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Associations Between Black Tea and Coffee Consumption and Risk of Lung Cancer Among Current and Former Smokers

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Abstract: *Although cigarette smoking is a clear risk factor for lung cancer, the other determinants of lung cancer risk among smokers are less clear. Tea and coffee contain catechins and flavonoids, which have been shown to exhibit anticarcinogenic properties. Conversely, caffeine may elevate cancer risk through a variety of mechanisms. The current study investigated the effects of regular consumption of black tea and coffee on lung cancer risk among 993 current and former smokers with primary incident lung cancer and 986 age-, sex-, and smoking-matched hospital controls with non-neoplastic conditions. Results indicated that lung cancer risk was not different for those with the highest black tea consumption (≥2 cups/day) compared with nondrinkers of tea [adjusted odds ratio (aOR) = 0.90; 95% confidence interval (CI) = 0.66–1.24]. However, elevated lung cancer risk was observed for participants who consumed 2–3 cups of regular coffee daily (aOR = 1.34; 95% CI = 0.99–1.82) or ≥4 cups of regular coffee daily (aOR = 1.51, 95% CI = 1.11–2.05). In contrast, decaffeinated coffee drinking was associated with decreased lung cancer risk for both participants who consumed ≤1 cup/day (aOR = 0.67; 95% CI = 0.54–0.84) and those who consumed ≥2 cups/day (aOR = 0.64; 95% CI = 0.51–0.80). These results suggest that any chemoprotective effects of phytochemicals in coffee and tea may be overshadowed by the elevated risk associated with caffeine in these beverages.*

Introduction

Coffee and tea are significant dietary sources of polyphenols, which include phytoestrogens, flavonoids, and catechins (1–5). Polyphenols have been shown to exert hormonal and antioxidant effects as well as other anticarcinogenic activities (6–8). In addition, tea and tea components have been shown to inhibit carcinogenesis by a variety of mechanisms (2,3,9–13), and the literature supports a risk-reducing effect of tea consumption on chronic conditions such as cardiovascular disease, cancer, bone health, oral health, cognitive health, and kidney stones (4).

Hormonal and antioxidant agents have the potential to reduce lung cancer among smokers; therefore, it is reasonable to hypothesize that polyphenol-containing beverages such as tea and coffee might affect lung cancer risk (2,3,8,11,13,14). The epidemiological evidence for a relationship between tea and lung cancer has been limited and inconsistent but in general has not supported a protective effect of higher tea consumption (15). Even fewer studies have examined coffee consumption and lung cancer; however, these studies suggested increased risks associated with higher coffee consumption (16,17). Comparison of findings in these studies is difficult as categories of consumption tend to be study specific. Given the limited literature available that has addressed this question, we examined usual consumption of tea and coffee with risk of lung cancer in a hospital-based case-control study using data collected at Roswell Park Cancer Institute (RPCI) between 1982 and 1998.

Methods

The study population included individuals who received medical services at RPCI in Buffalo, New York, between 1982 and 1998 and who agreed to complete a comprehensive epidemiological questionnaire. The case group consisted of 993 individuals (624 male, 369 female) with primary, incident lung

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cancer, identified from the RPCI Tumor Registry and Diagnostic Index. Histologies were based upon routine pathology at the time of diagnosis. Controls included 986 individuals (619 male, 367 female) randomly selected from a pool of 8,730 eligible individuals with complete data on the exposure of interest who had received medical services at RPCI for non-neoplastic conditions. These participants came to RPCI with a suspicion of neoplastic disease but were not diagnosed with either benign or malignant conditions. Selected controls were most frequently treated for gastrointestinal disorders (19%), infectious disorders (15%), and genitourinary disorders (15%). Controls were frequency matched approximately 1:1 to cases on sex, smoking status, and 5-yr age intervals. Statistical software was used to randomly select an appropriate number of controls in each age-, sex-, and smoking-specific strata. Smoking status of participants was classified as never smoker (44%), current smoker (31%; currently smokes or quit within the past year), or former smoker (25%; quit at least 1 yr ago). Nonsmokers were excluded as few nonsmoking lung cancer cases were identified and these cases were likely to have etiologies that differed from smokers.

