18, 19]. In a recent meta-analysis based on these studies, we concluded that coffee consumption might increase the risk of urinary tract cancer slightly [4].

Tea consumption was inversely associated with bladder cancer risk for both men and women. Evidence from animal studies shows that certain compounds present in tea may have inhibitory effects on bladder tumor formation and growth. This inhibitory activity is believed to be due mainly to the antioxidative and possibly antiproliferative effects of polyphenol compounds (*e.g.* flavonoids) [20–23]. It has been pointed out that no other agent tested for possible chemoprevention effects in animal models has elicited such strong activity as tea and its components at concentrations usually consumed by humans [22]. In the present study, we found an inverse association between tea intake and bladder cancer risk. Lack of a positive association of tea consumption is consistent with the results of two previous prospective studies [5, 24] and most case–control studies [4].

An inverse association between tea consumption and bladder cancer risk might be explained by the hypothesis that drinking more fluids is associated with a decreased risk of bladder cancer [5, 25]. The urogenous-contact hypothesis associates the development of bladder cancer with prolonged exposure to carcinogens in urine [5, 26]. High consumption of fluids may reduce this exposure by diluting the urine and reducing contact time through increased frequency of urination. However, total fluid consumption has also been hypothesized to increase the risk of bladder cancer by increasing the workload of the bladder or by exposing the bladder to specific fluids that contain carcinogens (*e.g.* in coffee or alcohol) or chemopreventive agents (*e.g.* in tea) [26, 27]. Neither total fluid consumption nor total water intake was associated with bladder cancer risk in the present study. Previous studies showed mixed results. Some case–control studies reported positive associations between total fluid consumption and bladder cancer [27–33], whereas others found no association [34, 35]. Only one case–control study reported an inverse association between total fluid consumption and bladder cancer risk in women, but not in men [36]. Only two follow-up studies to date were conducted to investigate this association [5, 18]. One follow-up study did not find an association between fluid consumption and bladder cancer [18]. Recently, a preventive effect of total fluid consumption was presented in another follow-up study [5]. Although the weight of evidence is not in favor of a protective effect of fluid intake, further research is needed to evaluate this matter.

In conclusion, the results of this prospective study suggest a possible positive association between coffee consumption and bladder cancer risk for men. Men consuming ≥ 7 cups per day were found to have the highest risk of bladder cancer. For women, a probable inverse association was found. Tea was inversely associated with bladder cancer for both men and women. The authors found no evidence for an association between total fluid consumption and bladder cancer risk.

Acknowledgements

The Netherlands Cohort Study was supported by the Dutch Cancer Society. The authors thank the regional cancer registries, the Dutch national database of pathology reports (PALGA), and the National Health Care Information Centre for providing incidence data; S. Van de Crommert, H. Brants, W. van Dijk, M. Moll, J. Nelissen, C. de Zwart, A. Pisters, H. van Montfort, R. Schmeitz, T. van Montfort, T. van Moergastel for assistance.

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