All participants completed the Patient Epidemiology Data System (PEDS) questionnaire, which is offered to all new patients as part of the admission process and is returned by approximately 50% of patients. The 16-page instrument covers information on tobacco and alcohol consumption, family history of cancer, occupational and environmental exposures, reproductive and medical histories, medication and vitamin usage, and diet. Diet was assessed using a 44-item food-frequency questionnaire that assessed usual intake during "the past few years before the current illness." The separate section on beverage intake assessed usual daily servings of black tea, decaffeinated tea, regular coffee, and decaffeinated coffee. Beverage intake was categorized based on the distribution of intake among the controls, with an emphasis on creating meaningful categories. Regular coffee intake was classified as none, ≤1 cup per day, 2–3 cups per day, or 4 or more cups per day. Decaffeinated coffee intake was classified as none, ≤1 cup per day, or 2 or more cups per day. Black tea intake was classified as none, <1 cup per day, 1 cup per day, or 2 or more cups per day. During the period covering data collection (1982–1998) intake of decaffeinated tea, green tea, and herbal teas was uncommon, preventing examination in this study.

Risk of lung cancer was estimated using unconditional logistic regression, adjusting for matching variables as well as identified confounders and multiplicative interaction terms that changed the odds ratio (OR) in any exposure stratum by at least 10%. Confounders were identified based upon statistically significant associations with both disease status and beverage intake. Confounders were evaluated separately for models examining regular coffee, decaffeinated coffee, and black tea. For all analyses, nondrinkers of the beverage were used as the referent group. *P* for trend was determined by evaluating the significance of the continuous variable in the logistic model. Multivariate models were evaluated for goodness of fit using the Hosmer-Lemeshow test (18).

Results

Descriptive characteristics of the study population are shown in Table 1. Due to matching procedures, there were no differences between cases and controls with respect to age, sex, or smoking status. Consistent with previously described risk factors for lung cancer, cases were significantly less likely to have taken vitamin C supplements but were more likely to report high alcohol intake, use of carotene supplements, and a variety of occupational exposures, including asbestos, various dusts, occupational smoke (not due to tobacco), and radiation. Lung cancer risk was also strongly associated with a personal history of chronic obstructive pulmonary disease or pneumoconiosis. Despite matching cases to controls on smoking status, participants with lung cancer reported smoking slightly more cigarettes per day and a smoking history that was somewhat longer than their counterparts without lung cancer.

As shown in Table 2, the highest intake of regular coffee was associated with a moderate increase in lung cancer risk [adjusted OR (aOR) = 1.51; 95% confidence interval (CI) = 1.11–2.05] compared with nondrinkers, with evidence of a dose-response relationship (P_{trend} = 0.01). However, there was no clear association between black tea consumption and lung cancer risk. In contrast, intake of decaffeinated coffee was associated with a dose-dependent decrease in lung cancer risk (P_{trend} = 0.02), with the highest intake group experiencing a 36% decrease in risk (aOR = 0.64; 95% CI = 0.51–0.80). Hosmer-Lemeshow test results for each adjusted multivariate model were nonsignificant (P = 0.40 for regular coffee, P = 0.25 for black tea, and P = 0.96 for decaffeinated coffee), indicating sufficient model goodness of fit.

Table 3 displays adjusted associations between beverage intake and lung cancer risk by histologic subtype. Although cell sizes decrease, resulting in less stable point estimates, results do not appear different for most subtypes of lung cancer. One exception is the association between regular coffee intake and adenocarcinoma. In contrast to the dose-dependent increase in risk observed for other histologies, moderate coffee intake may be associated with decreased risk of adenocarcinoma (aOR = 0.60; 95% CI = 0.30–1.21) despite elevated risk for individuals with the highest coffee consumption (aOR = 1.66; 95% CI = 0.90–3.04). Hosmer-Lemeshow test results for all models were nonsignificant ($P > 0.05$), indicating sufficient model goodness of fit.

Effects did not differ for men and women and do not appear to be driven by the effect in any subset of controls (data not shown). Results did not differ when models were adjusted for intake of other beverages (data not shown).

Discussion

Coffee and tea contain significant amounts of phytochemicals that could potentially affect cancer etiology.

Table 1. Characteristics of Lung Cancer Cases (n = 993) and Noncancer Hospital Controls (n = 986), Roswell Park Cancer Institute, 1982–1998[a]

Characteristic	Cases n (%)	Controls n (%)	Crude OR (95% CI)
Male[b]	624 (62.8)	619 (62.8)	1.00 (0.84–1.20)
High school graduate	610 (61.8)	701 (71.4)	0.65 (0.54–0.78)
Non-Hispanic White	931 (93.8)	959 (97.3)	0.42 (0.27–0.67)
Age group[b]			
26–30	3 (0.3)	3 (0.3)	0.96 (0.19–4.92)
31–35	7 (0.7)	7 (0.7)	0.96 (0.32–1.87)
36–40	8 (0.8)	8 (0.8)	0.96 (0.35–2.69)
41–45	44 (4.4)	44 (4.4)	0.96 (0.58–1.62)
46–50	58 (5.8)	58 (5.8)	0.96 (0.60–1.55)
51–55	94 (9.5)	94 (9.5)	0.96 (0.64–1.47)
56–60	182 (18.3)	182 (18.3)	0.96 (0.67–1.39)
61–65	197 (19.8)	197 (19.8)	0.96 (0.67–1.39)
66–70	187 (18.8)	187 (18.8)	0.96 (0.67–1.39)
71–75	129 (13.0)	125 (12.7)	1.00 (0.67–1.47)
>75	84 (8.5)	81 (8.2)	Reference
Current cigarette smoker[b]	491 (49.4)	484 (49.1)	1.01 (0.85–1.21)
Ever smoked cigars regularly for 1+ yr	97 (9.9)	126 (12.9)	0.74 (0.56–0.98)
Drinks >14 alcoholic beverages/wk	171 (17.2)	132 (13.4)	1.35 (1.05–1.72)
Ever took carotene supplements	41 (4.5)	25 (2.6)	1.73 (1.04–2.86)
Ever took vitamin C supplements	231 (24.5)	281 (29.3)	0.78 (0.64–0.96)
Known occupational exposure to asbestos	203 (33.2)	172 (25.2)	1.48 (1.16–1.88)
Known occupational exposure to coal dust	169 (21.7)	149 (17.6)	1.30 (1.02–1.66)
Known occupational exposure to wood dust	195 (24.9)	161 (18.8)	1.43 (1.13–1.81)
Known occupational exposure to other dust	261 (34.8)	234 (28.4)	1.35 (1.09–1.67)
Known occupational exposure to nontobacco smoke	217 (27.7)	197 (23.3)	1.26 (1.01–1.58)
Known occupational exposure to radiation	76 (10.2)	77 (9.3)	1.11 (0.79–1.54)
History of chronic obstructive pulmonary disease	95 (10.4)	42 (4.3)	2.62 (1.80–3.81)
History of pneumoconiosis	18 (2.0)	2 (0.2)	9.87 (2.29–42.5)
Family history of lung cancer among first-degree relative	129 (13.0)	88 (8.9)	1.52 (1.14–2.03)
	Mean (SD)	Mean (SD)	
Daily exposure to second hand smoke (h)	5.8 (6.3)	5.6 (6.2)	1.00 (0.99–1.02)
Total years cigarette smoking	39.4 (11.7)	32.2 (14.5)	1.04 (1.04–1.05)
Average cigarettes per day smoked	30.8 (14.6)	23.7 (13.5)	1.04 (1.03–1.05)
Monthly servings fruits and vegetables	113 (65.2)	121 (65.5)	0.64 (0.50–0.82)[c]

a: Abbreviations are as follows: OR, odds ratio; CI, confidence interval; SD, standard deviation.
b: Controls were frequency matched to cases on these characteristics.
c: For highest quartile of intake compared with lowest quartile.

Whereas experimental data suggest that higher consumption of tea and other polyphenol-containing beverages could reduce lung cancer risk, we observed in this study no association between tea drinking and lung cancer and, in fact, observed increased lung cancer risk with higher coffee intake. These findings are somewhat consistent with the epidemiological data, which, in general, do not find a protective effect for tea with lung cancer but report increased risks associated with coffee intake (15–17,19–28).

Several factors may have contributed to our findings. First, experimental data may not be directly extrapolated to humans. Human behavior is complex, especially with regard to diet. Furthermore, coffee drinking and cigarette smoking tend to be positively associated behaviors. Although we carefully controlled our analyses for cigarette smoking, unaccounted residual confounding can never be excluded as an explanation. Additionally, tea intake in our population was fairly low. Few subjects consumed more than 2 cups per day; these amounts may have been too low to exert a protective effect on lung cancer development. Finally, the questionnaire queried coffee and tea intake in the few years prior to diagnosis. It may be that longer-term high intakes are more relevant.

Interestingly, we observed a protective effect of higher decaffeinated coffee consumption on lung cancer risk. Decaffeinated coffee contains very little caffeine. In fact, our results tended to mirror a positive association with caffeine consumption (that is, higher risk with coffee, no risk with tea, reduced risk with decaffeinated coffee). Caffeic acid has been labeled by the International Agency for Research on Cancer as a possible human carcinogen (16,17), and caffeine has been shown to reduce the beneficial effects of flavonoids (7). Caffeine is a known inhibitor of ataxia telangiectasia mutated kinase, the enzyme responsible for phosphorylating and activating p53, thus regulating the p53-related apoptotic

Table 2. Crude and Adjusted Risk of Lung Cancer by Black Tea, Regular Coffee, and Decaffeinated Coffee Consumption, Roswell Park Cancer Institute, 1982–1998[a]

	Cases *n* (%)	Controls *n* (%)	Crude OR (95% CI)	Adjusted OR (95% CI)
Regular coffee consumption (cups/day)[b]				
None	201 (20.7)	231 (23.9)	Reference	Reference
≤1	157 (16.2)	198 (20.5)	0.91 (0.69–1.21)	1.03 (0.73–1.45)
2–3	293 (30.1)	275 (28.4)	1.22 (0.95–1.57)	1.34 (0.99–1.82)
4+	321 (33.0)	264 (27.3)	1.40 (1.09–1.79)	1.51 (1.11–2.05)
P for trend			<0.01	0.01
Black tea consumption (cups/day)[c]				
None	420 (42.3)	404 (41.0)	Reference	Reference
<1	250 (25.2)	265 (26.9)	0.91 (0.73–1.13)	0.87 (0.66–1.16)
1	118 (11.9)	114 (11.6)	1.00 (0.74–1.33)	0.97 (0.66–1.43)
2+	205 (20.6)	203 (20.6)	0.97 (0.77–1.23)	0.90 (0.66–1.24)
P for trend			0.26	0.93
Decaffeinated coffee consumption (cups/day)[d]				
None	564 (59.2)	473 (49.0)	Reference	Reference
≤1	198 (20.8)	244 (25.3)	0.68 (0.54–0.85)	0.67 (0.54–0.84)
2+	190 (20.0)	248 (25.7)	0.64 (0.51–0.81)	0.64 (0.51–0.80)
P for trend			0.02	0.02

a: Abbreviations are as follows: OR, odds ration; CI, confidence interval.
b: Adjusted for age, sex, smoking status, known occupational exposure to other kinds of dust, known occupational exposure to smoke, number of cigarettes smoked per day, and interaction between smoke exposure and cigarettes.
c: Adjusted for age, sex, smoking status, known occupational exposure to asbestos, number of cigarettes smoked per day, and interaction between asbestos and cigarettes.
d: Adjusted for age, sex, and smoking status.

pathway (29). Caffeine consumption has been positively associated with increased incidence of breast atypical hyperplasia, presumably due to accumulation of cyclic adenosine monophosphate (cAMP) and activation of protein kinase, which leads to the overproduction of fibrous tissue and cystic fluid (30). In renal epithelial cells from patients with polycystic kidney disease, clinically relevant concentrations of caffeine increased accumulation of cAMP, which resulted in activation of the extracellular signal regulated kinase pathway of cellular proliferation (31). Caffeine consumption has also been associated with risk of ovarian cancer (32), and this effect was modified by the CYP1A1 genotype. In animal studies, however, caffeine administration has been associated with some anticarcinogenic properties, particularly the inhibition of UVB-induced carcinomas in DMBA-initiated SKH-1 mice (33). Nevertheless, the results of the current study suggest that the carcinogenic effects of caffeine may outweigh the potentially protective effects of phytochemicals present in coffee and tea.

Several methodological issues should be considered in interpreting these results. As in all case-control studies, bias could have affected the validity of the current findings. Selection bias may have occurred in this investigation. The lung cancer patient group was restricted to individuals who were treated at RPCI, a large regional cancer treatment center, and is not likely to represent the general population of lung cancer patients in the western New York region. However, our sample of lung cancer cases represents the population with a high-risk profile (see Table 1) and is large enough to allow the investigation of rare histologic types of lung cancer. In addition, it is unlikely that self-reported tea and coffee consumption would be different for RPCI patients than from patients treated in different facilities. The use of hospital controls might introduce bias due to the possibility that some controls were suffering from conditions that might be associated with coffee consumption. However, greater likelihood of coffee consumption in the control group would only have attenuated the true risk estimate rather than produced spurious associations. In addition, hospital controls were selected from a large pool of eligible participants with a wide variety of noncancer conditions, minimizing bias arising from potential overrepresentation of patients with characteristics that may be associated with the exposures. In fact, no significant differences with respect to tea and coffee consumption were observed for the most common diagnostic categories of controls. Selection bias may have also been introduced due to the low participation rate in this study. Only about 50% of eligible cases and controls agreed to complete the PEDS questionnaire. We have no way of ascertaining whether or not those individuals who refused to complete the instrument differed from participants with respect to tea and coffee consumption. Nevertheless, previous studies that utilized the PEDS database and faced the same methodological issue consistently replicated established epidemiological associations for a variety of cancer sites, including ovary (34,35), colon (36), breast (37), prostate (38), and lung (39). Recall bias is always a problem in case-control studies of cancer. However, in this investigation it may have been less of an issue due to our use of hospital controls. Further, the questionnaire used in this investigation places no particular emphasis on any specific item. Thus, there is little reason to believe that cases were more motivated than controls to recall tea and cof-

Table 3. Adjusted Risk of Lung Cancer Among Smokers by Histologic Subtype and Consumption of Black Tea, Regular Coffee, and Decaffeinated Coffee, Roswell Park Cancer Institute, 1982–1998[a]

	All $n_{cases}/n_{control}$ aOR (95% CI) n = 993	Adenocarcinoma $n_{cases}/n_{controls}$ aOR (95% CI) n = 120	Large Cell Carcinoma $n_{cases}/n_{controls}$ aOR (95% CI) n = 170	Small Cell Carcinoma $n_{cases}/n_{controls}$ aOR (95% CI) n = 186	Squamous Cell Carcinoma $n_{cases}/n_{controls}$ aOR (95% CI) n = 366
Regular coffee consumption (cups/day)[b]					
None	201/231	36/231	27/231	38/231	70/231
	Reference	Reference	Reference	Reference	Reference
≤1	157/198	23/198	23/198	21/198	70/198
	1.03 (0.73–1.45)	0.90 (0.45–1.81)	1.12 (0.55–2.26)	0.67 (0.33–1.37)	1.12 (0.70–1.80)
2–3	293/275	23/275	54/275	54/275	101/275
	1.34 (0.99–1.82)	0.60 (0.30–1.21)	1.44 (0.78–2.66)	1.51 (0.88–2.60)	1.28 (0.84–1.97)
4+	321/264	36/264	60/264	68/264	119/264
	1.51 (1.11–2.05)	1.66 (0.90–3.04)	1.82 (1.00–3.29)	1.48 (0.86–2.53)	1.61 (1.05–2.47)
Black tea consumption (cups/day)[c]					
None	420/404	50/404	78/404	73/404	166/404
	Reference	Reference	Reference	Reference	Reference
≤1	250/265	32/265	36/265	53/265	89/265
	0.87 (0.66–1.16)	0.85 (0.46–1.58)	0.92 (0.55–1.55)	0.94 (0.57–1.57)	0.81 (0.55–1.19)
1	118/114	16/114	20/114	21/114	37/114
	0.97 (0.66–1.43)	0.81 (0.34–1.96)	0.88 (0.41–1.89)	1.06 (0.52–2.15)	0.75 (0.44–1.29)
2+	205/203	22/203	36/203	39/203	74/203
	0.90 (0.66–1.24)	0.71 (0.35–1.46)	0.82 (0.47–1.45)	0.65 (0.35–1.19)	0.88 (0.58–1.34)
Decaffeinated coffee consumption (cups/day)[d]					
None	564/473	65/473	97/473	109/473	211/473
	Reference	Reference	Reference	Reference	Reference
≤1	198/244	24/244	30/244	35/244	76/244
	0.67 (0.54–0.84)	0.66 (0.40–1.08)	0.61 (0.39–0.95)	0.63 (0.41–0.96)	0.69 (0.51–0.94)
2+	190/248	26/248	32/248	33/248	69/248
	0.64 (0.51–0.80)	0.72 (0.44–1.17)	0.64 (0.42–0.99)	0.60 (0.40–0.92)	0.61 (0.44–0.83)

a: Each type of lung cancer is compared with all hospital-based noncancer controls (n = 986). Abbreviations are as follows: aOR, adjusted odds ratio; CI, confidence interval.

b: Adjusted for age, sex, smoking status, known occupational exposure to other kinds of dust, known occupational exposure to smoke, number of cigarettes smoked per day, and interaction between smoke exposure and cigarettes.

c: Adjusted for age, sex, smoking status, known occupational exposure to asbestos, number of cigarettes smoked per day, and interaction between asbestos and cigarettes.

d: Adjusted for age, sex, and smoking status.

fee consumption. Additionally, recall for common foods, such as coffee and tea, has been demonstrated to be good, further minimizing the risk of recall bias (40,41).

In summary, similar to previous epidemiological studies, our results do not support a protective effect of tea consumption with lung cancer among current and former smokers but suggest that higher coffee intake may increase lung cancer risk. However, also similar to previous studies, tea consumption in our study was relatively low. Large prospective studies in populations with a greater range of tea consumption would help to disentangle the potential positive effects of phytochemical intakes in tea and coffee from the potential negative effects of caffeine contained in these beverages.

Acknowledgments and Notes

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